ISSN 2320-9623 (Print) ● ISSN-2321-1032 (Electronic)

Volume 5 / Number 1 / January-June 2017

INTERNATIONAL JOURNAL OF CONTEMPORARY MEDICINE

Website: www.ijocm.org.in

INTERNATIONAL JOURNAL OF CONTEMPORARY MEDICINE

International Journal of Contemporary Medicine is a double blind peer reviewed international journal which has commenced its publication from January 2013. The journal is half yearly in frequency. The journal covers all aspects of medical practice. The journal has been assigned ISSN 2320-9623 (Print Version) and ISSN 2321-1032 (Online Version). The journal is Indexed in many international data bases.

Website: www.ijocm.org.in

ISSN 2320-9623 (Print Version) and ISSN 2321-1032 (Online Version). Frequency: Half Yearly

Editor

Dr. R.K. Sharma
Institute of Medico-legal Publications
4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110 001

Printed, published and owned by

Dr. R.K. Sharma
Institute of Medico-legal Publications
4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110 001

Published at

Institute of Medico-legal Publications
4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110 001

INTERNATIONAL JOURNAL OF CONTEMPORARY MEDICINE

CONTENTS

Volume 5, Number 1 **January-June 2017**

DOI Number: 10.5958/2321-1032.2017.00001.8

ORIGINAL ARTICLE

Nerve Conduction Velocity (NCV) Study in Type 2 Diabetes Mellitus Patients to Evaluate Diabetic Peripheral Neuropathy

Pankaj Kumar Jain[1], Archana Kansal[2], Subhash Chandra[3], Bhupendra Singh Bhalavi[3]

[1]P.G. Student, Department Of Medicine, G. R. Medical College, Gwalior, [2]Associate Professor, Department Of Medicine, G. R. Medical College, Gwalior, [3]Senior Resident, Department of Cardiology, G. R. Medical College, Gwalior

ABSTRACT

Background – Diabetic peripheral neuropathy is the most commonly reported long term complication of Type 2 Diabetic patients. The sensory symptoms and signs are more common than motor symptoms and signs.

Objectives - To study and compare the Nerve Conduction study in type 2 Diabetes Mellitus patients with symptomatic and asymptomatic peripheral neuropathy.

Method – This study was conducted in 100 patients of type 2 Diabetes Mellitus age > 18 years. Sample size was divided in 50 symptomatic and 50 asymptomatic patients. The diagnosis of diabetes was based on the criteria given by the national Diabetes Data Group and World Health Organization. Each patient was questioned systematically with regard to symptoms of neuropathy and the areas of limbs involved. A full scale clinical examination, including a detailed neurological examination was done. A complete NCS was done for those patients, using a EMG/NCV/EP ALERON 201, 2 channel machine manufactured by RMS using the standard protocols and settings. Both motor conduction and sensory conduction studies were done with respect to latency, amplitude and velocity.

Results - Out of 100 patients studied, maximum number of cases (36%) observed were in age group of 51-60 years followed by in the age group 41-50 years (27%). The minimum age was 30 years and the maximum age observed was 70 years with ratio of M:F ≈ 2.33:1. The peripheral neuropathy can be the 1st presentation of type 2 diabetes mellitus patients. Most common symptoms were sensory i.e. tingling and burning sensation and the most common sign was the loss of vibration sense. In our study lower limbs affected more than upper limbs. The increased duration of diabetes, higher blood sugar levels and patients who were taken OHA's only were found to have more abnormal results by the Nerve Conduction Studies.

Conclusion - Nerve Conduction Velocity Study is more sensitive tool to detect the presence of neuropathy in diabetics especially in asymptomatic patients and the most common type of peripheral neuropathy detected is axonal sensory motor type neuropathy. The earliest change is the axonal degeneration that is the main pathology in diabetic peripheral neuropathy.

Keywords *– Type 2 Diabetes mellitus, Peripheral Neuropathy, Nerve Conduction Velocity (NCV) Study.*

Address for Correspondence:
Pankaj Kumar Jain
P.G. Student, Department of Medicine, G. R. Medical College, Gwalior, Email- drpankajjain07@gmail.com
Contact No. 9827785717

INTRODUCTION

Diabetic peripheral neuropathy (DPN) is the most commonly reported long term complication of Type 2 Diabetic patients (T2DM). Definition of Diabetic neuropathy is "the presence of symptoms and or signs

of nerve dysfunction in people with diabetes after the exclusion of other causes." The most common symptoms observed were sensory - pain and paraesthesia and the most common sign was loss of vibration sense.[1]

Distal symmetrical sensorimotor polyneuropathy is the most common type of diabetic neuropathy. It involves both small and large fibres and has insidious onset. The primary risk factor for diabetic neuropathy is hyperglycemia. The sensory symptoms and signs are more common than motor symptoms and signs. Its symptoms are extremely variable, ranging from severely painful symptoms at one extreme to the completely painless variety, which may present with an insensitive foot ulcer at the other end. Thus, screening and appropriate treatment for DPN is of paramount importance.

OBJECTIVES

- To study Nerve Conduction Velocity in type 2 Diabetes Mellitus patients with symptomatic and asymptomatic peripheral neuropathy.
- To compare the nerve conduction velocity study in above symptomatic and asymptomatic patients.

MATERIAL AND METHOD

The present study was conducted in J A group of hospitals, attached to G.R. Medical College, Gwalior (M.P.).

Study area: Department of Medicine, G.R. Medical College, Gwalior, Madhya Pradesh (M.P.).

Study design: Hospital based cross sectional study.

Sample size: 50 symptomatic & 50 asymptomatic patients

INCLUSION CRITERIA:

- All patients of type 2 diabetes mellitus age > 18 yrs.

EXCLUSION CRITERIA:

- Patients who have type 1 diabetes mellitus.
- Patients who are alcoholic, smokers and pregnant females.
- Diabetic subjects having acute diabetic complications, nutritional deficiency, endocrinal disorder.
- Neurovascular complications like stroke.
- Any pathology or injury to the upper limb and lower limb.
- Clinical evidence of any other advanced illness like severe liver disease or renal disease.
- Patients with myopathy, neuromuscular diseases, inherited neuropathy and all other causes of peripheral neuropathies.

METHODOLOGY

The diagnosis of diabetes was based on the criteria given by the national Diabetes Data Group and World Health Organization. Each patient was questioned systematically with regard to symptoms of neuropathy and the areas of limbs involved. A full scale clinical examination, including a detailed neurological examination was done. Among the sensory system parameters, all modalities of sensations were tested with a view to determining whether there was a glove & stocking pattern of sensory deficit or a dermatomal pattern. Vibration sensation was tested with a 128 Hz tuning fork, on both upper & lower limbs.

Electrophysiology

A complete NCS was done for those patients, using a EMG/NCV/EP ALERON 201, 2 channel machine manufactured by RMS using the standard protocols and settings. Motor conduction studies were done on median, ulnar, common peroneal and posterior tibial nerves with respect to latency, amplitude, velocity and F waves. Sensory conduction studies were done on median, ulnar, superficial peroneal and sural nerves with respect to latency, amplitude and velocity. Observer's variability was reduced to almost nil, as the study was conducted by the same staff for all the patients. The same specialist evaluated and commented on the results.

Statistical method and software

- **Chi square** test is the statistical method used in our study.
- Significant figures were analyzed
- Suggestive significance (**P value :** $P<0.05$)
- The statistical software namely **SPSS version 20.0** was used.

RESULTS

Distribution of patients according to sex

Out of 100 patients 70 were males (70%) and 30 were females (30%) with ratio of male: female ratio is ≈2.33:1.

Distribution of patients according to age

Minimum age observed was 30 year and maximum age observed 70 year. The mean age was 52.18±9.85 years. Maximum number of cases (36%) was in the age group 51-60 years.

Distribution of patients according to treatment history

The above table shows that maximum number of patients were in OHA's alone 59(59%) while 29(29%) were both on insulin and OHA's, 10(10%) were first time detected diabetes. Only 2(2%) were on insulin therapy alone.

Symptoms profile

The symptoms of diabetes noticed were polyuria (51.85%), polydipsia (37.04%), fatigue (18.52%), polyphagia (8.64%) and weight loss (7.41%).

The symptom of neuropathy noticed were tingling and numbness (100%), burning sensation (24%), cramps in calves/foot muscles (16%), pain in any limbs and weakness of limbs (10% each) and allodynia (4%).

Physical signs elicited

Among the physical signs, vibration sense was found to be lost in 18% of patient, ankle jerk lost in 11% of patients and power was elicited normal in all patients (100%).

Table No. 1: Clinical presentation of neuropathy in relation to NCV study report

S.No.	Clinical presentation	Normal NCV study (n=25)	Abnormal NCV study (n=75)	Total
1.	Asymptomatic (n=50)	20 (40%)	30 (60%)	50
2.	Symptomatic (n=50)	05 (10%)	45 (90%)	50
χ^2=10.45, p=0.001, significant				

Association found between the clinical presentation and NCV study report was statistically significant.

Table No. 2: Clinical presentation of neuropathy in relation to details of NCV study reports

S.No.	Electrophysiological type (n=100)	Asymptomatic (n=50)	Symptomatic (n=50)	Total (%)
1.	Normal (n=25)	20	5	25(25.00)
2.	Abnormal (n=75)			
	a. Axonal sensory motor	17	11	28(37.33)
	b. Axonal sensory	05	11	16(21.33)
	c. Demyelinating sensory motor neuropathy	05	09	14(18.67)
	d. Others (axonal + demyelination)	03	14	17(22.67)

Of the 100 patients studied, the type of nerve damage observed the most common was axonal degeneration (58.66%) found mostly in symptomatic patients, while only demyelinating type of damage was seen in 18.67% of patients and both (axonal + demyelinating degeneration) type of neuropathy was seen in 22.67% of patients.

The most common type of neuropathy observed was axonal sensorimotor type (37.33%).Also, 5 patients (10.00%) who were symptomatic were found to have a normal NCV study report.

Table No. 3: NCV report in relation to duration of diabetes

S.No.	Duration of diabetes (yrs)	Normal NCV study (n=25)	Abnormal NCV study (n=75)
1.	< 1	05 (20.00%)	01 (01.33%)
2.	1-5	17 (68.00%)	29 (38.67%)
3.	>5	03 (12.00%)	45 (60.00%)
χ^2=23.40, p=0.000009, **significant**			

A strong association is found between the NCV study report and the duration of diabetes.

Table No. 4: NCV study reports in relation to Fasting Blood Sugar (FBS) level

S.No.	Fasting Blood Sugar (FBS) mg/dl	Normal NCV study (n=25)	Abnormal NCV study (n=75)
1.	< 126	01 (04.00%)	00(00.00%)
2.	126-150	20(80.00%)	37(49.33%)
3.	150-200	04(16.00%)	35(46.67%)
4.	> 200	00(00.00%)	03(04.00%)
Mean		**156.7**	**156.8**
SD		**27.2**	**27.4**
χ^2=11.61, p=0.00008, **significant**			

There is found to be a strong association between the NCV study abnormalities and fasting blood sugar levels.

DISSCUSSION

This study was conducted to know the electrophysiological (NCV study) and clinical profile of diabetic peripheral neuropathy in symptomatic and asymptomatic patients. Another aim was to compare NCV study in above two groups.

Out of 100 patients studied maximum number of cases (36%) observed were in age group 51-60 years. The minimum age was 30 years and the maximum age observed was 70 years and the mean 52.18±9.85 years out of the 100 patients, 70 were males (70%) and 30 were females (30%) with the ratio of M:F ≈ 2.33: 1. These results were comparable with Garg R et al (2013)[2] and Gauhar H et al (2014)[3].

In our study, 10(10%) patients were found to be 1st time detected diabetics and out of which 8(80%) patients presented with symptoms of neuropathy (symptomatic) as their presentation of diabetes.

The most common diabetic symptoms observed in our study were polyuria (51.85%) of polydipsia (37.04%) with the most common neuropathy symptoms being sensory type in which tingling and numbness is the most common (100%) followed by others like burning sensation (24%), cramps in calves/foot muscles (16%), pain in any limb and weakness of limb (10% each).

The most common sign was loss of vibration sense (18%) followed by loss of ankle jerk (11%). Motor symptoms were found to be very less in our study (10%). The above findings are also found in Kumar and Gill (1988)[4] and Celiker et al (1996)[5]. Hence patients of diabetic neuropathy have sensory symptoms predominating motor symptoms. These sensory symptoms are mainly positive symptoms with loss of vibration sense indicating large fibre neuropathy in diabetes.

Clinical presentation of neuropathy in relation to NCV study (Table No.1) report suggests that 40% asymptomatic patients had normal NCV study and 60% had abnormal NCV study as compared to Cameron NE et al (1994)[6] in which 84.8% had normal and 15.2% had abnormal study and Misra UK et al (2005)[7] in which 20% had normal and 80% had abnormal study. Even though the diabetic patients are asymptomatic for the symptoms of neuropathy. NCV study abnormalities of neuropathy are present in them even at the time of diagnosis.

In present study; types of nerve damage in both asymptomatic and symptomatic patients are Axonal degeneration 58.66%, both Axonal and demyelination 22.67% and only demyelination 18.67% (Table No. 2) as compared to Harati et al (1996)[8] in which also most common involvement found to be of axonal degeneration.

So according to above the present study is comparable to another studies done in the past. In type 2 diabetics, the type of nerve damage that occurs in diabetic neuropathy is axonal degeneration and it is also the first change that occurs in diabetic neuropathy as evident from the asymptomatic group though the abnormal report were seen more commonly in symptomatic group.

In our study it was found that there is a significant association between duration of diabetes and the NCV study abnormalities (p=0.000009) (Table No. 3). Diabetic duration of less than one year had 1.33% of NCV study abnormality, while 1-5 years had 38.67% and > 5 years had 60% of patients with abnormal NCV study reports. Other studies like Ellenberg M. (1990)[9], Chuttani P.S. et al (1979)[10], Allen C. et al (1997)[11] and Sultana MS et al (2010)[12] have also confirmed significant association between duration of diabetes and the abnormal NCV study reports. As the duration of diabetes increases the abnormalities detected electrophysiologically (by NCV study) of diabetic peripheral neuropathy increase and thereby the prevalence also increases.

In our study it was found that there is significant association between the fasting blood sugar level (FBS) and the NCV studies reports abnormalities (p=0.00008) (Table No. 4). Maximum patients with abnormal NCV study were found in FBS range 126-150 mg/dl (49.33%).Other similar study done by Prasad N et al (2013)[13], Gauhar H. et al (2014)[3] and ChandraSekhar A. et al (2014)[14] have also found significant association between Fasting blood sugar levels (FBS) and abnormal NCV study.

As the Fasting blood sugar levels increases, the electrophysiological abnormalities also increases and thereby the prevalence of diabetic peripheral neuropathy also increases.

CONCLUSION

NCV study is more sensitive tool to detect the presence of neuropathy in diabetics especially in asymptomatic patients and the most common type of peripheral neuropathy detected is axonal sensory motor type neuropathy. The earliest change is the axonal degeneration that is the main pathology in diabetic peripheral neuropathy.

It is also concluded that the increased duration of diabetes, higher blood sugar levels (FBS) and patients treated with OHA's only are found to have more clinical symptoms of neuropathy (sensory > motor) and highly abnormal NCV Study. It is therefore recommended that the nerve conduction velocity study is powerful test of neurological assessment and it should be done for all patients of suspected neuropathy.

Ethical Clearance – Taken from Institutional Ethical Committee Gajra Raja Medical College, Gwalior M.P. Dated 26/05/2015.

Source of Funding – Nil

Conflict of Interest - Nil

REFERENCES

1. Dyck PJ, Thomas PK. Diabetic Neuropathy, Second Edition, Philadelphia, W.B. Saunders, 1999.

2. Garg R et al, A study of median nerve conduction velocity in diabetes mellitus type 2 in neurologically asymptomatic patients, IJHSR, 2013; 3(5): 42-49.

3. Gauhar H. et al. Nerve conduction velocity as an early predictor of diabetic peripheral neuropathy in type 2 diabetes mellitus patients, IJCMPR Vol. I Issue 1.

4. Kumar and Gill. Motor nerve conduction velocities and neuropathy amongst diabetics. JAPI 1988;36(10):589-593.

5. Celiker et al. Early detection of neurological involvement in DM. Electromyogr. Clin. Neurophysiol 1996;36(1):29-33.

6. Cameron NE, Cotter MA. Metabolic and vascular factors in the pathogenesis of diabetic neuropathy. Diabetes 1997;46(Suppl 2):S31-S37.

7. Misra UK, Kalita J. Clinical neurophysiology; 4th edition reprint, New Delhi, Elsevier, 2005.

8. Harati et al. Diabetes and the nervous system Endocr Clin of North America 1996; 332-347.

9. Ellenberg M. Diabetic neuropathy factors in onset. Ann Intern Med 1990; 52:1067-75.

10. Chuttani PS, Chawla LS. diabetic neuropathy in India. Indian J Med Research; 1979; 62:99-109.

11. Allen C, Shen G, Palta M. Long term hyperglycemia is related to peripheral nerve changes at a diabetes duration of 4 years. Diabetes care 1997;20(7): 1154-1158.

12. Sultana MS et al, Electrophysiological changes of sensory nerves in patients with type 2 diabetes mellitus of different duration. BSMMU J 2010; 3(1): 9-12.

13. Prasad N et al, Comparative analysis of electrophysiological parameters of median nerve in normal and diabetic subjects, Indian Medical Gazette, July 2013, Page 261-264.

14. Chandrashekar A. et al. Height, weight, BMI, FBS, PPBS correlated with nerve conduction velocity in type 2 diabetes mellitus patients, Int J Physiother Res 2014, vol. 2(1):308-93.

DOI Number: 10.5958/2321-1032.2017.00002.X

Study of Drug –Dosage in Tuberculosis of Childhood in Rajasthan Population

Jain Manish[1], Makandar UK[2]

[1]Associate Professor, Pharmacology, Pacific Medical College and Hospital Udaipur, Rajasthan,
[2]Associate Professor, Anatomy AIMS, BGNagar, Mandya (dist) Karnataka

ABSTRACT

In the present study, out of 80 tuberculosis children 50% were malnutritious,,25% were MDRTB ,25% were HIV infected tuberculosis .Peak concentration of anti-TB drugs of children of different ages. INH peak concentration was3.4µg/ml, in 1-3 years of age, 6.7µg/ml in 4-6years ,6.9µg/mi in 6-9 years 7.4µg/ml in 9-12 years of age. Rifampicin peak concentration was 3.2µg/ml in 1-3 years of age, 4µg/ml in 4-6 years, 7.2 µg/ml in 6-9 years.5.8µg/ml in 9-12 years of age. Pyrazinamide peak concentration was 32.1µg/ml in 1-3 years, 39.1µg/ml in 4-6 year, 41.2µg/ml in 6-9 years, 39.1 µg/ml in 9-12 years In daily dosage INH 5mg/kg body weight. Rifampicin 10/kg, PZA 25mg/kg. Ethambutol 15mg/kg and intermittent dosage (three times weekly) INH 10mg/kg, Rifampicin 10mg /kg.PZA 35mg/kg. This study is more or less in agreement with previous studies. The duration of treatment in pulmonary and extra pulmonary and hilar adinopathy the Rifampicin and INH is given for 6 months .In tuberculosis meningitis ,bone and joint TB Rifampicin ,INH, PZA for 2 months then Rifampicin and INH for 4 months .This study will be certainly help the pharmacist and pediatrician to treat the childhood tuberculosis efficiently because drug concentrations influences by several factors such as age, ethnicity, or genetic factors,nutritional status, human immune deficiency virus (HIV).hence incidence of Tuberculosis increasing worldwide.1 billion people will be newly affected with tuberculosis, 200 million people will develop the disease and 35 million will die from tuberculosis.(1) The profound influence on incidence of tuberculosis is HIV infection, particularly in illiterates and Slum dwellers.

Keywords: *INH=Isonized, RMP= Rifamplcin, PZA =pyrazinamide, EMB= Ethambutol MDRTB=Multi Drug Resistant TB.*

INTRODUCTION

The basic principles of treatment and recommended anti TB regimens for children are similar to those for adults. For children drug sensitive TB, a four drug regimen, INH, RMP, PZA, and EMB for two months followed by INH, RMP for four months (continuation phase), may be extended up to 9-12 months but management of drug dosage in children is a great challenge because response to treatment depends upon multiple factors ,drug concentrations are influenced by several factors such as, ethnicity, genetics, nutritional status, HIV infections, drug-drug interactions, drug –food interactions. Moreover low dosage serum concentrations of the drugs could potentially lead to un–satisfactory treatment. Hence attempt is made to study the peak concentrations of different anti-TB Drugs so that, justification of proper dosage of drug can be given to appropriate body weight and types of TB at various age of children because notable modifications have occurred in drug dosage management of TB infection in children including alternate regimens for the treatment of latent TB, MDRTB, preventive therapy in context of HIV infected children.

Address for Correspondence:
Dr. Manish Jain
Near Uttam Emporium.Ward no-11. MainRoad.
Parasia. Chhindwara (Dist).MP
Email id –drmanishjain76@gmail.com
Cell number -919407187773.

MATERIAL AND METHOD

80 (Eighty) Children of different age groups ,1-3,3-6-9,9-12 who are regularly visiting to Pacific medical college Hospital Udaipur –Rajasthan .These children's have undergone pathological tests like sputum for AFB (Acid –Fast –Bacilli),ELISA, positive Tuberculin SKIN Test (TST) false –positive TST are often attributed to asymptomatic infection by environmental non-tuberculosis mycobacterium[2] chest x-ray for PT.CT for tuberculosis meningitis ,however symptoms be non –specific with over half of children being asymptomatic with early disease [3] but family history plays vital role that if somebody in family suffers with TB. Among 80 children they are classified in three groups .1-malnutritiuos (40) ,2-MDRTB(20).3-HIV infected TB (20).The drugs were RMP. INH, PZA, EMB, and other antibiotics under the guide lines of WHO.

OBSERVATIONS AND RESULTS

Table-1 –out of 80 children of tuberculosis 40 were with malnutrition, (50%) 20 were MDRTB (25%), 20 were TB with HIV infected.

Table-2 study of peak concentration of anti-TB Drugs at different ages ,1-3,3-6 6-9 ,9-12 years .with INH, PZA ,EMB. .

Table-3 a) Duration of treatment in pulmonary, extra pulmonary and hilar adinopathy b).Tuberculosis meningitis, bone and joint TB.

DISCUSSION

In the present study 50% of children were with malnutrition, 25% were MDRTB, 25%HIV infected TB.(Table-1). The peak concentration of Drugs is also studied for different ages .1-3 years INH concentration is 3.4µg/ml. Rmp 3.2µg/ml, PZA 32.1 µg/ml, EMB 1.9µG/ml. In the age of 4-6 years the peak concentration of INH was 6.7µg/ml, Rmp 5.4µg/ml, PZA 39.1µG/ml .In the age of 6-9 years peak concentration of INH was 6.9µg/ml, Rmp was 7.2µg/ml ,PZA was 41.2µg/ml .In the age of 9-12 years peak concentration of INH was 7.2µg/ml Rmp was 5.8 µg/ml, PZA 39.1µg/ml..Daily dosage of treatment per kg bodyweight was for INH 5mg/kg, Rmp 10mg/kg ,PZA 25mg /kg EmB15 mg/kg and intermittent (three times weekly) dosage INH 10Mg/Kg, Rmp10mg/kg, PZA35mg/kg.EMB30mg/kg (Table-2). These peak concentrations of Drugs and Dosage are more or less in agreement with previous studies.[4],[5][6]. The duration of treatment for pulmonary ,extra pulmonary and hilar Adinopathy was about six months, and the Drugs are Rmp, INH. For Tuberculosis meningitis, Bone and joint TB was for two months, drugs were RMP,INH,PZA for four months, RMP ,INH PZA (3 times weekly) (Table-3). This study was also recommended by previous studies[7][8][9]. During the treatment of Tuberculosis of children nutritional status plays vital role because patho-physiological changes associated with mal nutrition can alter pharmo-kinetic processes ,drug responses and toxicity. Poor nutritional could cause mal-absorption of drugs, alter levels of hepatic drug metabolizing enzymes and enhance the renal clearance thus decreasing the drug concentrations of RMP, INH, PZA and EmB have reduced in malnourished children[10]. RMP resistance most commonly occurs in conjunction with INH resistance called Multidrug resistance TB.(MDRTB). Such patients needs to be admitted with appropriate isolation facilities .Treatment of MDRTB should be monitored closely not only for Drug toxicity but more importantly to ensure compliance. Treatment of more cases involve five or more drugs and the duration is two years. Several anti –TB drugs may need to be used although efficacy of these drugs has not been evaluated in children. Previously used drugs include amino glycosides, (streptomycin, amikacin capremycin kanamycin), Ethionamide, prothionamide, cycloserine, quinolones (ciprofloxacin, ofloxacin) rifabutin, Macrolides (Azithromycin, clarithromycin) and paraaminosalicylic acid and cortico steroids .Corticosteroids have been found to be beneficial in situations where host response to M.tuberculosis contributes to significant tissue damage. Corticosteroids have been shown significant decrease mortality and long term neurological sequelae in patients with tuberculosis meningitis[11]. When HIV influences the TB outcomes in different ways, the inability to achieve and sustain therapeutic levels of anti-TB Drugs (could be due to mal-absorption of drugs) hence treatment cannot be effective[6]. Hence highly active retroviral treatment should be initiated few weeks after anti-TB treatment. The advent of HIV has not changed the basic characteristic of tuberculosis and it has been suggested that, well organized tuberculosis control programmes might reduce the impact of HIV Considerably.[12]

SUMMARY AND CONCLUSION

The present study of Drug dosage in childhood tuberculosis certainly help the Pharmacist, pediatrician

to treat the TB in children but children should be monitored to identify the adverse reactions early and to promoted adherence. Childhood TB represents a sentinel event within the community suggesting recent transmission from an infectious adult. The early diagnose and adequate treatment of both adult and children with tuberculosis remains a key tuberculosis control strategy but there is an urgent need for studies of efficacy and safety of different drug combinations of retroviral and anti-TB drugs in the children with better diagnostic tests and vaccines are awaited for better healthy tomorrow.

This research paper is approved by Ethical Committee of Pacific medical college and Hospital Udaipur –Rajasthan.

Table –1: Classification of childhood patients of tuberculosis

No	Particulars	No of Patients	%
1	Mal nutritious	40	50%
2	Multidrug Resistant	20	25%
3	HIV infected TB	20	25%

Table- 2. Peak concentration of anti-TB Drugs in children with different Ages

Drugs	Age 1-3 years.	4-6 years	6-9 years	9-12 years
INH	3.4µg/mi	6.7µg/mi	6.9µg/ml	7.4µg/ml
RMP	3.2µg/mi	5.4µg/ml	7.2µg/ml	5.8µg/ml
PZA	32.1µg/ml	39.1µg/ml	41.2µg/ml	39.1µg/ml
EMB	1.9µg/mi			

Dosage. Daily .Body weight =INH 5mg /kg, RMP 10mg/kg, PZA=25mg/kg, EMB=15mg/kg.

Intermittent Dosage (Three times weekly). INH 10mg/kg, RMP 10 mg/kg, PZA 35mg/kg , EMB 30mg/kg.

Table-3. Duration of treatment for TB Children

Disease	Drug	Duration
Pulmonary, Extra pulmonary and Hilar Adinopathy.	Rmp, INH ,	SIX months
Tuberculosis meningitis ,Bone and Joint TB	a) RMP, INH, PZA. b) RMP,ISH,	Two months , Then four months (daily or 3 times weekly).

Conflict of Intrest: None

Source of Funding: None

REFERENCES

1- WHO Global tuberculosis control .WHO 2001.Publication .Geneva. Switzerland.

2- Larson L ,Benzton M ,Lind A-sensitivity to sestina and tuberculin in Swedish children in rural areas .Tuber lung Dis 1993, 74, 371-376.

3- Khan E, Starke J-Diagnosis of tuberculosis in children ,increased need for better method .J of Emerg.Infec.Dis.1995,115-123.

4- Swaminathan S.and Ramachandran G.— Challenges in childhood tuberculosis .J of clinicalpharmacology and therapeutics .2015.98(3), 240-244.

5- Verhagen LM –Pharmakinetics of anti-TB Drugs in Venezuelan children younger than 16 years of age .Trop.med.Int Health 2012, 17, 1449-1456.

6- Monosuthi W and wongsawat J-Treatment challenges in co-infected HIV and TB Children .Indian paedtr.2011, 48, 937-938.

7- Joint tuberculosis in in UK Recommendations in 1998.J.of Thorax 1998.53, 536-548.

8- American Academy of pediatrics .L Pickering (ed).Red book. Report of committee on infectious diseases 25th edition, 2000, Elk Groove village publications.

9- WHO Manual treatment of tuberculosis.,guidelines for national programmed 3rd edition 1997,WHO organization publication Geneva .Switzerland .

10- Graham SM, -Low levels of pyrazinamide and ethmbutol in children with tuberculosis and impact of age, nutritional status and human immunodeficiency virus infection .J of Anti microb.Agents chemother.2006.50,407-413.

11- Schoeman L, Vanzyl J. Laubscher P –Effect of corticosteroids on intra cranial pressure .computed topographic findings and clinical outcome. With tuberculosis meningitis .J Of pediatrics 1997, 99,226-231.

12- Emarson D—The international union against Tuberculosis and lung disease .Model national tuberculosis programmed .J of Tuber lung Disease 1995,76,95-99

DOI Number: 10.5958/2321-1032.2017.00003.1

Accuracy of Ultrasound in the Diagnosis of Abdominal Pain among Children

Ajay Punj[1], Sartaj Ahmad[2], Arvind Kumar Shukla[3], Bhawana Pant[4]

[1]Associate Professor Department of Pediatrics, Subharti Medical College Meerut, Swami Vivekananda Subharti University, Meerut, UP., [2]Assistant Professor, (Medical Sociology), Swami Vivekananda Subharti University, Meerut, UP., [3]Assistant Professor, Biostatistics, [4]Professor, Community Medicine, Subharti Medical College Meerut, Swami Vivekananda Subharti University, Meerut,UP.

ABSTRACT

Abdomen pain is a medical emergency, in which there is sudden and severe pain in abdomen of recent onset with accompanying signs and symptoms that focus on an abdominal involvement. It can represent a wide spectrum of conditions, ranging from a benign and self-limiting disease to a surgical emergency. The integrated imaging, and in particular the use of ultrasonography has revolutionized the clinical approach to this condition, simplifying the diagnosis but burdening the radiologists with the problems related to the clinical management. A paediatric abdominal ultrasound is an examination of the abdomen with an ultrasound machine that uses sound waves to form images of different organs within the child's body. Abdominal ultrasound studies are most commonly performed to investigate the causes of abdominal pain or whether there is a mass of tissue or "lump".

Objective: (1)To study the clinical profile of pain abdomen in children of age group 2-10 years (2) To establish the etiology of pain abdomen with the aid of ultrasonography (3) To study correlation of clinical and ultrasonographic findings

Materials and Method: A hospital based cross sectional study.

Results: This article shows the use of ultrasound in the evaluation of the abdominal pain in the pediatric patients. Ultrasound appearance of pathologic processes that result in abdominal pain in the pediatric patient and to understand the use and limitations of abdominal ultrasound in the acute pediatric abdomen.

Conclusions: The causes of the abdominal pain in children vary depending on the ages of the children. Ultrasound is a noninvasive modality and is useful for assessing these patients. Ultrasonography is quite sensitive for diagnosing. But utility of ultrasonography was found to be limited for diagnosing cases of acute gastroenteritis and urinary tract infection as a cause of abdominal pain.

Keywords: *Abdominal Pain, Clinical examination, Ultrasound, Diagnosis.*

INTRODUCTION

The term "abdomen" can be defined as a medical emergency, in which there is recently onset sudden and severe pain in the abdomen with accompanying signs and symptoms that focus on an abdominal involvement. Abdominal pain in children presents a diagnostic dilemma and is one of the most difficult and challenging clinical problem in pediatric medical practice.

Abdominal pain can be classified as visceral or referred pain that can be a manifestation of a wide array of systemic and local causes. More common causes are choliccystitis, acute appendicitis, bowel obstruction, visceral perforation, mesenteric ischemia and colitis in

Corresponding author:
Dr. Sartaj Ahmad
Telephone: 09897093882
Email: sartajsaleem@gmail.com

children patients. [1]

The causes of the acute abdomen in children vary depending on the ages of the children and can be divided into diseases that can be treated with medical care and those in which emergency surgical intervention must be considered. [2]

Therefore, a thorough and logical approach to the diagnosis of abdominal pain is necessary. Associated symptoms, medical history or drug therapy often allows the physician to further focus on the differential diagnosis. However a confident and accurate diagnosis can be made solely on the basis of medical history, physical examination, and laboratory test findings in only a small proportion of patients so that imaging plays a pivotal role. [3]

Today, surely the integrated imaging, and in particular the use of *Ultrasonography* has revolutionized. Ultrasound is highly sensitive and specific imaging modality for diagnosis of various etiologies of abdominal pain. It is simple, rapid, portable, relatively less expensive, safe, functionally independent along with good subjective acceptability and should be used as procedure of choice for evaluation of acute and chronic abdominal pathologies. Diagnosis is usually made on the basis of abdominal radiographs showing pneumatics, a thick-walled bowel, free air, and portal venous air. Sonography may be useful when perforation and abscess formation are suspected. [5]

The role of diagnostic imaging is to determine whether the acute abdominal pain is due to a surgically or medically treated disease and if possible to diagnose the exact nature of the ailment. Imaging usually begins with a supine and horizontal beam radiograph. A chest radiograph is also commonly included to show extra-abdominal causes of acute abdominal pain such as pneumonia. Because of the noninvasive nature of ultrasound and its sensitivity in finding the common lesions producing acute abdominal disease, it is often the next imaging procedure performed. Doppler Sonography is helpful for assessing organ perfusion and diagnosing inflammation. The examination can be performed portably in the neonatal intensive care unit with excellent resolution of bowel anatomic characteristics when high frequency (7- to 10-MHz) transducers are used.

The objective of this study was to know the role of Ultrasound in the diagnostic management of acute abdominal pain among children .

AIMS AND OBJECTIVES

1. To study the clinical profile of pain abdomen in children of age group 2- 10 years.

2. To establish the etiology of pain abdomen with the aid of ultrasonography.

3. To study correlation of clinical and ultrasonographic findings.

MATERIALS AND METHOD

Study was conducted on 85 children patients of age group 2-10 years presenting with pain abdomen to the out patients department and those admitted to indoor of Department of peadiatrics of Sardar Vallabh Bhai Patel Hospital in Lala Lajpat Rai Memorial Medical College Meerut UP, over the study period of I year from September 2015- August 2016.

Inclusion criteria:

All the children patients presenting with pain abdomen whether:

i) Acute

ii) Chronic

iii) Recurrent

All these nature were included in the study.

Exclusion criteria:

i) Children patients in whom surgical cause for abdominal pain has already been confirmed.

ii) Children patients who have already under gone any surgical intervention for abdominal pain.

Case Performa of Children patients under study comprised of documentation was obtained. Detailed history with special reference to abdominal pain and clinical examination findings along with investigation report was used. Finally all the data that was obtained after clinical evaluation and spectrum of essential investigations along with ultrasonographic examination was complied thoroughly, observation tables constructed along with statistical analysis and conclusions drawn regarding utility of ultrasonography in evaluation of etiology of abdominal pain in children patients.

RESULTS

Table 1: Socio-demographic status of Abdominal Pain among Children

Age wise distribution	Number and percentage
2-4 years	14 (16.47)
4-6 years	19 (22.35)
6-8 years	24 (28.23)
8-10 years	28 (32.94)
Sex wise Distribution	
Male	59(69.40)
Female	26(30.60).
Religion wise Distribution	
Hindu	43 (50.60)
Muslim	38 (44.70).
Sikh	*03 (3.53)*
Christian	*01(1.17)*
Time interval between onset of symptoms and reported to hospital	
<1day	*16 (18.82)*
1-2 days	26 (30.58)
2-3 days	21 (24.70)
3-4 days	*10 (11.76)*
4-5 days	*07(8.23)*
>5 days	5 (5.88)

After compiling all the data and statistical analysis, it was observed that, maximum 28 (32.94) cases were in the age group of 8 years – 10 years and minimum 14 (16.47) cases were in the age group of 2 years – 4 years. The difference was not statistically significant. The male children were predominantly found to have been effected. The male: female ratio comes out to be 2.27: 1 as percentage of male children was 59(69.40) whereas percentage of female children was 26 (30.60).

Hindu children were constituted 43 (50.60) while Muslim children were constituted 38 (44.70). The difference was not statistically significant. Maximum 26 (30.58) cases reported to hospital within 1-2 days of onset of symptoms followed cases who reported between 2-3 days were 21 (24.70) while those who reported after 5 days of onset were 5 (5.88). The difference was statistically significant.

Table 2: Accuracy of Ultrasound in the Diagnosis of Abdominal Pain among Children

Distribution according to presenting symptoms	Number and percentage
Abdominal tenderness	64 (45.20)
Abdominal distention	58 (68.20)
Fever	54 (63.40)
Dehydration	23(27.05)
Lymphadenopathy	16(18.80)
Shock	14 (16.47)
Ascities	13 (15.30)
Absence of movement of abdominal wall with respiration	11 (12.90)
Visible peristalsis	7(8.23)
Lump in abdomen	4 (4.70)
Pre rectal exam (Faccoliths)	9 (10.59)
Blood tinged mucus	3 (3.53)
Distribution of cases according to clinical diagnosis	.
Gastritis and dysentery	24 (28.23)
Worm infestation of GIT	11 (12.94)
Abdominal tuberculosis and recurrent abdominal pain	9 (10.56)
Acute intestinal obstruction	8 (9.41)
Acute appendicitis	4 (4.70)
Nonspecific mesenteric lymphadenopathy, peritonitis, inflammatory bowel syndrome diseases and liver abscess	3 (3.53)
Distribution of cases according to clinical / Medical diagnosis and surgical etiology	
Clinical / Medical diagnosis	63 (74.00)
Surgical etiology	22 (26.00)
Distribution of cases according to ultrasonography diagnosis	
Worm infestation of GIT	9(10.56)
Acute intestinal obstruction	7 (8.23)
Abdominal tuberculosis	6 (7.05)
Acute appendicitis, nonspecific mesenteric lymphadenopathy, inflammatory bowel syndrome diseases and liver abscess	3 (3.53)
Peritonitis, intussception, pyonephrosis	2 (2.35)
Indeterminate diagnosis	45 (52.91)

Most of common symptom observing along with abdominal pain was fever 74 (86.90). Other common associated symptoms were vomiting 41 (42.80), altered bowel habits 38 (44.70), abdominal distention 29 (34.11), reduced appetite 26 (30.59) along with burning micturation, restlessness, and dysponia.

Most common sign elicited was abdominal tenderness and was seen in 64 (74.20) of total patients followed by abdominal distension 58(68.20). Through clinical evaluation the most common etiology established for pain abdomen was acute gastritis and dysentery 24(28.23) of total cases followed by worm infestation of GIT 11 (12.94), abdominal tuberculosis and recurrent abdominal pain 9 (10.56), acute intestinal obstruction 8 (9.41), acute appendicitis 04 (4.70), nonspecific mesenteric lymphadenopathy, peritonitis, inflammatory bowel syndrome diseases and liver abscess 3(3.53) were diagnosed.

63 (74.00) cases turned out to be of medical etiology needing no immediate surgical intervention while 22 (26.00) cases demanded urgent surgical evaluation and were thus referred to surgery or further management.

The maximum no. of patients presenting with abdominal pain when evaluated with aid of abdominal ultrasonography were found to have no abnormality detectable and thus patients represented about 45 (52.94) of total cases.

Table 3: Correlation between clinical diagnosis and ultrasonographic diagnosis.

Distribution of cases according to clinical / Medical diagnosis and surgical etiology	Number and percentage
Worm infestation of GIT	9 (10.56)
Acute intestinal obstruction	7 (8.23)
Abdominal tuberculosis	6 (7.05)
Nonspecific mesenteric lymphadenopathy, inflammatory bowel syndrome diseases and liver abscess	3 (3.53)
Peritonitis,, intussection and pyonephrosis	2 (2.35)
Accuracy of Abdominal ultrasonographic in determining etiology of pain abdomen	
Accuracy of ultrasonographic was found nearly in diagnosing Nonspecific mesenteric lymphadenopathy, liver abscess , intussception, pyonephrosis and inflammatory bowel diseases	100%
Acute intestinal obstruction and abdominal tuberculosis, acute gastroenteritis and peritonitis.	60-80%

Positive findings on abdominal ultrasonography, the most common diagnosis was worm infestation of GIT 9 (10.56), acute intestinal obstruction 7 (8.23) and abdominal tuberculosis 6 (7.05) were diagnosed. Nonspecific mesenteric lymphadenopathy, inflammatory bowel syndrome diseases and liver abscess were found 3(3.53) although peritonitis, intussection and pyonephrosis were found in 2 (2.35) cases. Almost all clinically suspected cases of worm infestation of GIT , acute intestinal obstruction and abdominal tuberculosis 6(7.05), Nonspecific mesenteric lymphadenopathy, inflammatory bowel syndrome diseases and liver abscess were confirmed ultrasonographically while ultrasonographic confirmation could not be obtained in clinically suspected cases of acute gastroenteritis and dysentery.

Accuracy of ultrasonographic was found nearly 100% in diagnosing Nonspecific mesenteric lymphadenopathy, liver abscess, intussception, pyonephrosis and inflammatory bowel diseases while, it was in range of 60-80% in diagnosis for acute intestinal obstruction and abdominal tuberculosis, acute gastroenteritis and peritonitis.

DISCUSSION

In this study, it was observed that, maximum (32.94) cases were in the age group of 8 years – 10 years and minimum (16.47) cases were in the age group of 2 years – 4 years. The difference was not statistically significant. This difference seems to be quite significant when viewed in relation to previous studies on this aspect because complaints of abdominal pain along with other associated symptoms can be earlier and more accurately narrated by older peadiatrics age group as compared to others which is also reflected in the results of the present study.

The male children were predominantly found to have been effected. The male: female ratio comes out

to be 2.27:1 as percentage of male children was (69.40) whereas percentage of female children was (30.60). The reason for this seems to be that the female child is considered as a neglected member of the family. Second male children are considered as future earning members of the family and so medical advices for their illness are sought with utmost urgency. Traumatic abdominal emergencies are common in males because of their more outdoor activities as compared to female.

In this study, it was observed that, maximum (30.58) cases reported to hospital within 1-21 days of onset of symptoms followed cases who reported between 2-3 days were (24.70) while those who reported after 5 days of onset were (5.88). The difference was statistically significant. It is usually seen that as compared to adults the time interval between onset of symptoms and seeking medical advice is shorter in children. However even in this era of urbanization, it is not infrequent in our setup to come across cases who have reported late to hospital just because of lack of transport facilities especially in villages placed interiorly and ignorance, illiteracy and poverty.

In this study, it was observed that, most of common symptom observing along with abdominal pain was fever (86.90). Other common associated symptoms were vomiting (42.80), altered bowel habits (44.70), abdominal distention (34.11), reduced appetite (30.59) along with burning micturation, restlessness, and dysponia. In a study by S. Boukthir (2004) suggested on clinical examination were abdominal distension (60%), abdominal lump (50%), free or localized Ascities (20%) which is in partial agreement with our study. [6]

In the present study the greatest number of cases who came with complaints of abdominal pain were of acute gastroenteritis and dysentery which is in concordance with study of Alexnder KC (2003). [7]

Abdominal ultrasonography is of significant diagnostic value in evaluation of children with abdominal pain and is extremely beneficial in the evaluation of acute peadiatrics abdominal diseases. This statement earlier proved by P Vasauala (2004) is also consolidated in our study. [8]

In our study it was found that ultrasonography is quite sensitive for diagnosing acute intestinal obstruction and abdominal tuberculosis, acute gastroenteritis and peritonitis, Nonspecific mesenteric lymphadenopathy, liver abscess, intussception, pyonephrosis and inflammatory bowel diseases, worm infestation of GIT in peadiatrics age group, while at the same time its utility was found to be limited for diagnosing cases of acute gastroenteritis and urinary tract infection as a cause of abdominal pain. Ultrasonography was not helpful in reaching at final diagnosis in 52.94% of our patients and these cases were labeled as that of indeterminate diagnosis. This data is in partial agreement with the data obtained by Glassman (1988). [9]

CONCLUSION

Abdominal pain in children presents a diagnostic dilemma and is one of the most difficult and challenging clinical problem in pediatric medical practice. Today, the use of *Ultrasound* has revolutionized the clinical approach. ultrasonography is quite sensitive for diagnosing. But utility of ultrasonography was found to be limited for diagnosing cases of acute gastroenteritis and urinary tract infection as a cause of abdominal pain.

Acknowledgement: Nil

Declaration of Interest: The authors report no conflicts of interest.

Source of Funding: Nil

Ethical Clearance: Ethical clearance was taken from ethical committee of the institution

REFERENCES

1. Cartwright SL, Knudson MP: Evaluation of acute abdominal pain in adults. Am Fam Physician 2008, 77: 971–8.
2. Franken EA Jr, Kao SC, Smith WL, Sato Y. Imaging of the acute abdomen in infants and children. AJR Am J Roentgenol 1989; 153:921–928.
3. Stoker J, van Randen A, Laméris W, Boermeester MA: Imaging patients with acute abdominal pain. Radiology 2009, 253: 31–46. Review 10.1148/radiol.2531090302
4. Reginelli A, Mandato Y, Solazzo A, Berritto D, Iacobellis F, Grassi R: Errors in the radiological evaluation of the alimentary tract: part II. Semin Ultrasound CT MR 2012, 33(4):308–17. 10.1053/j.sult.2012.01.016
5. Miller SF, Seibert JJ, Kinder DL, Wilson AR. Use of ultrasound in the detection of occult bowel

perforation in neonates. J Ultrasound Med1993; 12: 531– 535.

6. S. Boukthir et al. (2004) abdominal tuberculosis in children. Report of 10 cases. Acute Gast.Belgum . July-Sep;67(3):245-249
7. Leung KC Alexnder et al. (2003). Acute abdominal pain in children, June 1,vol 67, Nov 11.www.aafp.org/afp 2021-2326
8. P Vasauala (2004). Ultrasound evaluation of acute abdominal emergencies in infant and children. Radiology clinics of North America 2004 March; 42 (2); 445-456
9. Glassman M.et al. (1988). Emergency ultrasound in the evaluation of acute – onset abdominal pain in children, pedi. emer. care. 1988 Sept;4 (3);169-171.

DOI Number: 10.5958/2321-1032.2017.00004.3

Association of Geophagia with Anemia in Children Age 2 to 5 Years and Effect of Oral Iron on Geophagic Behaviour

Pankaj Mittal[1], Mayank Rawat[1], Garima Saxena[2], Alka Agarwal[3]

[1]Assistant Professor, [2]Post Graduate, [3]Professor, Department of Pediatric, Santosh Hospital and Medical College, No 1, Ambedkar Road Ghaziabad

ABSTRACT

Objective: To assess the hematological profile in children with geophagia and study the response of oral iron on geophagia.

Method: This longitudinal observational study was conducted in the department of pediatrics at Santosh hospital.Children between the ages of 2-7 years of either sex with history ofgeophagia for at least 1 month duration were enrolled. 185 children completed study.Detailed history, anthropometry, baseline hematological profile and serum iron levels were done. An intervention in the form of oral iron in the dose of 3 mg/kg/day was initiated for a period of 6 weeks. Children were reassessed for therapeutic response, considered as adequate if there was either no geophagia or decreased geophagic behavior.

Result: 185 children completed the study. Majority of the children (78.5%) were between 24-48 months of age. Most commonly ingested substance were cement and dirt. Anemia was present in 96% and low serum iron level was present in 84% of children. After 6 weeks of oral iron therapy 68.7% of children showed adequate improvement in geophagia. Only 3.2% children showed no response.

Conclusion: Geophagia in children has a strong association with anemia and has good response to oral iron therapy. Therefore it may be recommended to evaluate and treat it as separate entity rather than pica in general.

Keywords: *Pica,Geophagia, Anemia, Oral iron*

INTRODUCTION

Geophagia is defined as habit of eating earth including clay and other types of soil for a period of at least 1 month[1]. The Diagnostic And Statistical Manual of Mental Disorder: 5th edition, defines Pica as "the persistent eating of non-nutritive substances for a period of at least 1 month that is inappropriate to the development level and is not a part of culturally supported or socially normative practice.[1] Infants and toddlers are typically excluded from this diagnosis since mouthing of objects is normal developmental behavior, pica after the second year of life needs evaluation.[2]

Danford and Huber described 36 different types of pica. Some of the most commonly described pica are geophagia (eating earth, soil or clay, sand), amylophagia(starch), pagophagy (ice), coprophagy(faces), trichophagia(hair), etc. Geophagia is the most common pattern of pica. It has been reported from all over the world with prevalence varying from 10 to 32.5 %, being more prominent in younger children[3,4]

Although pica has been described since antiquity, there is no single agreed-upon explanation of the cause of such behavior. Etiology of geophagia in children is different from adult and multifactorial. Different specific mechanism have often been associated with particular form of pica. That include nutritional deficiencies (e.g., iron, zinc, and calcium), psychosocial factors (low socioeconomic status, child abuse and neglect, family disorganization e.g. poor supervision), underlying biochemical disorder,habit disorders, cultural and familial factors.[5,6] Geophagia has been associated with iron deficiency based on cross-sectional studies, but it is not clear if iron deficiency leads to craving for earth, or

if earth eating impairs iron absorption[7]

In ourpediatric outpatient department (OPD) most common type of pica is geophagia. Evidence of association of anemia withgeophagia in children is limited and typically found under the broad category of pica.Hence the study has been aimed specifically to assess serum iron levels, hemoglobin, and RBC indices and clinical response to oral iron so that a definite protocol for managing geophagy in children can be formulated.

MATERIAL AND METHOD

This longitudinal observationalstudy was conducted inDepartment of Pediatrics, Santosh Hospital and Medical College,Ghaziabad for1 year from May 2014 to April 2015. In the study, the childrenbetween the age group of 2-7 years of either sex presenting with complaints ofgeophagy, i.e. eating earth/cement/sand/clay, for atleast 1 monthwere enrolled. Children with neurodevelopment disorder, severe acute malnutrition and psychosocial factors associated with pica were excluded. Consent was taken from parents for participation of their children and collection of blood specimens.This study was approved by the ethical committee of the institute.

The parents and children were interviewed in Hindi/English according to a predesigned questionnaire. It included information about the type of substance, duration, frequencyand quantity ofgeophagia. In order to determine the accurate amount of substance eaten, the parent/childwas asked to pick the amount of substance they consume and was estimated with the help of comparing with the 4 different sizes that measured 10 to 30grams. History of diarrhea, constipation or worm infestation during the pica habit was taken. History of pica in siblings and family, history pertaining to other behavior disorder like thumb sucking, nail biting & bed wetting were also asked for. A detailed psychosocial history was elicited with special reference to scholastic performance and adjustment problems at home.A detailed physical examination was done to look for any signs of any nutritional deficiency like signs of anemia or vitamin deficiency.Anthropometry was then recorded and was the compared with WHO standards for children between 2-5 years & IAP charts for 5-7 years.Complete Blood Count analysis was performed by SYSMEX K21. Serumiron was measuredbyBeckman coulter CX 9.

Anemia was defined ashemoglobin thresholds for age(0.5-4.99years) is 11 gm/dl.Severe anemia defined as hemoglobin < 7 gram/dl.The serum iron level of 50 - 150 ug/dl was taken as normal.[8] Reference range for RBC indices were: MCV 72 – 90 fL, MCH 24-31 pg/cell, MCHC 32-36 gm Hb/dL[2].

All the recruited children were given oral liquid preparation of ferrous sulphate in doses of 3 mg/kg in two divided doses for a period of 6 weeks. Children were advised to visit the OPD again after 5 days to look for any side effects. Non-compliant or non-tolerant children were excluded. All the patients were then dewormed.The patients were followed up after 6 weeks and assessed for clinical response in parameters of decrease in frequency and amount of geophagia.The clinical response was graded as described:

Grade 1	No improvement: No change in frequency and amount
Grade 2 Mild improvement	Either change in frequency or amount
Grade 3 Moderate improvement	Change in both frequency and amount
Grade 4 Cured	No substance eaten

Grade 3 and grade 4 respnse was labeled as adequate response and grade 1 and grade 2 response was labeled as inadequate response.

Statistical package for social science (SPSS)software (Trial version 22) was used for processing and analyzing data.

RESULTS

A total of 204 children were recruited. 6 patients did not give consent; 5 developed complication after consuming iron whereas 8 patients were lost to follow up. 185 patients completed the study.

Summarised data of demographic andhematological character are presented in the table 1. In our study 55.6% were male. Male female ratio was 1.25:1. Majority of children (78.5%)were between 24-48 months age. Mean duration of geophagiawas 11±6.1 months. 30% of children had duration of pica exceeding 1 year. Most common substance ingested was cement (74.5%) and 52% ate dirt.46% of children ingested 10 to 20gm of substance while more than 20 gm was ingested by almost one third of patients.70.8% children gave history of ingestion of substance one or two times in a day. In our study 75.7 % children had other habit disorder. Nail bitingbeing commonest was present in45.9%.6.2% children were moderately under nourished while the rest were normally nourished asper WHO charts (<5 years) &IAP charts (>5 years). Severe anemia was present in 9.71 % children.Hb>11gm% was found in 3.78%.Microcytosis (MCV<80fl)was present in 95% of children.Mean serum iron was 43.4±12.3µg/dl(males 43.4±11.49 µg/dl, in females 43.3±11.49µg/dl). 84% children had low serum iron level (less than 50 ug/ml).

After 6 weeksof oral iron therapymean hemoglobin of study population increased from8.43±1.23 to 10.67±0.80 gm %.(Table 2). Amount of substance ingested in grams, and frequency of ingestion decreased after 6weeks of oral iron therapy.Adequate response was seen in 68.7% children with geophagia on oral iron therapy in 6 weeks(Table 3). Only 3.2% children shows no response after oral iron therapy.

DISCUSSION

Geophagia is most common form of pica. It is still unclear, however, whether anemiaprompts geophagia (to compensate for iron deficiency) or whether geophagia is the cause of anemia[9].In the present study children with age more than 2 years were enrolled basically because normal mouthing behavior is expected till 18 months of age. Hence this period was extended to 2 years and above to get true picture of geophagia. In index study 78.4% children were between 24 to 48 months. Singhi et al also showed maximum incidence around 1-3 years to the tune of 80% and only 20 % were more than 4 years.[10]The age profile of our children is similar to other studies from India and west.

There was no statistical difference between mean age at presentation amongst males and females (p>0.5). In most of the available literature there is no significant difference seen between the two sexes. In our study there was a slight preponderance of male (55.7% vs 44.3%). Male to female ratio was 1.25:1. Similar result was also seen in study by Fathia Mohamed el Nemer et al with predisposition to males 63.2% of males[11]. Male female ratio was 1.71:1. Amieleena Chhabra et al also made a similar observation in her study with 64.4% males and 35.6% of females[12]. In our study mean duration was 11±6.1months. 30.8% of children had duration of pica exceeding 1 year.In the study by Singhiet al only 25% children had pica for more than 1 year[10]. In study by Alka Agarwal et almean duration of symptoms were 2.02±1.02 years[13]. In the present study only geophagic behavior was considered rest were excludedhence commonest substances ingested was cement (74.5%).Other substances ingested were dirt (51.9%), clay (34.5 %) and sand (14.6%).Bhatia et al has quoted in his study that 76.5% children were eating earth or gravel[14]. Singhi et al has described three fourth children eating mud, pieces of earthen pottery followed by coal, plaster, chalk and ash[10].

In our study 6.2% children were moderately undernourished while the rest were normally nourished as per WHO charts used for less than 5 years & IAP charts used for more than 5 years. Severe malnourished children were excluded from the study group because severely malnourished children are likely to beanemic and have depleted iron stores with other micronutrient deficiency. Hence they may not be truly representing adequate or inadequate response to iron in management of geophagy, which is the ultimate outcome variable in the present study.Nivedita et alin her study also excluded malnourished children from the study group because severely malnourished children have deficiency of trace elements[15].In our study mean Hb level of children was 8.43±1.23gm/dl.In study group mean MCV(64.5±7.3 fl),MCH(19.3±3.4 pg),MCHC(26.5±2.34gm/dl) was below the normal reference value.

Mean Hb level of study population was 8.43±1.23gm/dl after 6 weeks of oral iron therapy it increased to 10.67±0.80gm/dl.84% children had low serum iron level.We could not do mean serum iron after

oral iron therapy because of financial constrain.68.7% of geophagic children had adequate response (moderate improvement or cure) after 6 weeks of oral iron therapy.31.3% of geophagic children either mild improvement or no improvement, which was considered as inadequate response. Inadequate response may be due to shorter duration of follow up or another micronutrient deficiency or poor bioavailability of given iron form.

Lanzkosky first proposed a theory that iron deficiency is the major cause of pica and Crosbystated that cure of this compulsive behavior with therapeutic iron is the hallmark of pica[16]. On the contrary, Minnich et al and Okcuoglu et al stated that pica results in malabsorption of iron from the diet. They proposed that clay or starch may prevent the absorption of iron from the intestine and iron deficiency is a result of pica.[17] Coltman treated cases of pagopaghy with parenteral iron in a week and oral iron therapy in 2 weeks. Coltman reported iron deficiency in patients with pica for substances which could not conceivably decrease the absorption of iron[18]. These findings again created controversy that whether decreased plasma iron levels cause pica or is an effect of pica and the cause effect relationship is yet not resolved.

DRAWBACK

As 31.3% of children show inadequate response, iron may further be given for 4 week and followed up for improvement in geophagic behavior. In non-responder multiple other factors must be evaluated likemicronutrient deficiency and poor bioavailability of iron.

Tables 1: Demographic Characteristics and hematological parameters of study subjects

	Male (103)	Female (82)	Total (%)
Age in months			
24-36	33	33	66 (35.6%)
36-48	39	22	61 (32.9%)
48-60	18	16	34 (18.3%)
> 60	13	11	24 (12.9%)
Wt for Ht z scores			
-3 to -2	8	4	12 (6.2%)
-2 to -1	46	31	77 (41.6%)
-1 to 0	41	36	77 (41.6%)
0 to +1	8	10	18 (5.1%)
Duration of geophagia in months			
1-6	28	20	48 (25.9%)
6-12	41	39	80 (43.3%)
12-18	24	13	37 (20.0%)
>18	10	10	20 (10.8%)
Type of substances ingested			
Cement	80	58	138 (74.5%)
Dirt	53	52	96 (51.9%)
Clay	54	31	65 (34.5%)
Sand	18	9	27 (14.6%)
Amount ingested in grams			
< 10	29	17	46 (24.9%)
10-20	45	40	85 (46%)
20-30	29	24	53 (28.6%)
>30	0	1	1 (0.5%)
Frequency (no of times per day)			
1	36	31	67 (36.2%)
2	38	26	64 (34.6%)
3	21	20	41 (22.2%)
≥3	8	5	13 (7.0%)

Cont... **Tables 1: Demographic Characteristics and hematological parameters of study subjects**

Associated symptoms			
Abdominal pain	43	32	75 (40.5%)
Constipation	19	10	19 (10.3%)
Worm Infestation	29	25	54 (29.2%)
Diarrhoea	35	23	58 (31.4%)
None	24	22	46 (24.8%)
Other Habit Disorders			
Thumb sucking	9	6	15 (8.1%)
Bed wetting	9	6	15 (8.1%)
Nail Biting	44	41	85 (45.9%)
None	20	25	45 (24.3%)
Hemoglobin in gm%			
< 7 (Severe)	12	6	18 (9.7%)
7-9.9 (Moderate)	76	64	140 (75.7%)
10-10.9 (Mild)	12	8	20 (10.8%)
>=11 (Normal)	3	4	7 (3.8%)
RBC indices (Mean±SD)			
PCV	27.28±3.9	27.2±3.9	27.4±3.8
MCV	63.5±7.3	65.9±7.15	64.5±7.3
MCH	19.0±3.3	19.6±3.5	19.3±3.4
MCHC	26.4±2.8	26.73±2.4	26.5±2.4
Serum Iron (mcg/dl)	43.4±11.49	43.3±11.49	43.4±12.3
<30	12	7	19 (10.27%)
30-50	75	61	136 (73.5%)
>50	16	14	30 (16.2%)

Table 2: Impact of oral Iron therapy on anemia and geophagic behaviour

	Before iron therapy	**After iron therapy**	
Hemoglobin gm% mean±SD	8.43±1.23	10.67±0.80	P<0.01
Amount ingested in grams			
0	-	34	
< 10	46	77	
10-20	85	60	P < 0.01
20-30	53	14	
>30	1	0	
Frequency (no of times per day)			
0	-	34	
1	67	101	
2	64	43	P< 0.01
3	41	5	
>3	13	2	

Table 3: Degree of Improvement in geophagia after oral iron therapy

Degree of Improvement	Number	Percentage
No Improvement	6	3.2%
Mild Improvement	52	38.1%
Moderate Improvement	93	50.3%
Cured	34	18.4%

CONCLUSION

Pica is broad category in that geophagy is most common type in children. Research on etiology of geophagia is limited and typically found under broad category of pica.In a developmentally normal and anemic child probability of response to oral iron therapy after 6 weeks is high.

Conflict of Interest-None

Source of Funding -None

Ethical Clearance- Yes

REFERENCE

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5thed. Arlington, VA: American Psychiatric Association; 2013.
2. Nelson Textbook of Pediatrics, 20th Edition, 23.2: 139.
3. Sayetta R.B.: pica an overview Am,Fam, Physician,1986: 33:181-5
4. PV Aparna, Austin RD, Matthew P, "PICA" Indian J Dent. Res., 23(3), 2012, 426-427. PMID 23059587
5. Barltrop D. Prevalence of pica. Am J Dis Cild1966; 112:116-123.
6. Millican FK, Layman EM, Lowrie RS, Takashashi L, Dublin CC. Prevalence of ingestion and mouthing of non-edible substances by children. Clin Proc Child Hosp Wash 1962; 18 :207-214.
7. Geissler PB Mwaniki DL, thiong o F, Friis H. Geophagyamong school children in western Kenya. Trop Med Int Health1997; 7: 624-630.
8. Haemoglobin concentrations for the diagnosis of anemia and assessment of severity http: //www.who.int/vmnis/indicators/haemoglobin.pdf (last accessed on 7/7/2016)
9. Christopher Rodgman, Daniel K. Winstead, A taste for the unusual. Current psychiatry, 12(3), 2013, 46-49
10. SumitSinghi: Nutritional statusand psychosocial stress in children with pica. Indian pediatrics1983,20 :345-359
11. Fathia Mohamed El nemeret al.: Prevalence of Pica Among Children Attending Pediatrics Clinic At El-Menoufiya university Hospital American Journal of BioScience 2014; 2(4): 147-152.
12. Amieleena Chhabra, et al. a study of anemia in hospitalized children in tertiary care hospital in northern india ;Journal of Biomedical and Pharmaceutical Research 3 (2) 2014, 80-83.
13. Alkaagarwal et al : A Study to Assess the Therapeutic Response of Iron and Zinc in Children with PIC AInt. J. Pharm. Sci. Rev. Res., 28(1), September – October 2014; Article No. 44, Pages: 233-236.
14. Bhatia M.S., SinghalP.k.: Habit disorder, prevelance and etiology, Indian pediatrics1981,24 : 475-479
15. Nivedita Gupta: The Serum Levels of Iron, Zinc, Calcium and Selenium in Children with Pica IJBAP, Vol 3(1) 2014.
16. Lanzkowsky P: Investigation into the etiology and treatment of pica. Arch Dis , Child 1959 ; 34 :140.
17. Minnich V et al. Pica in turkey II. Effect of clay on iron absorption. Am J ClinNutr 1968; 21:78-86.
18. Coltman CA: Pagophagia and iron lack. J. Am. Med. Assoc. 1969; 207:513

DOI Number: 10.5958/2321-1032.2017.00005.5

Study of Cardiovascular Diseases in Women of Malwa Region of Punjab

Choudhary Veerendra

Assistant Professor, Medicine Department, Adesh Institute of Medical Sciences and Research, Bhatinda, Punjab

ABSTRACT

95 Adult females aged between 45 to 70 years of age were selected for study. Among them 33.6% had Ischemic Heart Disease,14.7% had arrhythmia ,15.7% had stroke, 24.2% had peripheral vascular Disease, 2.1% had Aortic aneurysm. Out of 95 women patients 56.8% were post menopausal, 5.2% were infertile due to Poly cystic ovarian syndrome, 73.6% had elevated lipid profile. This study of various cardiovascular diseases will certainly help the Physician, Cardiologist for proper approach to the women with different cardiovascular diseases so that, they can prevent the future risk of Coronary Heart Diseases, which are life threatening diseases in India and abroad.

Keywords *- CVD= Cardio Vascular Diseases, IHD =Ischemic Heart Disease, CAD= Coronary Artery Disease , PCOS =Poly Cystic Ovarian Syndrome.*

INTRODUCTION

The latest medical census has revealed that, CVD is an alarming fact that, out of 5 women 3 women are at high risk of CVD especially in the adult women.[1] and at the age of menopause also.[2] CVD means damage to or narrowing of Arteries due to atherosclerosis. Therefore it is a systemic disease that can lead to variety of end organ manifestation like Coronary Artery Disease (CAD) with or without coronary syndrome ,heart failure (Ischemic), Arrhythmia (arterial fibrillation), Stroke especially related to carotid artery stenosis and cerebro-vascular disease, Aortic Aneurysm, chronic renal disease etc. There are multiple causes of CVD like irregular menses, obesity, sedentary life, PCOS, history of migraine, complications during pregnancy. Hence attempt was made to rule out different types of CVD in adult and post-menopausal women, infertile women with PCOS.because CVD are challenging problems for physician and cardiologist as well.

Corresponding author :
Dr. Veerendra Choudhary
Faculty quarter no-B 102, Adesh Institute of Medical sciences and Research Campus, Bhatinda- 151101, Punjab, Email id -veerendrachoudhary@yahoo.co.in
Cell number - +919314722800.

MATERIAL AND METHOD

95 (Ninety five) adult females aged between 45 to 70 who were regularly visiting to Adesh Institute of Medical Sciences and Research Hospital selected for study. Among these 95 patients, 32 had IHD,14 had Arrhythmia, 15 had Stroke, 23 had Peripheral vascular Disease, 2 had Aortic aneurysm .in the present study Diabetic women patients were excluded. Out of 95 patients 54 were post menopausal, 5 were infertile due to PCOS and 70 patients had elevated lipid profile. The duration of this study of was about two years.

OBSERVATION AND RESULTS

Table--1

IHD patients were 32 (33.68), Arrhythmia 14 (14.7%), Stroke 15(15.78%), peripheral vascular diseases 23(24.2%), Aortic aneurysm 2 (2.1%).

Table-2

Out of 95 women patients, 54 (56.8%) were post-menopausal, 5(5.26%) were infertile due to PCOS.70 (73.6%) had elevated lipid profile.

DISCUSSION

In the present study of CVD in women between the

age of 45 to 70. The IHD patients were 32 9(33.6%), Arrhythmia patients were 14 (14.7%), stroke 15(15.7%), peripheral vascular Diseases were 23(24.2%) ,Aortic aneurysm were 2 (2.1 %) (Table-1) Moreover post-menopausal were 54 (56.8%), Infertile women with PCOS having CVD were 5(5.26%) ,CVD with elevated lipid profile were 70 (73.6%) These present findings were more or less in agreement with previous studies.[3],[5]. Untreated IHD leads to myocardial infarction ,CVD which claims 50% of death and/ or stroke.[6] Major risk factors for CHD ,CAD, peripheral vascular Diseases in India are Tobacco chewing, dyslipidemia, obesity, sedentary life style, poor nutrition, stress and strain, increased serum cholesterol and low density lipoprotein which is main cause of morbidity and mortality in women[7].moreover early surgical menopause also linked to the increased risk of CHD.[8] As hypertension is a clearly major risk for stroke which is higher ratio in females than males. Apart from these number of CAD factors there are ischemic strokes, congestive heart failure ,angina pectoris, myocardial infarction ,IHD ,mitral valve Diseases ,left ventricular hypertrophy and atrial fibrillation .It is also observed that, persistent atrial fibrillation with or without hypertension is a great risk of stroke in women than men.[9] The peripheral vascular diseases include claudication, there is absence of posterior tibial or dorsalis pedis artery which is also lined with CVD. Apart from this oral contraceptives lower the LDL and raise HDL Cholesterol which increases major risk of CVD in young adult women associated with hemorrhagic stroke.[10] Although estrogen therapy is called cardio protector in post menopausal women but early age of CVD outcomes in post menopausal are osteoporosis, breast or uterine cancer[11] Apart from this in the post menopausal life women go in to depression due to withdrawal of hormones and undergo anxiety, helplessness ,sleep disturbance. These factors elevates the blood pressure which results into CVD. It is established fact that, majority of Indian women are suffering with Obsessive Compulsive Disorder.(OCD) due to moral and social bindings. This obsessive compulsive disorder leads to leads to hypertension, lethargy, sedentary life, obesity which results into atherosclerosis and ultimately end into CVD.

Table 1: Study of types of CVD in women of Punjab.

Sl No	Particulars	No of Patients	Percentage
1	IHD	32	33.6
2	Arrhythmia	14	14.7
3	Stroke	15	15.7
4	Peripheral vascular disease	23	24.2
5	Aortic Aneurysm	2	2.1

Table 2: Study of different types of physio-pathological conditions of women with CVD of Punjab.

Sl No	Particulars	No of Patients	Percentage
1	Post Menopausal	54	56.8
2	Infertile with polycystic ovarian syndrome	05	5.26
3	CVD with elevated Lipid profile	70	73.6

SUMMARY AND CONCLUSION

The present study of CVD in females is quite helpful for Physician and cardiologist to take preventive measures to avoid the risk of CVD in women. Apart from this it requires to create awareness among women to avoid sedentary life style, obesity ,stressful work conditions, compromised diet, pregnancy complications ,pros and cons of hormone and statin medication in both house wives and working women .CAD predominantly affects older women but atherosclerotic CAD are quite common in young adult women. This study demands further genetic study because CAD are not modifiable and exact cause of thrombotic, haemostatic, and inflammatory markers of CHD are yet to be known. Developmentally exact mechanism of angiogenic tissue which gives origin to heart and blood vessels is still unclear.

This research paper is approved by Ethical committee of Adesh Institute of Medical sciences and research, Bhatinda - 151101, Punjab

Conflict of Intrest : None

Funding : None

REFERENCES

1- Pravin Chandra -Study reveals that, 3 in 5 women in India are high risk of cardiovascular diseases as early as 35 years of age. Facts about cardiovascular risk in Indian women September 29,2014.

2- Richard .F.Gillium - menopause and coronary heart disease .The Framing ham study ,Ann.Intern .med.1978,89 (2), 157-161.

3- Goff D.C, Lioyd. D Bennet .G- A report of cardiology / American heart Association .Task force on practice guide lines .Circulations 2014, 129, 549-73

4 - Stone .N J, Robinson J.G Lichten .A.H --Guide lines on the treatment of blood cholesterol to reduce atherosclerotic cardio vascular risk in adults. Circulation .2014,129,51-55.

5 - Lori Mosia Joann.E, Manson, Susan E and Elizabeth Berrett -connar-- Cardiovascular diseases in women .http;//dx.do .org /10.1161/01.CIR.96.7 2468.october 7 1997.Viewed on 24-october 2016.

6- Eaker .ED, Chesebro JH,Sacks .F.M Winstone .M--Cardiovascular diseases in Women .Circulation 1993 ,88,1999-2009.

7- Sempos C T,Cleeman .J I.Caroll .M.D,Johnson CL,Lippell K ---Prevalence of high blood cholesterol among US adults ,an updated based on national cholesterol programme JAMA 1993,269,3009-3014.

8- Kennedy J.W, Killip .T. Fisher .L D,Mock M.B -- The clinical spectrum of coronary artery disease and its surgical and medical management .Circulation ,1982 ,66 16-23

9 - Njolstad I ,Amesen ,E ,Lund,Larsen .P G --Body height ,cardiovascular risk factors and risk of stroke in middle aged women and men .Circulation 1996,94, 2877-2882.

10- WHO collaborative study of cardiovascular Diseases and steroid hormone .Contraception, Ischemic stroke and combined oral contraceptives Lancet .1996,348 .498-505.

11- Psaty .B M,Heckbert S R,Atkins .D----- Effects of estrogen or estrogen progesterone regimes on heart diseases risk factors in post menopausal women.JAMA.1995,273,199-208..

DOI Number: 10.5958/2321-1032.2017.00006.7

A Pilot Study of High-sensitivity C-reactive Protein as Inflammatory Biomarker in Type 2 Diabetic Mellitus

Hemant Kumar Sharma[1], S C Chadha[2], Manisha Arora[3]

[1]AssociateProfessor, [2]Assistant Professor, Department of Medicine, [3]Professor, Department of Biochemistry, Muzaffarnagar Medical College Muzaffarnagar, U.P., India

ABSTRACT

Systemic inflammatory activity has turned out to play a key pathogenic role in vascular atherosclerosis, insulin resistance, and type 2 diabetes mellitus (T2DM). Inflammatory biomarkers may therefore be a valuable tool for risk evaluation. Data suggest that High sensitive C reactive protein (hs-CRP) may participate directly in the process of atherogenesis. The analyses were done with 90 type 2 diabetic and 60 non-diabetic individuals. Anthropometric and biochemical parameters were studied to assess the association of hs-CRP with in T2DM. T2DM encompasses -90% of the diabetic subjects, and it is characterized by insulin resistance often accompanied by obesity and dyslipidemia. High sensitive C reactive protein, the golden marker of inflammation was analyzed in diabetic subjects. Serum hs-CRP levels were positively related to anthropometric parameters. Elevated level of hs-CRP in diabetic subjects was observed with insulin resistance and has strong cardio vascular risk marker in these individuals.

Keywords: *Cardio vascular disease (CVD), High sensitive C-reactive protein (hs-CRP), Type 2 diabetic mellitus (T2DM), Insulin resistance (IR)*

INTRODUCTION

The relation between chronic subclinical low-grade inflammation and insulin resistance (IR) has long been known[1,2]. IR is the major contributor and mediating factor in the development of type 2 Diabetic mellitus (T2DM) along with concomitant hypertension (HT) and cardiovascular disease (CVD)[3,4]. The relationship between the development of T2DM and some markers of inflammation such as C-reactive protein (CRP) has been described previously. Serum concentration of CRP increases in both impaired glucose tolerance (IGT) and overt T2DM[3]. On the other hand, some studies reported that elevation of CRP is an indicator of development of T2DM[4].

Correspondence to :-
Dr. Hemant Kumar Sharma
Associate Professor, Department of Medicine
Muzaffarnagar Medical College
Muzaffarnagar, U.P. India. Tel: +91 9758417852
E-mail: hemantkumarsharma1959@gmail.com

Diabetes is a metabolic -disorder with inappropriate hyper glycemia either due to an absolute or relative deficiency of insulin secretion or reduction in the biologic effectiveness of insulin or both. It is also associated with disturbances concerned with protein, carbohydrate and lipid metabolism. The decreased uptake of glucose into muscle and adipose tissue leads to chronic extra cellular hyper glycemia which results in tissue damage and chronic vascular complications in both type I and II Diabetes Mellitus[5].

Among several markers of inflammation, hs –CRP is found to be significant in people with diabetes. CRP, a pentameric protein produced by the liver has emerged as the 'golden marker for inflammation'. It is a non- immunoglobin protein having five identical sub units. It is a member of pentraxin family proteins. The C-reactive protein derives from the fact that it reacts with capsule polysaccharide of streptococcus pneumonia. It is an acute phase response protein markedly increased in both inflammatory and infectious diseases. It plays an important role in innate immunity. It assists in complement binding to foreign and damaged cells and enhances phagocytosis. It was also noticed that

the elevated levels of IL18/IL18BP in plasma during active stages of disease suggest a possible role in the pathogenesis and course of idiopathic thrombocytopenia (ITP)[6]. Hyper glycemia is an associated factor to the increase of serum CRP levels, non-controlled type II diabetic subjects[7]. Several studies demonstrate that hs-CRP remained a significant predictor of diabetes risk even after adjusting with body mass index, family history of diabetes mellitus, smoking and other factors[8,9]. In people with diabetes, CRP levels is highest tertile (> 0.28 mg/dl) were associated with a 2 fold increase in CV mortality after adjusting for age, sex and glucose tolerance tests[10] .

Hypertensive patients with T2DM had higher levels of hs-CRP, a circulating inflammatory marker, than normal subjects. This finding suggests that patients with two associated diseases have a more active inflammatory state[11]. Though we have several studies on hs-CRP and diabetes mellitus association with different age groups is limited. So current study was focused on high-sensitivity C-reactive protein as inflammatory biomarkers in type 2 diabetic mellitus.

MATERIAL AND METHOD

A pilot study was conducted from December 2015 to November 2016 in Department of Medicine, Muzaffarnagar Medical College Muzaffarnagar, U.P, India. Ninety subjects diagnosed as T2DM by Fasting plasma glucose (FPG) and haemoglobin A1c (HbA1c) test were enrolled as study group and randomized sixty non- diabetic healthy individuals were selected as control. A written informed consent was obtained from each participant. The study was approved by the local ethical board.

All biochemical tests including glucose, insulin, and lipid profile were measured in fasting blood samples using Auto analyzer in the Central Biochemistry Laboratory, Muzaffarnagar Medical College Muzaffarnagar, U.P. India. The concentration of hs-CRP was analyzed by immune turbid metric assay and HbA1c by turbid metric inhibition immunoassay.

A detailed medical history of each participant was obtained, and measurements of anthropometry (height, weight, waist, and hip circumference) and systolic and diastolic blood pressure (SBP, DBP) were done. Body mass index (BMI), HOMA-IR (= fasting glucose × fasting insulin/405), and non-HDL-cholesterol (= total cholesterol − HDL-cholesterol) were calculated accordingly.

STASTICAL ANALYSIS

Data analysis was performed using Epi info software version 3.5.1. Descriptive statistics, including mean, range, and standard deviations, were calculated for all variables. Proportions were compared using Chi- square tests and chi square for trend at 0.05 level of significance.

FINDINGS

Demographic characteristics and laboratory findings of study group and healthy control group are presented in Table1. In brief, T2DM subjects had significantly higher BMI, SBP, DBP, FPG, HbA1c, Triglycerides (TG), Non HDL-cholesterol, Fasting Plasma Insulin and HOMA-IR values than non – diabetic subjects ($p < 0.001$). The level of hs-CRP in T2DM subjects had also significantly higher than in healthy non – diabetic control ($p < 0.001$).

Table 1: Clinical characteristics and laboratory findings between the study groups (Type 2 diabetic subjects) and control group (Non – diabetic subjects)

Parameters	Study group (no=90) Mean ± S.D.	Control group (no=60) Mean ±S.D.	P value
Age (years)	52 ± 12	48 ± 10	*N.S.*
BMI (kg/m^2)	28.6± 4.1	23.7 ± 4.6	$p < 0.001$
SBP (mmHg)	128.4 ± 19	117.5 ± 16	$p < 0.001$
DSP (mmHg)	76.2 ± 12	73.1 ± 11	$p < 0.001$
FPG (mg/dl)	173± 38	84 ± 12	$p < 0.001$

Cont... **Table 1: Clinical characteristics and laboratory findings between the study groups (Type 2 diabetic subjects) and control group (Non – diabetic subjects)**

HbA1c (%)	8.2 ± 2.5	5.1± 0.7	$p < 0.001$
hs-CRP (mg/L)	4.9 ± 2.4	2.7± 1.6	$p < 0.001$
Triglycerides (mg/dl)	147.5± 28.8	102.6± 17.3	$p < 0.001$
HDL-cholesterol (mg/dl)	22.5± 12.6	28.6± 10.3	$p < 0.001$
Non-HDL-cholesterol (mg/dl)	205.5± 29.8	142.5± 18.9	$p < 0.001$
Fasting Plasma Insulin (uU/ml)	8.66 ± 1.9	5.72 ± 1.2	$p < 0.001$
HOMA-IR	3.69 ± 0.8	1.18 ±0.5	$p < 0.001$

DISCUSSION

The clinical and biochemical characteristics in relation to hs-CRP of the study group were shown on the table 1. In comparison with non-diabetic subjects, T2DM subjects were older and had higher body Mass Index BMI (P<0.001). They also had significantly higher systolic blood pressure (P<0.001), diastolic blood pressure. (P<0.001), fasting plasma glucose (P<0.001), HbA1C % (P<0.001), fasting insulin (P<0.001), hs-CRP(P<0.001) and insulin resistance (P<0.001).

Several studies have suggested that inflammation is associated with insulin resistance that takes part in the pathogenesis of T2DM and atherosclerotic disease[1-4,6.] Environmental factors such as infections, over nutrition, and lack of physical activity are believed to contribute serum CRP levels although the mechanism is not properly understood. On the other hand, hyperglycaemia per se may induce inflammation and this may enhance the development of T2DM[12,13].

In our study, we found a positive correlation between hs-CRP levels and all glycaemia and IR parameters. However, after adjustment for age, sex, smoking, BMI, waist, and HT, positive correlations were maintained with HbA1c, fasting insulin, and HOMA-IR but not with FPG. In their later report stated that post challenge glucose but not FPG was strongly correlated with baseline CRP[16]. Other studies have also shown an association between CRP and T2DM, which remained significant after adjusting for BMI or other covariates[17]. Our findings and others suggested that adiposity is not sufficient to explain the relationship between high levels of inflammatory markers and increased DM risk.

Atherosclerosis, the underlying pathology responsible for CHD, is an inflammatory disease. Recent observations suggest that the atherosclerotic process is characterized by a low-grade inflammation altering the endothelium of the coronary arteries and is associated with an increase level in markers of inflammation such as acute phase proteins and cytokines. Cumulative evidence indicates that inflammation, at both focal and systemic levels, plays a key role in destabilization and rupture of atherosclerotic plaques, leading to acute cardiovascular events[18]. In consideration of the important role that inflammatory processes play in determining plaque stability, recent work has focused on whether biomarkers of inflammation may help to improve risk stratification and identify patient groups who might benefit from particular treatment strategies. Among them, C-reactive protein (CRP), a prototype marker of the inflammatory process, is the most studied both as a causal factor and in the prediction of CHD[19].

One of the greatest strengths of the present study is its national representative sampling with a large sample size and wide age range. In this study where two currently proposed methods (FPG, and HbA1c) were used to define T2DM and each of them was compared with the inflammation marker, hs-CRP.

CONCLUSION

Possible reasons for the higher CRP values in this population include a very high prevalence of Diabetes Mellitus and obesity since Diabetes and high body mass index are associated with elevated CRP. In conclusion, the present study showed that hs-CRP has a strong association with diabetes. It is also concluded that age, body mass index, hyper sensitivity and body weight has strong association with diabetic individuals and high levels of hs-CRP groups predicts the high risk of

diabetes mellitus type 2. It is very well understand that the levels of hs-CRP significantly associated with age and positively related to insulin resistance, BMI, systolic and diastolic pressure. It is also observed that hs-CRP levels are the sensitive biomarker for inflammation.

Conflict of Interest – None

Source of Funding – Self

Ethical Clearance – Taken

REFERENCES

1. Pickup J. C., Crook M. A. Is type II diabetes mellitus a disease of the innate immune system? D iabetologia.1998;41(10):1241–1248.
2. Donath M. Y., Shoelson S. E. Type 2 diabetes as an inflammatory disease. Nature Reviews Immunology.2011;11(2):98–107.
3. Festa A., D'Agostino R., Jr., Howard G., Mykkänen L., Tracy R. P., Haffner S. M. Chronic subclinical inflammation as part of the insulin resistance syndrome: the insulin resistance atherosclerosis study (IRAS) Circulation. 2000;102(1):42–47.
4. Ridker P. M., Buring J. E., Cook N. R., Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. Circulatio[n.]2003;107(3):391–397.
5. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Follow- up report on the diagnosis of diabetes mellitus. Diabetes Care. 2003;26(11):3160–3167.
6. Hotamisligil G. S., Peraldi P., Budavari A., Ellis R., White M. F., Spiegelman B. M. IRS- 1-mediated inhibition of insulin receptor tyrosine kinase activity in TNF-α- and obesity- induced insulin resistance. Science.1996;271(5249):665–668.
7. Pradhan A. D., Manson J. E., Rifai N., Buring J. E., Ridker P. M. C-reactive protein, interleukin 6, and risk of developing type 2 diabetes mellitus. The Journal of the American Medical Association. 2001;286(3):327–334.
8. de Rekeneire N., Peila R., Ding J., et al. Diabetes, hyperglycemia, and inflammation in older individuals: the health, aging and body composition stud. Diabetes Care. 2006;29(8):1902–1908.
9. Barzilay J. I., Abraham L., Heckbert S. R., et al. The relation of markers of inflammation to the development of glucose disorders in the elderly: the Cardiovascular Health study. Diabetes. 2001; 50(10):2384–2389.
10. Freeman D. J., Norrie J., Caslake M. J., et al. C-reactive protein is an independent predictor of risk for the development of diabetes in the west of Scotland Coronary Prevention Study. Diabetes. 20 02;51(5):1596–1600.
11. Schmidt M. I., Duncan B. B., Sharrett A. R., et al. Markers of inflammation and prediction of diabetes mellitus in adults (Atherosclerosis Risk in Communities study): a cohort study. The Lancet. 1999;353(9165):1649–1652.
12. Aronson D., Bartha P., Zinder O., et al. Association between fasting glucose and C-reactive protein in middle-aged subjects. Diabetic Medicine. 2004;21(1):39–44.
13. Fröhlich M., Imhof A., Berg G., et al. Association between C-reactive protein and features of the metabolic syndrome: a population-based study. Diabetes Care. 2000;23(12):1835–1839.
14. Festa A., D'Agostino R., Jr., Tracy R. P., Haffner S. M. Elevated levels of acute-phase proteins and plasminogen activator inhibitor-1 predict the development of type 2 diabetes: the insulin resistance atherosclerosis study. Diabetes. 2002;5 1(4):1131–1137.
15. Rubio-Martín E., Soriguer F., Gutiérrez-Repiso C., et al. C-reactive protein and incidence of type 2 diabetes in the Pizarra study. European Journal of Clinical Investigation. 2013;43(2):159–167.
16. Festa A., D'Agostino R., Jr., Tracy R. P., Haffner S. M. C-reactive protein is more strongly related to post-glucose load glucose than to fasting glucose in non-diabetic subjects; the Insulin Resistance Atherosclerosis study.Diabetic Medicine. 2002;19(11):939–943.
17. Lee C. C., Adler A. I., Sandhu M. S., et al. Association of C-reactive protein with type 2 diabetes: prospective analysis and meta-analysis. Diabetologia. 2009;52(6):1040–1047.
18. Lu B., Yang Y., Yang Z., et al. Insulin resistance in Chinese patients with type 2 diabetes is associated with C-reactive protein independent of abdominal obesity. Cardiovascular Diabetology. 2010;9, article 92.
19. J.P. Casas, T. Shah, A.D. Hingorani, J. Danesh, M.B. PepysC-reactive protein and coronary heart disease: a critical reviewJ Int Med, 264 (2008), pp. 295314.

DOI Number: 10.5958/2321-1032.2017.00007.9

Coverage of Mass Drug Administration for Filariasis Elimination in Thiruvananthapuram District of India

Anil Bindhu S[1], Nazeemabeevi[2], Ranu Rawat[2], Benny PV[1], Jeesha C Haran[1]

[1]Professor, [2]Associate Professor, Department of Community Medicine, Sree Gokulam Medical College, Venjaramoodu, Kerala, India

ABSTRACT

Introduction: Lymphatic Filariasis is responsible for considerable suffering, deformity and disability, although it is not a fatal disease. The current estimate reveals that 120 million people in the world are infected with lymphatic filarial parasites, which includes 40 million people with overt disease like lymphoedema and scrotal hydrocele. The National Health Policy (2002) has envisaged elimination of Lymphatic Filariasis in India by 2015. Mass drug administration for elimination of Filariasis has been implemented in India since 2004. The objectives of the study were to assess the coverage and compliance of mass drug administration in Thiruvananthapuram district in Kerala for 2014 round, to find out the reasons for non-consumption of the drugs & to find out the side effects experienced among those who consumed the drugs. **Materials and method**: A community based cross sectional study was conducted through house to house survey. Data regarding 864 individuals from 243 households were collected from the selected clusters. **Results:** 87.8% (95% CI: 85.5-89.9%) of the population received the antifilarial drugs. The proportion of population who consumed the drugs was 68.8% (95%CI: 65.6-72.0%). The most common reason for non-consumption was not receiving the drug followed by fear of side effects, and thought of "no Filariasis". Side effects reported in only 6.7% among those consumed. The most common side effect was dizziness or sedation (3.9%). No significant difference was observed in the consumption pattern among the residents in rural and urban areas (p = 0.10), gender (p=0.41).

Keywords: *Mass drug administration, coverage, Elimination; Lymphatic Filariasis, Kerala*

INTRODUCTION

Globally 120 million are infected with Filariasis and approximately 25 million men suffer from LF-associated uro-genital disease (most commonly hydrocele), and almost 15 million people, have lymphoedema. These chronic manifestations of LF cause major disability, social and stigma loss of productivity. Global Programme to Eliminate Lymphatic Filariasis was initiated by the World Health Organization. The central strategy of the GPELF is Mass Drug Administration (MDA) of anti-filarial medication to reduce the prevalence of microfilaria to below one percent in endemic communities. Global population requiring Preventive Chemotherapy for Lymphatic Filariasis(LF) was 1.242 billion in 2013.[1] Elimination of lymphatic Filariasis is defined as the reduction in infection prevalence below threshold levels at which transmission is no longer considered sustainable and ensuring access to a recommended basic package of care to manage morbidity and prevent disability.

Mass drug administration (MDA) is recommended to stop the spread of LF and involves a single, combined dose of medications given annually to all persons living in endemic areas for 4–6 years. For the strategy to be effective, more than 65% of those living in endemic areas should receive and swallow the recommended medication. To find out whether infection prevalence is reduced below threshold levels after intervention, a standardized transmission assessment survey (TAS) is recommended by WHO, in the districts in which

Correspondence to:
Anil Bindhu S,
Professor, Department of Community Medicine,
Sree Gokulam Medical College, Venjaramoodu, Kerala, India, E-mail: dranilbindu@gmail.com

minimum five rounds of MDA with more than 65% coverage against total population. About 56.5% of the populations requiring MDA are in South East Asian Region, where it is endemic in 9 countries. In 2013, overall 357.6 million people in the Region were targeted for MDA, and 253.6 million (70.9%) were treated.1 Filariasis has been a major public-health problem in India. The disease is reported to be endemic in 255 districts in 21 states and UTs.[2] The Government of India launched administration of annual single-dose DEC in 2004. The strategy for achieving the goal of LF elimination is by annual mass drug administration (MDA) with Diethylcarbamazine (DEC) to the entire population at risk and morbidity management of lymphedema, along with the other vector management strategies.[3] There are 8 lakhs cases of lymphoedema and 4 lakhs cases of hydroceles, as per the morbidity surveys till October 2014.[4] India accounts for 68.5% of the total population requiring MDA in the Region (489.1 million people. 248.7 million people were targeted for MDA in 2013 and 177.6 million were treated in 102 IUs in India.

The first round of MDA, covering eleven endemic districts, was launched in Kerala, in March 2005. The State is taking the first steps towards Filariasis elimination. MDA was conducted in 6 districts (Palakkad, Malappuram, Thiruvananthapuram, Kozhikode, Kannur and Kasaragod.) for 2014 round. The present study attempted to assess the coverage and compliance of mass drug administration in Thiruvananthapuram district in Kerala for 2014 round, to find out the reasons for non compliance of the drugs and to find out the side effects experienced by individuals after consumption of drugs

MATERIALS & METHOD

A community based cross sectional study was conducted in Thiruvananthapuram district in Kerala State of India. We assessed the compliance and coverage of mass drug administration for Filariasis for 2014 round of Mass Drug Administration programme for elimination of Filariasis. Two Taluks in Trivandrum district, Nedumangad and Chirayinkil were selected as study settings. These two Taluks belongs to the field practicing areas of rural and urban health centres of a tertiary care teaching hospital in South India. Cluster sampling technique was used, and four clusters were assessed from each Taluks. Two clusters from urban area and six clusters from rural area were selected. At least 30 households from each cluster were included in the study. Study period was December 2014 to march 2015. A total 864 people of all age group were studied from 243 households from the selected clusters through house to house survey. An independent evaluation of MDA for 2014 round is done. Data on drug distribution of anti filarial drugs, consumption, side-effects following Diethyl Carbamazine Citrate (DEC) consumption, reasons for non consumption and sources of information on MDA were collected by interviewing the head of the family or other responsible member present at the time of survey, with the help of predesigned semi-structured questionnaire. An informed consent was obtained before the commencement of the study. IBM SPSS statistics 20 version was used for analysis. The proportion and percentages were calculated. The coverage rate is presented as proportion with 95% confidence interval. The chi-square test was ($\chi 2$) test was used to test the significance of difference between proportions. *P* value <0.05 was considered as statistically significant.

RESULTS

Two forty three households from eight clusters (two urban and six rural) resulted in a total of 864 individuals. Of the 243 families surveyed, 207 were Hindu families, 8 were Christian families and 28 families belonged to Muslim religion. Data were collected by interviewing one of the responsible family members who is considered as the informants. Data of 864 people regarding coverage and compliance of MDA were collected of which, 600 participants were from rural area and 264 are from urban area. Among them, 46.9 % (405) were males and 53.1% (459) females. The sex ratio obtained was 1.13 which is comparable with the sex ratio of Kerala. Mean age of the study population was 34.68 (95% CI: 33.4 -35.9) years. Among the participants, 88.9 % (768) belonged to Hindu religion, 9.0 % (78) belonged to Muslim religion and 2.1 % (18) belonged to Christian religion.

Distribution of Antifilarial Drugs in the Population

In the study area, 87.8% (95%CI=85.5-89.9%) of the population (759) received antifilarial drugs while 12.2% did not receive the drugs for MDA**.** Of 243 families, only 89.3% (95% CI: 85.2-93.0) of households (217) received drugs; rest of the families did not receive antifilarial drugs. 88.4 %(358) males and 87.4 %(401)

of females received drugs (p=0.6). 86.5 %(519) people in rural area and 90.9 %(240) in urban area received the antifilarial drugs (p=0.06).

Consumption of drugs in the population

Only 68.8% (95% CI=65.6-72%) of the total population (594) Consumed DEC and albendazole. There was no statistically significant difference found between rural urban population in coverage and compliance of mass drug administration. And 67 %(402) of rural and 72.7% (192) of urban population had consumed the drugs, 33 %(198) rural and 27.3 %(72) urban population did not consume antifilarial drugs (p=0.09). Consumption of drugs was not significantly associated with gender, 70.1 %(284) males and 67.5 %(310) females had consumed anti filarial drugs, while 29.9 %(121) males and 32.5% (149) females did not consume the (p=0.41). Consumption of DEC and albendazole was higher among the age group 6-14 and 15-60 years (Table No.1). Also, 66.1% of Hindus, 77.8% of Christians and 92.3% of Muslims had consumed DEC and albendazole and this difference is found to be statistically significant (p<0.001).

Table 1: Consumption of DEC and Albendazole in different Age groups, Gender, Place of residence and Religion

Variable name	Categories	Consumed (%)	Not Consumed (%)	P-value
Age Groups	2-5 Years	9(47.4%)	10(52.6)	0.002
	6-14 years	89(73.6)	32(26.4)	
	15-60	449(71.4)	180(28.6)	
	>60 years	47(55.3)	38(44.7)	
Sex	Male	284(70.1)	121(29.9)	0.41
	Female	310(67.5)	149(32.5)	
Place of residence	Rural	402(67)	198(33)	0.09
	Urban	192(72.7)	72(27.3)	
Religion	Hindu	508(66.1)	206(33.9)	<0.001
	Muslim	72(92.3)	6(7.7)	
	Christian	14(77.8)	4(22.2)	

Regarding the compliance of antifilarial drugs, among those who received DEC and albendazole, only 78.3 % (95%CI: 75.5-81.2%) (594) had consumed the drug. The non-compliance rate among those received drugs for MDA was 21.7 % (95% CI: 18.8-24.5%).

The proportion of eligible individuals who has consumed appropriate dose of DEC in the selected areas was 70.37%. The major reasons for non-consumption of DEC and albendazole were observed as non receipt of the drug (not received), fear of side effects, and thought of they are free from disease (no filariasis).

Table 2: Reasons for not consuming MDA

Reasons for non-consumption of drugs For MDA	Frequency	Percent
NOT RECEIVED	99	36.7
FEAR OF SIDE EFFECTS	51	18.9
NO FILARIASIS	45	16.7
SICK AT THE TIME	3	1.1
CO MORBIDITIES	29	10.7
NOT ELIGIBLE(PREG,<2YRS, VERY ILL)	20	7.4
NO SPECIFIC REASON	23	8.5
Total	**270**	**100.0**

Side effects among those who consumed DEC and albendazole

Side effects reported in only 6.7% among those consumed. 93.3 %(554) did not report any side effects. The most common side effect was dizziness or sedation (3.9%), followed by head ache (1.3%), fever (0.8%), nausea (0.7%).

Compliance, coverage & perceptions among the informants

Among the informants only 217 (89.3%) received the drugs and 69.5 %(169) of them have consumed it. Only 76 (31.3%) of the informants reported that they met the volunteer when they came for the distribution of drugs. But 10.7% reported that the volunteer did not come to their home for distributing the medicines. 141(58%) answered they "don't know", when they were asked whether volunteer visited their house. Among those who met the volunteer, 26 (34.2%) informants reported that the volunteer was a Kudumbasree worker, 50 (65.8%) informants reported that the volunteer was an ASHA worker.

None of the informants think that Filariasis is a health problem in their area. Among the informants (86.3%) believe that Filariasis can be eliminated by consuming the drugs of mass drug administration yearly, while 13.7% do not believe in that.

Table 3. Source of information regarding MDA

Source of knowledge	Frequency	Percent
NOT HEARD	53	21.8
TV	24	9.9
RADIO,TV	44	18.1
RADIO, TV, NEWS PAPERS	13	5.3
RADIO, TV, NOTICE	12	4.9
RADIO	42	17.3
NEWS PAPER	31	12.8
Health staff	24	9.9
TOTAL	**243**	**100**

DISCUSSION

In the present study 68.8% of the population has consumed the drugs. There is a major increase in the coverage and compliance of MDA now, compared to the reports by Nujum ZT5 ,in which 52.3% received drugs and Compliance rate was only 39.5% in Thiruvananthapuram for the MDA round of 2007.[5] In our study, 87.8% (95%CI=85.5-89.9%) of the population has received antifilarial drugs. 78.3 % of those who received DEC and albendazole, had consumed the drug. In a study conducted by Hussain et al., in Odisha,[6] it is reported that ninety-nine percent of the eligible study participants received DEC and Albendazole tablets during MDA for 2011 round, while Roy et al [7] reported effective coverage rate of 34.16% in Burdwan district of West Bengal in 2011 and 51.24% of eligible beneficiaries did not receive drugs. In a systematic review conducted by Babu et al. (2014), MDA coverage rates varied between 48.8% and 98.8%, and the compliance rates ranged from 20.8% to 93.7%. [8] The coverage rate of 68.8% (95% CI=65.6-72%) obtained in this study is less than the reported coverage rate of 82% of population in Kerala in 2014. [9] In a study reported by Haldar D et al., Consumption of antifilarial drugs among the Muslim was found to be lower in West Bengal.[10] But in this study, the consumption among Muslims were higher.

Most important reason for non-consumption was due to no receipt of the drugs. Only 87.8% of the population received the antifilarial drugs. Among 270 who did not consume MDA, about 37% of was reported the reason as they did not received the drugs. If the coverage can be increased further, higher consumption rate can be achieved, if the proportion of population receiving drugs can be increased further. The consumption can be further improved by conducting BCC activities and drug distribution in the, work places, hostels and other institutions.

The compliance of antifilarial drugs, among those who received DEC and albendazole was only 78.3%. There is a gap between MDA drug distribution and compliance. Compliance rate of 88.7% was reported from Puduchery.[11] As per the systematic review by Babu et al.[8], the compliance rate of MDA ranged from 20.8% to 93.7%. The average coverage-compliance gap is reported to be 22%.

In the study by Nujum ZT[5] major reason for noncompliance was fear of side effects in this district in Kerala. The fear of side effects was a major reason for non compliance in this study also, even though the non compliance rate has been reduced. Kumar *et al*. also reported "fear of side-effects" as the main cause (80.6%) for non-consumption. [12] In many other studies also, fear

of side-effects was the major reason for not consumption of the antifilarial drugs.[8] In the study by Marian Offei et al. also, there was a strong association between dislike for the side effects of the drugs and drug intake.[13] Awareness programs and follow up visits can be further intensified to increase the compliance rate further. Involvement of professional organizations and Private practitioners in the conduct of MDA is to be enhanced.

Another important barrier to compliance was that people do not perceive Filariasis as a health problem to their families. People do not want to be treated for a disease, which they believe they will not get. As many of the infected individuals continue to harbour the parasite for many years without any sign and symptoms of disease, people may not realize that they could personally benefit from DEC. The message that all people living in endemic areas are at risk of infection and that one could be infected even if asymptomatic, should reach the people.

There was a significantly higher compliance among males in compliance in Odisha.[6] But in our study, there was no statistically significant difference in compliance between males and females, as well as between the places of residence (rural/urban). This could be due to the high literacy rate in both gender and rural and urban areas in Kerala.

Side effects were reported in only 6.7% among those consumed with the most common side effect being dizziness or sedation (3.9%). In a study conducted in West Bengal also, only 2.91% reported side-effects and the most common side-effect was dizziness.[7]

CONCLUSION

In this study, 68.8% of population consumed the antifilarial drugs. The complete elimination of Filariasis depends on the sustained pursuance of high MDA coverage. The IEC programs to sensitize the population about the risk and benefits of MDA should be intensified further so that preventive chemotherapy reaches more people who can benefit from it.

Limitation

The sample was selected from a limited geographical area i.e., the two selected Taluks in Trivandrum district.

Conflict of Interest: The authors declare that they have no conflict of interest.

Funding: This work has not been funded by any external agency

Ethical Clearance- Taken from institutional ethics committee

REFERENCES

1. WHO, Weekly epidemiological record,19 SEPTEMBER 2014, No. 38, 2014, 89, 409-420 http://www.who.int/wer
2. http://nvbdcp.gov.in/Doc/Annual-report-NVBDCP-2014-15.pdf accessed on 2-7-2015
3. Govt of India (2011). Ministry of Health and Family Welfare, Department of Health and Family Welfare. Annual report 2010-2011. New Delhi accessed on 24-7-2015
4. Govt of India (2014), Annual report 2013-2014, Ministry of Health and Family welfare, NewDelhi. accessed on 24-7-2015
5. Nujum ZT. Coverage and compliance to mass drug administration for lymphatic filariasis elimination in a district of Kerala, India. Int Health. 2011 Mar;3(1):22-6. doi: 10.1016/j.inhe.2010.12.001.
6. Mohammad A Hussain, Ashok K Sitha, Subhashisa Swain*, Shridhar Kadam, Sanghamitra Pati. Mass drug administration for lymphatic filariasiselimination in a coastal state of India: a study on barriers to coverage and compliance Infectious Diseases of Poverty 2014, 3:31 http: //www.idpjournal.com/content/3/1/31
7. RabindraNathRoy, AdityaPrasadSarkar, Raghunath Misra, Amitava Chakroborty, Tusar Kanti Mondal, and Kanad Bag Coverage and Awareness of and Compliance with Mass Drug Administration for Elimination of Lymphatic Filariasis in Burdwan District, West Bengal, India J Health Popul Nutr. 2013;31(2):171-177
8. Babu.BV,BabuGR. Coverage and compliance with , mass drug administration under the programme to eliminate lymphatic filariasis in India: a systematic review. Trans R Soc Trop Med Hyg. 2014;108(9): 538-49. doi: 10.1093/trstmh/tru057. Epub 2014 Apr 11
9. Govt of India. Ministry of Health and Family Welfare, National Vector Borne Disease Control Programme, Directorate General of Health Services. http://www.nvbdcp.gov.in/filariasis.html

accessed on 24-7-2015,

10. Haldar D, Ghosh D, Mandal D, Sinha A, Sarkar G N, and Sarkar S. Is the coverage of mass-drug-administration adequate for elimination of Bancroftian filariasis? An experience from West Bengal, India Trop Parasitol. 2015;5(1): 42–49. doi: 10.4103/2229-5070.149921
11. T. Mahalakshmy, G. Kalaiselvan, Jeram Parmar & Amol Dongre. Coverage and compliance to diethylcarbamazine in relation to Filaria Prevention Assistants in rural Puducherry, India. J Vector Borne Dis 2010;47: 113–115
12. Kumar A, Kumar P, Nagaraj K, Nayak D, Ashok L, Ashok K. A study on coverage and compliance of mass drug administration programme for elimination of filariasis in Udupi district, Karnataka, India. J Vector Borne Dis. 2009;46:237–40. [PubMed]
13. Offei M, Anto F. Compliance to Mass Drug Administration Programme for Lymphatic Filariasis Elimination by Community Members and Volunteers in the Ahanta West District of Ghana. J Bacteriol Parasitol 2014; 5: 180. doi: 10.4172/2155-9597.1000180

DOI Number: 10.5958/2321-1032.2017.00008.0

A Study of Association between Severe Periodontitis and Subclinical Atherosclerosis in Young Subjects

U M Natarajan[1], Midhun M[2]

[1]Professor, Department of Medicine, Kerala Medical College, Mangode, Cherpulassery, Palakkad District, Kerala, [2]Assistant Professor, Department of Medicine, Malabar Medical College, Modakkallur, Atholi, Kozhikode, Kerala

ABSTRACT

Backround : Periodontitis plays a central role in complex multifactorial chronic inflammatory diseases and cardiovascular disease (CVD).

Objective: To evaluate association between severe generalized periodontitis and subclinical atherosclerosis in young, otherwise systemically healthy individuals.

Method: 60 systemically healthy individuals of age between 20-40 years were included. Group I consisted of 30 subjects with healthy periodontal tissue & group II with 30 subjects with severe generalized periodontitis. Ultrasonographic evaluation of bilateral carotid intima media thickness (IMT)at the level of common carotid artery was done.

Results: The overall mean IMT in group I was 0.52±0.07mm and in group II was 0.61±0.07mm. Bivariate analysis considering the binomial IMT (≥0.6) as outcome variable showed odd's ratio=16 for probing depth and clinical attachment loss. Final model of stepwise logistic regression using binomial IMT (> 0.6) as outcome variable showed statistical significance with clinical attachment loss suggesting that, as the clinical attachment loss increases the IMT also increases.

Conclusion: Severe generalised periodontitis is associated with sub-clinical atherosclerosis in young systemically healthy patients.

Keywords: *Periodontitis, Atherosclerosis, carotid intima-media thickness*

INTRODUCTION

Periodontitis is a chronic 'infectious/inflammatory' disease of multifactorial etiology.[1] Though it is initiated by dental plaque associated microorganisms, the inflammatory process is sustained by the host. Inflammation referring to a protective tissue response to injury has been implicated in the pathogenesis of many human diseases. It plays a central role in complex multifactorial chronic inflammatory diseases including periodontitis and cardiovascular disease (CVD).

The periodontium thus serves as a renewing reservoir for inflammatory mediators,that is spilled over into systemic circulation thereby inducing and perpetuating the systemic effects.[2] IL-1α favours coagulation, thrombosis and retards fibrinolysis. Chemical mediators IL-1, TNF-α, and thromboxane can cause platelet aggregation and adhesion, formation of lipid-laden foam cells and deposition of cholesterol in the arteries.

B-mode ultrasonography is a non- invasive and highly reliable tool for assessing the early stages of atherosclerosis by measuring the thickness of the inner layer of the vessel walls.[3] This procedure is been used widely for monitoring the carotid artery and to identify

Correspondence author
Dr. U.M. Natarajan
Professor, Department of Medicine,
Kerala Medical College Hospital
Mangode, Cherpulassery, Palakkad District, Kerala

the sub-clinical atherosclerosis condition.

The present study was performed to assess the link between severe generalized periodontitis and carotid intima media thickness in young otherwise systemically healthy individuals. The Intima media thickness of the carotid artery indicates the subclinical atherosclerosis status of an individual.

METHOD

60 out-patients who were referred to Department of General Medicine, Kerala Medical College Hospital during June 2015- July 2016 were enrolled for the study . This study was conducted in collaboration with faculty of Dentistry of our Hospital. . Informed consent was obtained from all the patients. Ethical approval was obtained from institutional Ethical committee.

INCLUSION CRITERIA:

- Subjects within the age range of 20 to 40 years,
- Individuals with healthy periodontal tissue (group I)
- The subjects diagnosed with severe generalized periodontitis (group II, with clinical attachment loss ≥5mm in more than 30% of the sites).
- Smokers who have the habit for greater than 5 years

EXCLUSION CRITERIA:

- Subjects who had systemic antibiotic treatment within 3 months or any other regular medication
- Pregnant mothers
- Individuals involved in intense sporting activity
- Smokers who have the habit for less than 5 years

60 systemically healthy individuals were divided into Group I (Control group) consisting of 30subjects with healthy periodontal tissues and Group II (Test group) contained of 30 subjects with severe generalised periodontitis.

All 60 subjects underwent a physical examination. Medical history was determined from each patient by the interview method.

Periodontal Disease assessment

A single trained dentist assessed the full mouth plaque score, bleeding score, probing depth and clinical attachment level in the study participants.

Blood collection and laboratory analysis

Venous blood samples were taken from each subject at least 2 weeks after periodontal examination by a single venipuncture in the antecubital fossa. Tubes containing blood without an anticoagulant were centrifuged at room temperature (2000 ×g) for 15 min. Within 1 hour of collection, aliquots of serum samples were stored at -80°C until samples from all participants were collected.

The following were assessed

- High-sensitivity C-reactive protein
- Random Glucose
- Triglycerides
- High-density lipoprotein cholesterol (HDL-cholesterol)
- Low-density lipoprotein cholesterol (LDL-cholesterol)
- Total serum cholesterol
- Haemoglobin A1c%
- Cardiac risk ratio

Ultrasonographic measurement of carotid IMT

Carotid IMT was bilaterally assessed at the common carotid artery in both group I and group II patient in the supine position. A single experienced physician blinded with respect to periodontal condition assessed both the groups.

Carotid IMT was measured with an orthogonal incidence of the ultrasonic beam to the axial course of the artery, on a 10mm segment of the far wall of the common carotid artery (longitudinal projection) avoiding non-linear segments, using a dedicated software (Acuson X300 version 2.0, Swami Vivekananda Diagnostic Centre). The real-time measurement of carotid IMT represented the mean of 10 measures on each side. The average of both right and left IMT was considered for all subsequent computations [4].

STATISTICAL ANALYSIS

Statistical analysis was done using software SPSS (17.0, version for windows). Descriptive statistics were expressed as Mean± Standard Deviation for both the groups. Odd's ratio was calculated using IMT (≥0.6mm) as outcome variable. The correlation between periodontal parameters, cardiac risk ratio and carotid intima media

thickness was assessed using Karl Pearson's correlation coefficient. Multiple linear regression model (Forward Stepwise method; Criteria: Probability-of-F-to-enter ≤ 0.05, Probability-of-F-to-remove ≥0 .10) was assessed with mean IMT as outcome variable. Final model of stepwise logistic regression using binomial IMT (>0.6) as outcome variable was fitted.

RESULTS

The study sample consisted of a total number of 60 subjects in two groups(group I and group II).Descriptive statistics and details of matching criteria for group I and group II are shown in Table 1 and Laboratory variables in group I and control group II are shown in Table 2.

The odd's ratio (OR) of random blood sugar level, serum cholesterol level, triglyceride level were <1 which was statistically significant.The random blood sugar level was with OR of 0.66 with upper limit of 0.87 and lower limit of 0.51 which was statistically significant.The serum cholesterol level was with odd's ratio of 0.69 with the upper limit of 0.88 and lower limit of 0.54 which was statistically significant.The triglyceride level was with OR of 0.69 with the upper limit of 0.88 and lower limit of 0.54 which was statistically significant.

Final model of forward stepwise logistic regression using binomial IMT (> 0.6) as outcome variable showed BMI, random blood sugar, triglycerides and serum cholesterol were not statistically significant (p- value > 0.05). Whereas clinical attachment loss showed statistical significance (p – value 0.009) suggesting that as the clinical attachment loss increases the carotid intima thickness also increases.

The mean carotid intima thickness in male (0.64mm) had higher value compared to females (0.59mm) in the group II

DISCUSSION

The association between periodontal disease and increased carotid IMT has been described only in the middle-aged to elderly population with chronic/adult periodontitis [5,]. The present study was conducted to evaluate the association between severe periodontitis and subclinical atherosclerosis in young otherwise systemically healthy individuals in the age range of 20 to 40 years.

The Group I included periodontally healthy subjects and Group II consisted of subjects with severe generalized periodontitis.

It has been recognized that smoking habit is a risk factor for both periodontal disease and atherosclerosis[6].

In this study patient with smoking habit in group I and group II had higher IMT compared to non- smokers. Recent experimental and clinical data support the hypothesis that cigarette smoke exposure increases oxidative stress which acts as a potential mechanism for initiating cardiovascular dysfunction.

Genco et al 2005 [7] analyzed National Health and Nutrition Examination Survey (NHANES III) data and demonstrated that BMI was positively correlated with the severity of periodontal attachment loss; they found that this relationship is modulated by insulin resistance.Inthis study the body mass index for group II was higher compared to group I and it was statistically insignificant.

The mean plaque index score, mean papillary bleeding index score, mean probing depth and mean clinical attachment level was higher in group II and was statistically significant as these individuals were diagnosed with periodontitis.

Emerging evidence suggests that periodontitis may have a role in chronic infection, the associated inflammatory responses in atherosclerosis and its complications, or both, and experimental and clinical studies have indicated a potentially deleterious effect of periodontitis[8] Periodontal pathogens in vitro can promote platelet aggregation and foam-cell formation.[12] severe periodontal disease had 1.3 times the odds of having thick carotid arterial walls (≥1 mm) compared with individuals with less severe disease, after adjustment for traditional risk factors for atherosclerosis.[5] In this study the right and left carotid intima thickness and mean carotid intima thickness were higher in group II when compared to group I.

Women tend to develop heart disease later in life than men. This difference has been attributed to the loss of estrogen during the menopausal transition [13]. It is proposed that cholesterol losing effects of estrogen causes movement of cholesterol from atheroma towards plasma and thereby retards the progress of atherosclerosis. These cholesterol-losing effects of estrogen enable women to enjoy freedom from CHD

during their reproductive age, as compared to men of comparable age group [14] . As the females included in this study was within age range of 20- 40 yrs they showed lesser IMT value compared to males. The mean carotid intima thickness in male had higher value compared to females in the group II and the mean IMT in group II males and females was higher compared to group I males and females.

CRP describes the inflammatory status of the individual.[15] Periodontitis may add to the inflammatory burden of the individual and may result in increased levels of cardiovascular risk based on serum CRP concentrations. In group II subjects with increased high sensitivity C reactive protein level the odds for having increased IMT was 7.6.

The mean glucose level and HbA1C% in group II was higher when compared with group I and the difference was not statistically significant but the odds for having increased IMT was 0.66 and was statistically significant, Chronic gram negative periodontal infection may result in increased insulin resistance and poor glycemic control.[16] Uncontrolled diabetes may lead to cardiovascular complications.[17]

The odd's for increased IMT in subjects with high serum cholesterol level and triglyceride level was 0.69 which was statistically significant.Increase in pro-inflammatory cytokine in response to chronic periodontitis causes a rise in serum lipid levels.[18]

Although IMT increase in the elderly [5] might have been caused by periodontitis, this finding cannot rule out the well-known influence of aging on both IMT thickening and the prevalence of periodontal disease[19]. The correlation between periodontal parameters and the carotid intima media thickness in group I and II suggest that probing depth significantly correlates with right IMT (p-0.015), left IMT (p-0.018) and mean IMT (p-0.001).

Periodontal patients showed severe tooth loss, generalized loss of attachment and periodontal pockets and extensive gingival inflammation, with aesthetic, functional and psychological problems. When compared with the healthy individuals without signs of periodontitis.[20]

Positive relationship exist between the increased tooth loss and increased IMT in the arteries, Severe bone loss, overall periodontal bacterial burden and tooth loss [21] were associated with increased carotid IMT. In this study the clinical attachment level shows statistical significance (p – value- 0.001) suggesting that when the clinical attachment loss increases the mean carotid intima thickness level also can increase. The odd's for increased IMT in subjects with increased probing pocket depth and clinical attachment level was 16. The bivariate analysis was associated with binary IMT, with threshold value of greater than or equal to 0.6mm.

Relatively young patients with severe periodontal disease exhibit perturbed flow-mediated dilatation of the brachial artery compared with carefully matched controls. [22] Endothelial dysfunction occurs early in the pathogenesis of arterial disease, in response to a wide range of risk factors that have been shown to predict cardiovascular events in epidemiologic studies[23]. This study showed statistical significant clinical attachment level with p–value of 0.009. The odd's for having increased carotid IMT in subjects with increased clinical attachment level was OR=16 which was statistically significant. This suggest that as the clinical attachment loss increases the carotid intima thickness also increases

Limitations of the present study include the differences in age between group I and group II. Even if a minimal age-related increase (~0.02 mm/year)[20] in carotid IMT was reported the difference between group I and groups II is only partially explained in this study by age difference.

TABLE 1 Descriptive statistics and details of matching criteria for group I and group II

Variables	Group I (Control group) (N=30)	Group II (Test group) (N=30)	p- value
Gender (females, males)	16(53%),14(47%)	14(47%), 16(53%)	-
Age (years)	27.73±9.59	29.93±10.03	0.540
Smoking habits (yes)	3(20%)	3(20%)	-

Cont... TABLE 1 Descriptive statistics and details of matching criteria for group I and group II

Body mass index	22.39±1.82	23.74±2.42	0.090
Plaque index	0.86±0.31	2.04±0.46	0.001*
Papillary bleeding index	0.86±0.40	2.76±0.71	0.001*
Mean Clinical attachment level (mm)	2.65±0.43	7.94±1.23	0.001*
Mean Probing depth (mm)	2.54±0.45	7.13±1.07	0.001*
Right IMT (mm)	0.53±0.09	0.62±0.07	0.008*
Left IMT (mm)	0.51±0.12	0.60±0.011	0.050*
IMT mean (mm)	0.52±0.07	0.61±0.07	0.002*

*statistically significant†IMT- carotid intima media thickness

TABLE 2 Laboratory variables in group I and control group II

Variables	**Group I (Control group) (N=30)**	**Group II (Test group) (N=30)**	**p- value**
High sensitivity-C-Reactive Protein (mg/l)	0.27±0.12	0.56±0.51	0.04*
Glucose (mg/l)	96.06±13.12	100.66±13.8	0.35
Total serum cholesterol (mg/dl)	162.18±16.22	176.34±20.85	0.04*
Triglycerides (mg/dl)	95.93±15.90	114.26±45.36	0.15
High Density Lipid-cholesterol (mg/dl)	58.70±8.71	40.13±6.92	0.001*
Low Density Lipid -cholesterol (mg/dl)	100.96±17.98	117.38±26.41	0.05*
Haemoglobin A1C%	5.18±0.59	5.46±0.57	0.31

*statistically significant

CONCLUSION

Periodontitis seems to contribute to systemic inflammation and subjects with increased clinical attachment loss are more prone to have increased carotid intima thickness. Thus periodontal disease may predict a systemic atherosclerosis condition decades before the occurrence of clinical cardiovascular events. Further studies are required to assess the stronger association between periodontitis and subclinical atherosclerosis.

Conflict of Interest: Nil

Source of Funding : Nil

REFERENCE

1. Hugoson A, Norderyd O, Slotte C, Thorstensson H. Distribution of periodontal disease in a Swedish adult population 1973, 1983 and 1993. J ClinPeriodontol 1998;25:542–548.
2. Ross R. Atherosclerosis – an inflammatory disease. N Engl J Med 1999;340**:**115-126.
3. Vieira CLZ, Caramelli B. The history of dentistry and medicine relationship: could the mouth finally return to the body? Oral Dis 2009;15:538–546.
4. Alipour M, Doan HA, Bean B. Normal values of Intima-Media Thickness (IMT) in patients with no traditional Risk Factors (RF) for Atherosclerosis. Society of Vascular Ultrasound; Annual Conference 2009. Arch Cardiovasc Imaging 2013;1:27-31.
5. Beck JD, Elter JR, Heiss G, Couper D, Mauriello SM, Offenbacher S. Relationship of periodontal disease to carotid artery intima-media wall thickness. ArteriosclerThrombVascBiol 2001;21: 1816–1822.
6. Hujoel PP, Drangsholt M, Spiekerman C, DeRouen TA. Periodontitis-systemic disease associations in the presence of smoking-causal or coincidental?.Pe

riodontol 2000 2002;30:51-60.

7. Genco RJ, Grossi SG, Ho A, Nishimura F, Murayama Y. A proposed model linking inflammation to obesity, diabetes and periodontal infections. J Periodontol 2005;76:2075–2084.
8. Herzberg MC, Weyer MW. Dental plaque, platelets, and cardiovascular diseases. Ann Periodontol 1998;3:151-160.
9. Qi M, Miyakawa H, Kuramitsu HK. Porphyromonasgingivalis induces murine macrophage foam cell formation. MicrobPathog 2 003;35:259-267
10. Herzberg MC, Weyer MW. Dental plaque, platelets, and cardiovascular diseases. Ann Periodontol 1998;3:151-160.
11. Bhupathy P, Haines CD, Leinwand LA. Influence of sex hormones and phytoestrogens on heart disease in men and women. Womens Health (LondEngl) 2010 Jan;6(1):77-95.
12. Paranjape SG, Turankar AV, Wakode SL, Dakhale GN. Estrogen protection against coronary heart disease: are the relevant effects of estrogen mediated through its effects on uterus--such as the induction of menstruation, increased bleeding, and the facilitation of pregnancy? Med Hypotheses 2005;65(4):725-7.
13. D'Aiuto F, Parkar M, Andreou G. Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers. J Dent Res 2004; 83:156-160.
14. Katz J. Elevated blood glucose levels in patients with severe periodontal disease. J ClinPeriodontol 2001;28:710–712.
15. Hayashida H, Kawasaki K, Yoshimura A, Kitamura M, Furugen R, Nakazato M et al. Relationship between periodontal status and HbA1c in nondiabetics. J Public Health Dent 2009;69:204-206.
16. Iacopino AM, Cutler CWPathophysiological relationships between periodontitis and systemic disease: recent concepts involving serum lipids.J Periodontol 2000 Aug;71(8):1375-84.
17. Howard G, Sharrett MD, Heiss G, Evans GW, Chambless LE, Riley WA, Burke GL.Carotid artery intima-medial thickness distribution in general populations as evaluated by B-mode ultrasound. Stroke 1993;24:1297–1304.
18. Hugoson A, Norderyd O, Slotte C, Thorstensson H. Distribution of periodontal disease in a Swedish adult population 1973, 1983 and 1993. J ClinPeriodontol 1998*;*25:542–548.
19. Cairo F, Castellani S, Gori AM, Nieri M, Baldelli G, Abbate R et al. Severe periodontitis in young adults is associated with sub-clinical atherosclerosis. J ClinPeriodontol 2008;35: 465-472.
20. Albandar JM, Brunelle JA, Kingman A. Destructive periodontal disease in adults 30 years of age and older in the United States, 1988–1994. J Periodontol 1999;70:13–29.
21. Chin UJ, Ji S, Lee SY, Ryu J, Lee JB, Shin C et al. Relationship between tooth loss and carotid intima-media thickness in Korean adults. J AdvProsthodont 2010;2:122–127.
22. Engebretson SP, Lamster IB, Elkind MS, Rundek T, Serman NJ, Demmer RT et al. Radiographic measures of chronic periodontitis and carotid artery plaque. Stroke 2005;36: 561-566.
23. Tonetti MS, D'Aiuto F, Nibali L, Donald A, Storry C, Parkar M, SuvanJ, Hingorani AD, Vallance P, Deanfield J. Treatment of periodontitis and endothelial function. Engl J Med. 2007 Mar 1;356(9):911-20.

DOI Number: 10.5958/2321-1032.2017.00009.2

To Study the Role of Metadoxine on Liver Function Tests in the Management of Chronic Hepatitis B Infection

Sharma H[1], Chadha S C[2], Gupta R[3]

[1]Associate Professor, [2]Assistant Professor, [3]Senior Resident, Department of General Medicine, Muzaffarnagar Medical College & Hospital, Muzaffarnagar, Uttar Pradesh, India

ABSTRACT

Hepatitis B causes both acute and chronic liver damage where a greater proportion of patients with chronic disease end up with liver cirrhosis and hepatocellular carcinoma (HCC). Despite advances in modern medicine, there is no effective drug available that stimulates liver function, protects the liver from damage or helps to regenerate hepatic cells. Hence, there is a need for safe and effective remedy. The present study was planned to evaluate the role of metadoxine in treatment of patients with chronic hepatitis B (CHB) infection. A total of 40 male and female patients aged between 30-65 years with positive hepatitis B surface antigen were included in the study for six month and informed consent was taken. Patients were treated with 1500mg/day of metadoxine for six months. Liver function tests including total bilirubin, aspartate and alanine transaminase, serum albumin and alkaline phosphatase were done at baseline and repeated at the end of 24 weeks. Statical analysis was carried using Graphpad Prism, version 4.03 for windows, graphpad software. No significant evidence of improvement of biochemical parameters was observed at the conclusion of study.

Keywords*: Metadoxine, Chronic hepatitis B.*

INTRODUCTION

Hepatitis B is a serious and common infectious disease of the liver caused by the hepatitis B virus (HBV), an enveloped virus containing a partially double stranded, circular DNA genome and classified within the family hepadnavirus.[1] The average estimated carrier rate of HBV is 4%, placing India in the intermediate range for hepatitis B endemicity[2] with an approximate total of 36 million carriers.[3] Among the estimated 400 million hepatitis B surface antigen (HBsAg) carriers worldwide, India alone contributes 9% of the total.[4] There are wide variations in social, economic and health factors in different regions of India, which may explain the differences in HBV carrier rates reported by investigators in different parts of thecountry.[5-8] The virus is transmitted by exposure to infectious blood or body fluids such as semen and vaginal fluids, while viral DNA has been detected in the saliva, tears and urine of chronic carriers. Perinatal infection is a major route of infection in endemic (mainly developing) countries during the preschool years.[9] In areas of intermediate endemicity, transmission is either perinatal or horizontal.[10,11] The route of transmission has important clinical implications, as there is a very high probability of developing chronic hepatitis B (CHB) if the infection is acquired prenatally or in the preschool years.[12] Other risk factors for developing HBV infection include working in a healthcare setting, transfusions, dialysis, acupuncture, tattooing, extended overseas travel and residence in an institution.[13-15] The virus does not spread by holding hands, sharing eating utensils or drinking glasses, kissing, hugging, coughing, sneezing or breastfeeding.[16,17] The acute illness causes liver inflammation, vomiting, jaundice and, rarely, death. CHB may eventually cause cirrhosis and liver cancer - a disease with poor response to all but a few current therapies.[18] The infection is preventable by

Author for Correspondence
Dr. Hemant Kumar Sharma
Associate Professor, Department of Medicine
Muzaffarnagar Medical College
Muzaffarnagar, U.P. India.
Tel:+91 9758417852
E-mail: hemantkumarsharma1959@gmail.com

vaccination.[19] If the host is able to clear the infection, the HBsAg will eventually become undetectable and will be followed by immunoglobulin G (IgG) antibodies to the HBsAg and core antigen (anti-HBs and anti-HBc IgG).[20] A person negative for HBsAg but positive for anti-HBs either has cleared an infection or has been vaccinated previously. Individuals who remain HBsAg-positive for at least six months are considered to be hepatitis B carriers.[21] Carriers of the virus may have CHB reflected by elevated serum alanine aminotransferase (ALT) levels and hepatic inflammation. Carriers who have seroconverted to hepatitis B e-antigen (HBeAg)-negative status, especially those who have acquired the infection as adults, have very little viral multiplication and hence may be at little risk of long-term complications or of transmitting infection to others.[22] Antiviral treatment is the effective way to reduce morbidity and mortality from chronic HBV infection. Conventional interferon (IFN)-α and lamivudine have been the primary treatments to date. IFN-α produces a durable response in a moderate proportion of patients but has undesirable side effects and must be administered subcutaneously three times per week, an inconvenient regimen for patients. These disadvantages may be partially overcome with pegylated IFN (PEG-IFN). Lamivudine offers the advantages of minimal side effects and ease of administration. The major disadvantages are its modest efficacy rate, the need for long-term therapy to maintain response and its association with a high rate of viral resistance, particularly with prolonged use.[23-27] However, prolonged treatment is often necessary to prevent relapse on cessation of therapy[28] and continuous treatment can lead to the development of lamivudine resistance. Promising emerging treatments include adefovir,[29] entecavir[30] and PEG-IFN α-2a (40 kDa).[31] The current treatment of care is costly, has significant side effects and fails to cure about half of all infections. Hence, there is a need to develop new treatment from medicinal plants, which are less toxic, more efficacious and cost-effective.

Metadoxine is a medicine that is used for the treatment of liver damage due to alcoholism , alcoholic fatty liver acute and chronic liver disease and other conditions. Metadoxine works by increasing the alcohol elimination from the blood and tissues, thus preventing liver damage. Side effects include sleepiness, numbness, skin rash and loose motion.

MATERIALS AND METHOD

The study was conducted in the department of medicine of Muzaffarnagar Medical College and Mahesh Hospital, Muzaffarnagar from March 2016 through August 2016. The study included patients of Hypertension of age 30 years to 65 years of both sexes attending the medicine outpatient department of Muzaffarnagar Medical College and Mahesh Hospital. The number of patients included in the study was 50. Inclusion criteria: Patients with a history of hepatitis B or HBsAg carriers for at least six months, who still had symptoms and signs of hepatitis B as well as abnormal liver function and positive HBsAg, were diagnosed as having CHB infection in the present study. Patients who were willing to give a written informed consent and follow the schedule and who had not participated in a similar investigation in past four weeks were enrolled. Exclusion criteria: Patients aged >60 years or <18 years, pregnant or lactating women, patients who had hepatitis C or other hepatic viral infection, autoimmune hepatitis and drug-induced hepatitis or alcoholic hepatitis; patients with severe complications of the cardiovascular, renal or hematopoietic systems and mental diseases, were excluded. Patients were excluded if they had decompensated liver disease (serum albumin ≤360 g/l, bilirubin ≥150 g/l, prothrombin time [PT] ≥2s prolonged or a history of ascites, variceal hemorrhage or hepatic encephalopathy), pancytopenia (hemoglobin [Hb] <110 g/l, total leukocyte count [TLC] <4,000/mm3 or platelets <105/mm3). Patients with a history of using IFN or antiviral agents or corticosteroids or immunosuppressive drugs and who are unwilling to give written informed consent were also excluded. Study procedure: Each patient was asked to take 1500mg of metadoxine in two divided doses for a period of six months. . Liver function tests including total bilirubin, aspartate and alanine transaminase, serum albumin and alkaline phosphatase were done at baseline and repeated at the end of 24 weeks.

RESULTS

Fifty patients (32 males and 18 females) with a mean age of 43.90±10.60years participated in the study. All the patients completed the study and their data was available for analysis. No significant evidence of hepatoprotective effect of metadoxine was seen in chronic hepatitis B patients in terms of reduction in biochemical parameters.

There were no clinically significant adverse reactions either reported or observed during the entire study period. The overall compliance to the treatment was good and no treatment discontinuations were reported.

Table1: Comparison between the Biochemical parameters (Mean±2S.D.) of Study group after two months.

Parameters	Initial	After treatment	P value
T.Bilirubin (mg/dl)	2.372±1.704	2.264±0.704	NS
Albumin(g/dl)	3.582±0.904	3.590±0.982	NS
Total protein(g/dl)	6.864±0.643	6.790±0.785	NS
SGOT levels(U/I)	126.90±1.48	120.74±2.89	NS
SGPT levels(U/I)	246.86±0.78	240.87±2.67	NS
ALP levels(U/I)	104.54±2.84	98.45±1.87	NS

DISCUSSION

Our study demonstrates that six months treatment with metadoxine show no significant evidence of improvement in biochemical parametersin patients with chronic hepatitis B

From our study it may be summarised that metadoxine therapy was not beneficial for the chronic hepatitis B patients and further long term metastudies should be done in the future for more detailed beneficial effects of Metadoxine.

CONCLUSION

The role of metadoxine in liver function tests including total bilirubin, aspartate and alanine transaminase, serum albumin and alkaline phosphatase were done at baseline and repeated at the end of 24 weeks during the treatment of patients with chronic hepatitis B (CHB) infection. There is no significant evidence of improvement of biochemical parameters was observed at the conclusion of study.

Conflict of Interest - None

Source of Funding – Self

Ethical Clearance - Taken

REFERENCES

1. Ganem D, Schneider RJ. Hepadnaviridae: The viruses and their replication. In: Fields Virology. 4th edition, Knipe DM et al. (Eds.), Lippincott Williams & Wilkins: Philadelphia 2001:p.2923-69.
2. Suzuki H, Woodfield G. Viral hepatitis in Asia: summary of a plenary session. In: Viral hepatitis and Liver Disease. Nishioka K, Suzuki H, Mishiro S, Oda T (Eds.), Springer Verlag: Tokyo 1994:p.385-6.
3. Agarwal R, et al. Natl Med J India 1994;7(5): 216-20.
4. Andre FE. Vaccine 1990;8(Suppl):S74-8; discussion S79-80.
5. Irshad M, et al. Natl Med J India 1994;7(5): 210-2.
6. Singhvi A, et al. J Trop Med Hyg 1990;93(3):178-82.
7. Prasad SR, et al. Indian J Med Res 1983;78: 300-6.
8. Joshi SH, et al. Indian J Med Res 1990;91:340-3.
9. Coopstead, Lee-Ellen C. Pathophysiology. Saunders: Missouri 2010:p.886-7.
10. Lok AS. N Engl J Med 2002;346(22):1682-3.
11. Gust ID. Gut 1996;38(Suppl 2):S18-23.
12. Chen CJ, et al. J Gastroenterol Hepatol 2000;15 Suppl:E3-6.
13. World Health Organization, Hepatitis B, Fact sheet No. 204. Available at: http://www.who.int/ mediacentre/ factsheets/fs204/en/
14. Sleisenger MH, et al. In: Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management. 8th edition, Saunders: Philadelphia 2006.
15. Kidd-Ljunggren K, et al. J Hosp Infect 2006;64(4): 352-7.
16. Hepatitis B. National Institute of Health. Available at: http:// www.ncbi.nlm.nih.gov/pubmedhealth/ PMH0001324. Retrieved 2010-11-23.
17. Hepatitis B FAQs for the Public - Transmission. U.S. Centers for Disease Control and Prevention (CDC). Available at: http://www.cdc.gov/ hepatitis/b/bfaq.htm

18. Chang MH. Semin Fetal Neonatal Med 2007;12(3):160-7.
19. Pungpapong S, et al. Mayo Clin Proc 2007;82(8): 967-75.
20. Gocke DJ, et al. Lancet 1970;2(7684):1149-53.
21. Lai KN, et al. N Engl J Med 1991;324(21):1457-63.
22. Takekoshi Y, et al. Lancet 1978;2(8099):1065-8.
23. Zuckerman AJ. Hepatitis viruses. In: Baron's Medical Microbiology. Baron S, et al (Eds.), 4th edition, University of Texas Medical Branch, 1996.
24. Lok AS, et al. Hepatology 2007;45(2):507-39.
25. Chu CM, et al. Gastroenterology 2007;133(5): 1458-65.
26. Liaw YF, et al. Gastroenterology 2000;119(1): 172-80.
27. Dienstag JL, et al. Hepatology 1999;30(4):1082-7.
28. Perrillo R, et al. Hepatology 2000;32(1):129-34.
29. Yang H, et al. Hepatology 2002;36(2):464-73.
30. de Man RA, et al. Hepatology 2001;34(3):578-82.
31. Cooksley WG, et al. J Viral Hepat 2003;10(4): 298-305.

DOI Number: 10.5958/2321-1032.2017.00010.9

A Comparative Study of Serum Calcium and Electrolytes in Adult Patients with or without Hypothyroidism

Midhun M[1], Rashmi[2]

[1]*Assistant Professor, Department of Medicine, Malabar Medical College, Modakkallur, Atholi, Kozhikode,*
[2]*Assistant Professor, Department of Medicine, Government T D Medical College, Alappuzha*

ABSTRACT

Introduction: Different electrolyte disorders in association with thyroid dysfunction were observed in the literature. The effect of thyroid hormones on minerals has not been well established and the underlying mechanism is not well understood too.

Objective to assess the alterations in the levels of serum calcium, sodium, potassium and chlorides and to correlate these minerals with TSH in hypothyroidism.

Materials and method: A case control study is taken up on 50 subjects with hypothyroidism and 50 apparently normal healthy subjects. Venous blood sample is collected from all the subjects. Serum TSH, calcium, sodium, potassium and chlorides are estimated in all the subjects.

Results: A significant decrease in serum calcium, sodium and potassium is observed in cases in comparison to controls *(p<0.0001).* A significant increase in serum chlorides is ob-served in cases *(p=0.03)* compared to controls. When correlat-ed with TSH, serum calcium, sodium, potassium and chlorides showed negative correlation in subjects with hypothyroidism.

Conclusion: The present study indicates the profound influence of thyroid hormones on serum electrolytes. This study concludes that serum calcium, sodium and potassium levels are decreased whereas serum chloride levels are increased in hypothyroidism in comparison to euthyroid subjects.

Keywords: *Calcium, Hypothyroidism, Potassium, Sodium, Thyroid Stimulating Hormone (TSH).*

INTRODUCTION

Thyroid hormone is a central regulator of body haemodynamics, thermal regulation and metabolism. Profound in-fluence of thyroid hormones is observed on renal haemody-namics, glomerular filtration, renin-angiotensin aldosterone system and electrolyte handling.[1] Hypothyroidism is the most common form of thyroid dysfunction resulting from the deficiency of thyroid hormones or from their impaired activity. Different electrolyte disorders in association with thyroid dysfunction were observed in the literature.[2] Thyroid hormones by stimulating bone resorption directly increase serum calcium and serum phosphorus concentra-tions. The decrease in the bone resorpting hormone in hypothyroidism leads to hypocalcemia.[3] Enhanced renal water retention mediated by vasopressin was a consequence of hypothyroidism.[2] Thyroid hormones regulate the activity of sodium-potassium pumps in most of the tissues. Studies re-vealed that hypothyroidism is associated with hyponatrem ia.[4-6] Impaired urinary dilution capacity due to non-osmotic release of vasopressin as well as increased urinary sodium loss would be the major mechanism for hypothyroid induced hyponatremia.[7] Hyperkalemia and hyperchloremia were also observed in hypothyroid patients.[8]

Correspondence author:
Dr Midhun M
Assistant Professor, Department of Medicine,
Malabar Medical College Hospital,
Modakkallur,Atholi, Kozhikode

Indian patients are different from western patients from bone mineral homeostasis point of view. On one hand, thyroid dis-orders are most prevalent and on the other hand, Indian stud-ies focusing on the blood levels of calcium and electrolytes in thyroid disorders are sparse. The effect of thyroid hormones on minerals has not been well established and the underlying mechanism is not well understood too. So, the present study is undertaken to assess the alterations in the levels of serum calcium, sodium, potassium and chlorides and to correlate these minerals with TSH in hypothyroidism.[9]

METHOD

Study design and Subjects

This study is a hospital based case-control study conducted at Malabar Medical College Hospital, Kozhikode between July 2015 to December 2015. The study consisted of 50 Subjects who are known patients with hypothyroidism attending the outpatient department of Medicine at Malabar Medical College Hospital as cases and 50 normal apparently healthy age and sex matched subjects from general population as controls. Institutional Ethical Clearance was obtained. The objectives of the study are explained to all eligible subjects. Informed consent of all subjects included in the study is obtained for involvement in study groups and for venipuncture.

Selection Criteria

Inclusion Criteria: Age group between 20–50 years. Subjects who are known patients of hypothyroidism with

TSH more than 10μIU/ml are the cases

Exclusion Criteria: Patients with history of hepatic disease, renal disease, bone diseases, alcoholism, diabetes mellitus, pediatric age group, other major medical conditions and those who were on mineral supplementation or any medi-cations that might affect serum electrolyte levels were excluded. Institutional Ethical Clearance was obtained. The objectives of the study are explained to all eligible subjects. Informed consent of all subjects included in the study is obtained for involvement in study groups and for venipuncture.

Blood Sample Collection

A 3ml of venous blood is drawn from each volunteer using a disposable plain vacutainer system in fasting condition. Se-rum is separated within half an hour by centrifugation and stored at 2-8°C temperature till analysis is done.

Analysis of Serum TSH is measured by Monobind Acculite Thyroid TSH kit by using neolumax's Chemiluminescence Immunoassay. Serum total calcium level is estimated by Ar-senazo III method and Serum electrolytes are measured by Easylyte's Ion Selective Electrodes. Data is expressed as Mean ± S.D. Comparison between cases and controls for all variables is performed by student t-test and correlation between parameter is studied by Pearson's correlation coefficient using SPSS Package Version 20 sta-tistical software. $p<0.05$ is considered as statistically signifi-cant and <0.01 is considered as highly significant.

RESULTS

The mean age among the cases and controls are 35.68±8.91 and 35.78±8.85 respectively with no statistical significant difference. Among the cases and controls there are 24 males, 26 females and 27 males, 23 females respectively. This is a age and sex matched study. The mean TSH in cases and controls are 52.53±27.25 and 2.70±1.37 respectively. Statistically highly significant in-crease is seen in cases compared to controls *(p<0.0001)*. The mean Serum Calcium in cases and controls are 8.58±0.46 and 10.04±0.56 respectively. Statistically significant decrease is seen in cases compared to controls *(p<0.0001)*. The mean So-dium in cases and controls are 125.23±1.12 and 139.05±2.88 respectively. Statistically highly significant decrease is seen in cases compared to controls *(p<0.0001)*. The mean Serum Potassium in cases and controls are 3.48±0.30 and 4.31±0.60 respectively. Statistically highly significant decrease is seen in cases compared to controls *(p<0.0001)*. The mean Se-rum Chlorides in cases and controls are 103.43±7.52 and 100.58±3.45 respectively. Statistically significant increase is seen in cases compared to controls *(p=0.03)* (Table 1). The serum TSH values are correlated with the values of Serum Calcium, Sodium, Potassium and Chloride levels among the cases. On analyzing the values, a statistically significant strong negative correlation is observed between serum TSH with calcium, weak negative correlation is observed with So-dium, Potassium and Chlorides (Table 2)

DISCUSSION

Thyroid hormone is a central regulator of body hemodynamics, thermoregulation and metabolism. It has an influence on renal hemodynamics, glomerular filtration and electrolyte handling.[10] Thyroid hormone affects the glomerular filtration rate and blood flow and has a direct effect on Ca and Mg resorption.[11]

The aim of this study was to investigate the effects of hypo-thyroidism on serum calcium and electrolytes. According to different case reports in the literature, electrolyte disturbanc-es in any sort of thyroid dysfunction are possible. Our study demonstrated a significant low level of serum calcium in cas-es than controls *(p<0.0001)* There was a significant negative correlation between TSH and serum calcium level among cases. Our study is in accordance with study conducted by Shivallela et al[12], Roopa et al[13] and animal study by Kumar et al.[14]

Thyroid hormone is most essential for normal growth and maturation of the skeletal system. Depressed turnover due to impaired mobilization of calcium into the bone is observed in hypothyroidism leading to decreased blood calcium. In-creased production of thyroid calcitonin which promote the tubular reabsorption of phosphate and favor the tubular ex-cretion of calcium, leading to hypocalcemia and hyperphos-phatemia as seen in hypothyroidism.[9]

A statistically significant decrease in serum sodium is ob served in cases compared to controls in our study *(p<0.0001).* Negative correlation between TSH and serum sodium level among cases is observed. Our study is in accordance with study conducted by Derubertis et al.[15] Montenegro et al.[16] and Arvind Bharti et al.[8]

A statistically significant decrease in serum potassium was observed in cases compared to controls in our study *(p<0.0001)*. Negative correlation between TSH and serum potassium level among cases was observed. Our study is in accordance with study conducted by Kavitha et al[17] Schwarz et al[18] and Jaskiran kaur et al.[19]

Our findings are contradictory to Abedelmula M, *et al*[20], concluding that significant increase in serum potassium levels in hypothyroid group compared to controls.

Sodium and potassium make vital composition of the en-zyme Na-K ATPase, which is an enzyme on the cell mem-brane helping in the transport of water and essential nutrients across the cell membrane. Sodium potassium pump in most of the tissues are regulated by thyroid hormones. Deficien-cy of thyroid hormones leading to low potassium levels in hypothyroidism, affect the Na-K ATPase activity leading to accumulation of water inside the cells and causing oedema. This could be one of the mechanisms responsible for weight gain seen in hypothyroid patients.[13]

A statistically significant increase in serum chlorides is ob-served in cases compared to controls in our study *(p=0.03).* Negative correlation between TSH and serum chloride level among cases was observed. Our study is in accordance with study conducted by Arvind Bharti et al[8] and contradictory to Kavitha et al.[17]

Table-1: Comparision of Age, Sex, TSH, Serum Calcium, Sodium, Potassium and Chlorides in Controls and Cases

Parametres	Controls (n = 50)	Cases (n = 50)	P Value
Age (Years)	35.78 ± 8.85	35.68 ± 8.91	
Sex (M/F)	26/24	27/23	
TSH (Thyroid Stimulating Hormone)	2.70 ± 1.37		
Calcium Ca^{+2} 10.04 ± 0.56	10.04 ± 0.56	8.58 ± 0.46	< 0.0001*
Sodium Na^{+}	139.05±2.88	125.23±1.12	<0.0001*
Potassium K^{+}	4.31±0.60	3.48±0.30	<0.0001*
Chloride Cl^{-}	100.58±3.45	103.43±7.52	0.03**

(* is highly significan

Table-2: Correlation of Serum Calcium, Sodium, Potassium and Chlorides with TSH among Cases

Parametres	Correlation coefficient (r value)	P Value
TSH Vs Calcium	-0.79	< 0.0001*
TSH Vs Sodium	-0.03	= 0.85
TSH Vs Potassium	-0.03	= 0.85
TSH VsChloride	-0.16	= 0.31
(* is highly significant)		

CONCLUSION

The present study indicates the profound influence of thyroid hormones on serum electrolytes. This study concludes that serum calcium, sodium and potassium levels were decreased whereas serum chloride levels were increased in hypothy-roidism in comparison to euthyroid subjects. We suggest that hypothyroid patients should be regularly monitored for se-rum electrolytes. Early detection and treatment can prevent the further complications like electrolyte imbalance and will be helpful during the management of hypothyroidism.

Conflict of Interest: Nil

Source of Funding : Nil

REFERENCES

1. Mariani LH, Berns JS. The renal manifestations of thy-roid disease. J Am Soc Nephrol. 2012;23: 22–6.
2. Iwasaki Y, Oiso Y, Yamauchi K, Takatsuki K, Kon-do K, Hasegawa H, et al. Osmoregulation of plasma vasopressin in myxedema. J Clin Endocrinol Metab. 1990;70:534–9.
3. Auwerx J, Bouillon R. Mineral and bone metabolism in thyroid disease. The Quarterly journal of medicine. 1986;60:737-52.
4. Capasso G, De Tommaso G, Pica A, Anastasio P,Capas-soj KR, De Santo NG. Effects of thyroid hormones on heart and kidney functions. Miner Electrolyte Metab. 1999;154:197-212.
5. Adrogue HJ, Madias NE. Hyponatremia. N Engl J Med. 2000; 342:1581-9.
6. Gross P, Benzing T, Hensen J, Moning H. Practical ap-proach to hyponatremia. Dtsch Med Wochenschr. 2011; 136:1728-32.
7. Schmitt R, Klussmann E, Kahl T, Ellison Dh, Bachmann S. Renal expression of sodium transporters and aquaporin-2 in hypothyroid rats. Am J Physiol Renal. Physiol. 2003; 284:F1097-104.
8. Arvind Bharti, Shailaza Shrestha, Rahul Rai and Mukesh Kumar Singh. Assessment of serum minerals and electrolytes in thyroid patients IJASR. 2015;1:259-263.
9. Mukesh G Gohel, Aashka M Shah, Akash M Shah, Je-mil S Makadia.A Study of Serum Calcium, Magnesium and Phosphorous Level in Hypothyroidism Patients. Int J Med Health Sci. 2014:3;308-312.
10. Laura HM, Jeffrey SB. The Renal Manifestations of Thyroid Disease. J Am SocNephrol. 2012;23: 22–26.
11. McCaffrey C, Quamme GA. Effects of thyroid status on renal calcium and magnesium handling. Can J Comp Med. 1984;48:51–57.
12. Shivallela MB, Poornima RT and Jayaprakash Murthy DS. Serum calcium and phosphorous levels in thyroid dysfunction. Indian journal of fundamental and applied life science. 2012;2:179-83.
13. Murgod R, Soans G. Changes in Electrolyte and Lipid profile in Hypothyroidism. International Journal of Life science and Pharma research. 2012;2:185-194.
14. Kumar V, Prasad R. Molecular basis of renal handling of calcium in response to thyroid hormone status of rat. Biochem Biophys Acta. 2002;1586:331-43.
15. Derubertis, F.R., Jr.; Michelis, M.F.; Bloom, M.E.; Mintz, D.H.; Field, J.B.; Davis, B.B. Impaired water excretion in myxedema. Am. J. Med. 1971,51,41–53.
16. Montenegro, J.; Gonzalez, O.; Saracho, R.; Aguirre, R.; Gonzalez, O.; Martinez, I. Changes in renal function in primary hypothyroidism. Am. J. Kidney Dis. 1996;27: 195–198.
17. Kavitha M M, Pujar S, Hiremath C S, Shankar Prasad, Mahanthesh Evaluation of serum electrolytes in hy-pothyroid patients. MedPulse – International Medical Journai. 2014;1:393-395.

18. Schwarz C, Alexander BL, Spiros A, Georg MF, Hein-zZ, Aristomenis E, et al. Thyroid function and serum electrolytes: does an association really exist? Swiss Medical Weekly. 2012;142:w13669.

19. Kaur J, Ahemad N, Gupta A. Changes in the electro-lyte profile of patient having hypothyroidism.Journal of Medical Science and Clinical Research. 2014;2:633-37.

20. Abedelmula M, Abdealla, Fadwa AS. Serum elec-trolytes and Bone mineral status in Sudanese patients with thyroid dysfunction. Neelain Medical journal. 2013;3:52-60.

DOI Number: 10.5958/2321-1032.2017.00011.0

Clinicopathological Study of Malignant Soft Tissue Neoplasms at a Tertiary Teaching Hospital

B Narasimha Rao

Associate Professor, Department of Pathology , Al-Azhar Medical College and Super Specialty Hospital, Thodupuzha, Kumaramangalam,Kerala, India

ABSTRACT

Introduction: Malignant mesenchymal neoplasms amount toless than 1% of the overall human burden of malignant tumors but they are life threatening and may pose a significant diagnostic and therapeutic challenge

Objectives: To study the frequency of malignant soft tissue neoplasms among all other neoplasms and all soft tissue neoplasms and to note any variation regarding age, sex and histopathological features

Method: This is descriptive study conducted in the department of pathology . In this study we collected clinical profile of the 150 patients and correlated with gross and histopathological features. For histopathological study samples were collected, processed to prepare paraffin embedded sections and stained by H and E stains.

Results: Malignant soft tissue neoplasms contributed 1.63 %of all types of neoplasms. Among all soft tissue neoplasms, malignant soft tissue neoplasms accounted only 10.38 %. Commonest encountered histological group was the fibrohistiocytic tumors. Malignant soft tissue neoplasms showed equal predilection for sex and the mean age was 50.8 years.

Conclusion: Malignant soft tissue neoplasms accounts very small percentage among all neoplastic lesions reported. The majority of soft tissue neoplasms were from fibrohistiocytic tumor group. The mean age of malignant soft tissue neo-plasms is 50.8 years with equal sex predilection.

Keywords: *Malignant soft tissue neoplasms, Histopathological study.*

INTRODUCTION

Malignant soft tissue neoplasms contribute less than 1% of the overall human burden of malignant tumors but they are life threatening and having significant diagnostic, therapeutic challenge since there are more than 50 histological sub-types of soft tissue neoplasms, which are often associated with unique clinical, morphological, prognostic and thera-peutic features.[1,2]

Correspondence author:
Dr. B Narasimha Rao
Associate Professor, Department of Pathology, Al-Azhar Medical College and Super Specialty Hospital, Thodupuzha, Kumaramangalam,Kerala, India
Email Id: doctorbnr@gmail.com

Malignant lesions were more commonly noted in elderly patients except embryonal rhabdomyosacroma that was ob-served in a younger age group patients.[3] Soft tissue sarcomas occur more commonly at the deep soft tissues of the extrem-ities and the retroperitoneum, but certain types of sarcomas have site-specific incidence rates.[4]

Histopathology is the most reliable and definitive guide for accurate diagnosis and predicting the clinical behavior of these neoplasms. Recently these neoplasms offer a better clinicopathological correlation due to availability of modernhistogenetic classification and standard nomenclature.[5]The pathogenesis of most soft tissue neoplasms is still unknown. The recognized possible causes may be various physical fac-tors,

chemical factors, ionizing radiations, and inherited or acquired immunologic, genetic disorders.[1]

The definitive and accurate diagnosis of soft tissue neo-plasms is dependent on detailed history, clinical exami-nation, advanced radiology support with subsequent core needle biopsy under organ imaging control. Portions of the biopsy should be submitted for histopathology, immunohis-tochemistry, genetics, electron microscopy, and any other ancillary techniques.[6]

Data regarding clinicopathological study of malignant soft tissue neoplasms in rural set up are lacking in literature. Here an attempt has been made to collect and evaluate same in institution and compare available data is exercised.

Objectives of the study were to study the frequency of malignant soft tissue neoplasms (STN) among all other neoplasms in population attending rural based hospital, to find out the relative frequency of malignant STN among all STN in hospital population over period of eight months and to note any variation regarding age, sex and detailed histopathological features of these neoplasms.

METHOD

This is descriptive study conducted in the department of pathology at over the period of Jan 2016 – September 2016. Cases of malignant soft tissue neoplasms diagnosed on the basis of history and clinical examination and subjected to biopsy or surgery and subsequent histopathological examination were included in this study.Patients who were treated conservatively or patients referred to other hospitals were excluded from this study. Soft tissue neoplasms of systemic organs (like leiomyoma of uterus) were excluded from this study.

In this study, we collected clinical profile of the patients according to the age, sex, anatomical location, clinical di-agnosis, relevant investigations, histopathological features and immunohistochemistry wherever necessary. Anatomical sites were categorised as - upper extremity (including shoulder, arm, forearm, wrist and hand), lower extremity (including buttock, thigh, leg and foot), trunk (including abdomen, back and chest wall), head and neck.

The specimens were received in 10% formalin as a fixative. After fixation gross findings like size, shape, colour and consistency were recorded. Then sections of size 1 X 1.5 cm and 4 mm thick were taken from representative areas. Very tiny specimens received in the form of biopsy were wrapped in the filter paper. In selected cases, photographs of the speci-men were taken.

Tissue processing was done to prepare paraffin embedded sections and there after stained by H and E stains. Slides were studied under light microscopy. Correlation of gross and histopathological examination will be carried out.

All soft tissue neoplasms were classified according to WHO classification of soft tissue tumors (2002)[2] and histologic classification of soft tissue tumors[1] (in cases of PNST related lesion group).

Here, an attempt was made to correlate clinical presentation and histopathological diagnosis.

Statistical analysis was done with basic statistical tests like mean, range, percentage, standard deviation.

RESULTS

The present study includes 150 cases of soft tissue neo-plasms. Total number of malignant soft tissue neoplasms was 16. Malignant soft tissue neoplasms contribute 1.63% of all types of neoplasms in the present study. The present study includes 16 cases of malignant soft tissue neoplasms out of 150 soft tissue neoplasms. Malignant soft tissue neoplasms contributed 10.38% amongst all soft tissue neoplasms.

The majority of malignant soft tissue neoplasms were from fibrohistiocytictumor group (5.2%) followed by neoplasms of uncertain differentiation (3.3%). (Table No. 1). In this study we reported 8 cases each of male and female. Malig-nant soft tissue neoplasms showed equal sex wise distribu-tion with M: F ratio of 1:1.

Malignant soft tissue neoplasms encountered in adults with peak distribution in fifth and sixth decades and mean age 50.8 years (SD: ± 13.87). The age range was 25 to 70 years. Fibrohistiocytictumors were more common in 41-60 years age group and tumors of uncertain differentiation were com-mon in 21-40 years age group.

The largest number of malignant soft tissue neoplasms were accounted in extremities [Upper

(37.5%) >Lower(31.25)], followed by trunk (25%) and head neck region (6.25%).

Fibroblastic tumors

A case of sclerosing epithelioid fibrosarcoma accounted in a 65 years old man over neck region. Grossly, tumor was 4 cm, nodular, hard in consistency grey white on cut surface. Microscopy revealed tumor tissue arranged in cords, strands and nests. Tumor cells were round epithelioid with prom-inent nucleoli in densely sclerotic collagenous background with areas of necrosis and haemorrhage.

Single case of fibromyxoid sarcoma accounted in a 35 years old female over thigh region. Microscopy revealed tumor tissue arranged in fascicular pattern in alternating hypercellular fibrous and hypocellularmyxoid area.

Malignant fibrohistiocytic neoplasms

Malignant fibrohistiocytic neoplasms [8 cases (50%)] were the most common malignant soft tissue neoplasms. They found in adult age group from 35-70 years, peak in sixth dec-ade of life with equal predilection for sex with M: F ratio 1:1. They showed striking predilection for extremities.

Five cases (31.2%) of undifferentiated pleomorphic sarcoma (UPS) were found in older age group ranging from 35-70 years with predilection for lower extremity. Grossly, tumor varied from 7–10 cm, irregular and grey white to black on cut surface with areas of haemorrhage and necrosis. Microscopy revealed tumor tissue composed of plump bizarre spindle cells and giant cells arranged predominantly in storiform and fascicular pattern. Individual tumor cells are highly pleomorphic with round to oval nuclei and prominent nucleoli with abundant eosinophilic cytoplasm and high mitotic activity.

Uncertain differentiation tumors

Neoplasms of uncertain differentiation [5 cases (31.25%)] were second most common malignant soft tissue neoplasms observed. They were found in age group of range from 25-65 years with slight female predominance and predilection for extremities.

Single case of extra skeletal myxoid chondrosarcoma was observed in 40 year female over right buttock. Microscopy revealed tumor tissue composed of round uniform cells ar-ranged in lobules and cords separated by myxoid material.

Only one case of alveolar soft part sarcoma was encountered in 60 year female over trunk region. Single case of extraskel-etal Ewing's sarcoma was observed in 40 year female at right scapular region. Microscopy revealed tumor tissue com-posed of uniform small round cells arranged in lobules sep-arated by thick fibrous septa. At places cells were arranged around central fibrillary material forming rosettes.

Paraganglioma neoplasm

Single case of malignant Paraganglioma was accounted in 45 year old male at retroperitonium, which later on confirmed on immunohistochemistry. Grossly, tumor was fungating, smooth in consistency brown on cut surface. Microscopi-callytumor cells were arranged in trabecular, zellbalen and nest pattern separated by vascular septa. Areas of necrosis and vascular invasion were evident.

DISCUSSION

In the present study, soft tissue neoplasms comprised 154 of all types of neoplasms received over a period of two and half years in the department of pathology. Out of which, malignant soft tissue neoplasms contributed 1.63 % of allneoplasms.

A total of 154 soft tissue neoplasms were studied in the present study. Benign soft tissue neoplasms contributed [138 cases (89.6%)] and malignant tumours contributed [16 cases (10.38%)].

Malignant soft tissue neoplasms accounted small percent-age amongst all soft tissue neoplasms, which is comparable with all the studies. The percentage of malignant neoplasms (10.4%) was relatively more than the study of Myhre-Jensen O 1981[9] (5.4%) and Agravat AH et al 2010[3] (6.5%) which can be explained by the inherent bias in a referral population. Relatively increased percentage of malignant neoplasms in the study of Kransdorf 1995[7,8] (39.8%) from AFIP records and Bashar AH et al 2010[10] (24.8%) may be due to the case material referred to a highly specialized centre. (Table No. 3) In this study, the commonest malignant soft tissue neoplasm was undifferentiated pleomorphic sarcoma (31.2%) followed by DFSP (18.8%), Fibrosarcoma (12.5%) and SS (12.5%). The

percentage of undifferentiated pleomorphic sarcoma (31.2%) was comparable with study of Kransdorf MJ 1995(24.1%). The percentage of fibrosarcoma (12.5%) was comparable with Agravat AH et al 2010[3] (16.7%). Malignant fibrohistiocytictumors (50%) were most common malignant soft tissue neoplasms. In fibrosarcoma group, Sclerosing epitheliod fibrosarcoma (SEFS) and fibromyxoid sarcoma were noticed as variants of fibrosarcoma.

Fibrosarcoma was categorised under malignant fibroblastic group, undifferentiated pleomorphic sarcoma and dermatofibrosarcoma protuberans were categorised under malignant fibrohistiocytic group. Synovial sarcoma, extraskeletalmyxoid chondrosarcoma, alveolar soft part sarcoma, extraskeletal Ewing's sarcoma were categorised under malignant uncertain differentiation tumor group whereas malignant paraganglioma included under separate group.

In present study, malignant neoplasms presented with a male to female ratio of 1:1 while in the study of Myhre-Jensen O 1981[9], it was 2: 1. This difference may be due to inherent bias in a referral population.

The mean age in malignant soft tissue neoplasm was 50.8 years comparable with studies of Myhre-Jensen O 1981[9] (49.5) and more than Kransdorf MJ 1995[8] (42) and Bashar AH et al 2010[10] (39.1) may be due to inherent bias in a referral population. Malignant soft tissue neoplasms encountered in adults with peak distribution in fifth and sixth decade. The age range was 25 years to 70 years.

In the present study, malignant neoplasms showed predilec-tion for the upper extremity (37.5%) followed by lower extremity, trunk and head and neck. Kransdorf MJ 1995[8] found predilection for lower extremity (37.1%) fallowed by upper extremity (18%).

Table 1. Showing the group of neoplasms

Sr. No.	Group of neoplasms	Malignant soft tissue neoplasms	Frequency %
1.	Adipocytic	0	0
2.	Fibroblastic	2	1.4
3.	Fibrohistiocytic	8	5.2
4.	Smooth and skeletal muscle	0	0
5.	Vascular	0	0
6.	Chondro-osseous	0	0
7.	Uncertain differentiation	5	3.3
8.	PNST and related lesion	0	0
9.	Paraganglioma	1	0.6
	Total	**16**	**10.4**

CONCLUSION

Malignant soft tissue neoplasms accounts very small percentage among all neoplastic lesions reported. Benign soft tissue neoplasms outnumber the malignant neoplasm by a marginal difference. The majority of malignant soft tissue neoplasms were from fibrohistiocytictumor group followed by neoplasms of uncertain differentiation. The commonest accounted tumor is undifferentiated pleomorphic sarcoma. The mean age of malignant soft tissue neoplasms is 50.8 years with equal sex predilection. Commonest involved site is upper extremity. Haematoxylin and Eosin (H and E) stained sections remain the best method for establishing the primary diagnosis. Immunohistochemistry is very helpful in accurate categorization of soft tissue neoplasms when there is dilemma in histopathological diagnosis.

Conflict of Interest: Nil

Source of Funding : Nil

Ethical Clearance: Approval of Institutional ethics committee

REFERENCES

1. Weiss SW, Goldblum JR, editors. Enzinger and Weiss's Soft Tissue Tumors. 5th ed. Philadelphia: Mosby Else-vier; 2008.
2. Fletcher CDM, Unni KK, Mertens F, editors. World Health Organization Classification of Tumours - Pathol-ogy and Genetics of Tumours of Soft Tissue and Bone. Lyon, France: IARC Press; 2002.
3. Agravat AH, Dhruva GA, Parmar SA. Histopathology study of human's soft tissue tumours and tumour like lesions. J Cell Tissue Research. 2010;10:2287-92.
4. Weiss LM. Soft tissues. In: Waidner N, Cote RJ, Suster S, Weiss LM, editors. Modern surgical pathology. 2nd ed. Philadelphia: Saunders Elsevier; 2009
5. Coindre JM. Grading of Soft Tissue Sarcoma: review and update. Arch Pathol Lab Med. 2006;130:1448-53.
6. Allen PW. The diagnosis, classification and grading ofsoft tissue tumors. J Orthop Sci.1996;1: 148-56.
7. Kransdorf MJ. Benign soft tissue tumors in a large re-ferral population: distribution of specific diagnosis by age, sex and location. AJR. 1995;164: 395-402.
8. Kransdorf MJ. Malignant soft tissue tumors in a large referral population: distribution of diagnosis by age, sex and location. AJR.1995;164:129-34.
9. Myhre-Jensen O. A consecutive 7 year series of 1331 benign soft tissue tumours. Clinicopathological data. Comparison with sarcomas. ActaOrthop Scand. 1981; 52:287-93.
10. Bashar AH, Abdulkarem YS, Intisar SH. Soft tissue to-mors – histopathological study of 93 cases. Ann Coll Med Mosul. 2010;36:92-8.

DOI Number: 10.5958/2321-1032.2017.00012.2

Analysis of Gallbladder Diseases Diagnosed at a Tertiary Care Hospital: A Retrospective Study

B Narasimha Rao

Associate Professor, Department of Pathology, Al-Azhar Medical College and Super Specialty Hospital, Thodupuzha, Kumaramangalam, Kerala, India

ABSTRACT

Background: Gallbladder is one of the most commonly encountered specimen in a pathology laboratory. A diverse spectrum of diseases affect the biliary system, often presenting with similar clinical signs and symptoms.

Objective: To evaluate the profile of gallbladder diseases and also to determine potential correlations between histopathologic features noted.

Method: This study reviewed all cholecystectomies processed in Department of Pathology of Al Azar super specialty Hospital between June 2014 and July 2016. Gross and histopathologic features of the specimens were reevaluated.

Results: Among 250 patients; 69.9% were women and 30.1% were men. This study found out that fourteen primary gallbladder carcinomas (5.6%) with adenocarcinomas being the most frequent type (78.57%). The rate of cholelithiasis was found as 89.9%. The most common type of gallstones was mixed cholesterol type gallstones with 67.5% followed by black pigment and brown pigment types as 23.83% and 5.89%, respectively. The association of metaplasia with dysplasia and also gallstones were statistically significant ($p<0.001$, $p<0.005$). The rate of the gallbladder polyps was 2.6% with the cholesterol polyps being the most common type (56.4%).

Conclusion: Gallbladder diseases often present with similar clinical signs and symptoms and a surgical pathologist should be alert especially of precancerous lesions. With our results, it is concluded that elderly women with longstanding gallstone disease should undergo elective surgery even when no symptoms are present.

Keywords: *Cholelithiasis, Gallbladder diseases, Precancerous conditions, Gallbladder neoplasms.*

INTRODUCTION

The gallbladder (GB) is one of the most commonly encountered specimens in a pathology laboratory. A diverse spectrum of diseases affect the biliary system, often presenting with similar clinical signs and symptoms. Although cancer arising in this organ is very rare, a surgical pathologist should be alert especially of precancerous lesions while processing and evaluating the specimen. In this study, we reviewed all cholecystectomies that were processed at the pathology department of Al-Azhar Medical College and Super Specialty Hospital between June 2014 and July 2016. The present study aimed to define the profile of GB diseases, and to determine possible correlations between histopathologic features.

Correspondence author :
Dr. B Narasimha Rao,
Associate Professor, Department of Pathology, Al-Azhar Medical College and Super Specialty Hospital, Thodupuzha, Kumaramangalam,Kerala, India, Email Id: doctorbnr@gmail.com

METHOD

Two hundred and fifty consecutive cholecystectomies

conducted at Al-Azhar Medical College and Super Specialty Hospital between June 2014 and July 2016 were included in this study. All patients provided informed consent. This study was a retrospective study which evaluated the patients in two groups as those with or without cancer. All macroscopic descriptions were reviewed and the slides reexamined. The paraffin blocks were recut when needed. The specimens were known to have been processed under standard protocols. At least 2 standard sections were examined for each case. The following gross and histological features were detected by previously determined criteria1-6: Gross type of gallstones, thickness of the GB wall and other gross descriptions based on the patient's final pathology reports, the type of inflammation, cholesterolosis, polypoid lesions, metaplastic (pyloric and intestinal) and dysplastic changes. Another 14 primary GB carcinomas out of the 250 materials are reevaluated separately. The SPSS version 15 program was used to perform all statistical analysis.

RESULTS

Overall, 250 patients were women (69.9%) whereas 451 (30.1%) were men. The mean age of the patients was 51.94±14.22 for women with an age range of 16-97 and 55.40±14.07 for men with an age range of 13-92. The majority of these GBs were removed for symptoms related to cholelithiasis and chronic cholecystitis.

Fourteen patients had primary gallbladder cancer (0.93%) whereas 1486 were diagnosed as having benign gallbladder diseases. The rate of cholelithiasis, inflammation, cholesterolosis, polypoid lesions, and some precancerous lesions such as adenoma, antral and intestinal type metaplasia and dysplasia in 250 patients.

The rate of cholelithiasis in our series was 89.9%. Sixty two percent of these patients were females and twenty eight percent were males. We were able to fully identify the type of the gallstones in 97 patients including the 7 cases of cancer with gallstones whereas the gross descriptions were inadequate to define the stone type in all patients. We classified the gallstones as pure cholesterol, black and brown pigment stones and mixed cholesterol stones according to previously defined criteria1. The most common type of gallstone was the mixed cholesterol type (67.50%) (Figure 3) followed by the black pigment type (23.83%); brown pigment type (5.89%) and pure cholesterol type (2.76%). We observed cholesterolosis in 13.45% of the specimens with significant female preponderance (82%). The great majority of the stones (79 %) were of the mixed cholesterol type as seen in seventy eight stone-type-defined cholesterolosis cases.

This study observed metaplasia of either antral or intestinal type in 171 among 250 nonneoplastic materials (11.50%) and 164 of these cases also had gallstones (95.9%). The association of metaplasia with gallstones was significant ($p<0.005$). It was also significant that 29 of 30 gallbladders with intestinal metaplasia also had gallstones (96.66%). On the other hand, we found dysplasia in 24 cases (24/1500-1.60%). Metaplasia was also observed in 18 of these dysplastic GBs either adjacent to or within the dysplastic epithelium. We found a significant association of metaplasia with dysplasia ($p<0.001$). We had 14 primary GB carcinomas in our series (0.93%). The most common type was adenocarcinoma (11 cases, 78.57%) (Figure 4) followed by one adenosquamous carcinoma (7.14%), one squamous cell carcinoma (7.14%) and one undifferentiated carcinoma (7.14%). Among the cancerous cases, metaplastic and dysplastic changes adjacent to the malignant tissue were observed in only three (21.42%) and five (35.78%) cases, respectively.

DISCUSSION

Gallstones are simply classified on the basis of their gross features as cholesterol stones, pigment stones and as mixed ones. Cholesterol stones are single, spheroidal and coarsely nodular and they have a translucent bluish white color[5]. Pigment gallstones contain large amounts of pigment material and little cholesterol. They can be divided into black and brown stones according to their colors: Brown stones are brownish yellow, soft and show alternate dark and light layers in cross-section whereas black stones are black in color, hard in consistency and show an amorphous appearance on cross section[7]. Cholesterol and black pigment type gallstones form in the GB, whereas brown pigment stones form mainly in the intra or extrahepatic bile ducts[8]. It has been generally accepted that women are afflicted more often by GB stone disease than men. The female preponderance may be attributable to multiparity[9] or ingestion of certain drugs such as estrogen and oral contraceptives[8,10]. Other suggested risk factors are obesity, a diet rich in cholesterol and saturated fats, intake of hypolipidemic agents, low physical activity[9], increased body mass index, positive family history, and increased age[11].

Pathogenetic mechanisms in the formation of macroscopic gallstone starts with GB hypomotility that results in impaired GB emptying and then leads to bile stasis and subsequent cholesterol precipitation and crystal growth[10].

Black stones in the GB consist predominantly of insoluble unconjugated bilirubin polymers and mucin glycoproteins. The main cause of their formation is excessive bilirubin secretion into the bile based upon the increased production of bilirubin, i.e. hemolytic anemia, and previous or current liver damage[1].

The rate of black pigment stones among gallstone patients from Italy and Korea is reported as 5.3% and 25.2%, respectively [1,7]. In our study, the proportion of black pigment stones among total gallstone cases was 12.6 %. A sharp distinction of black pigment stones from other stone types is crucial for therapeutic purposes including the determination of the underlying disease such as a hematological or liver disorder.

Brown pigment type stones are formed with the stasisinfection mechanism1,8,10. Certain infectious agents such as Clonorchis sinensis, Opistochus vivarini or Ascaris [8,10] as well as conditions such as old age, intestinal motor disorders or gastric pathology may be involved in their formation. They used to be the predominant type of gallstones in Asia, but are reported to have a decreasing prevalence. This may perhaps be related to multiple factors including the eradication of parasites and westernization of the diet.

Cetta et al[1] found a brown pigment stone frequency of 5.2% in their series from Italy. They found that these stones were usually located in the common bile duct and associated with bile infection. Another study on Korean patients revealed that the rate of brown pigment stones in GB and intrahepatic bile duct are 12.1% and 61.4%, respectively. The frequency of brown pigment type stone was only 5.9% in our study. The design of our study was focused on gallbladder diseases, and gallstones of any other parts of the biliary tract were therefore not evaluated in our study. However, This study concluded that such parasitic infestations are rare in our region and brown pigment stones are not as commonly encountered as cholesteroltype stones.

Gallbladder polyps (GBP) are simply described as elevated lesions[2] and represent many benign conditions such as cholesterol polyps, adenomyomatous hyperplasia, and adenoma as well as GB carcinoma[11]. The detection rate for these lesions has increased with the widespread use of USG in recent years, but it is difficult to define the biologic nature of them radiologically [12]. It is suggested that sessile polyps, those are echopenic at USG, with a diameter of greater than 10 mm [2,13] and associated with gallstones [12] are highly suspicious for malignancy and should be removed, whereas asymptomatic patients with polyps smaller than 10 mm are subject to follow-up. Cholesterol polyps are the most frequent [11,14,15] or the second most frequent type of all GBPs.

This research found 39 polyps (2.6%) in the series with the most common type being cholesterol polyps (56.4%) followed by adenomyoma (20.5%), hyperplastic-type (10.2%), and inflammatory-type (7.69%) polyps. And also found that 2 of our cancer cases were also polypoid according to their final pathology report.

Cholesterol polyps are suggested to represent the polypoid variation of cholesterolosis[16]. The latter are characterized by mucosal villous hyperplasia with excessive accumulation of cholesterol esters within epithelial macrophages[2]. The frequency of cholesterolosis was found 13.33% in our study. We observed cholesterolosis in all the patients with cholesterol polyps. This might be due to their having a very thin and fragile stalk resulting in its detachment and floating along the bile while evaluating the specimen grossly.

The epithelial lesions involved in gallbladder carcinogenesis are dysplasia and adenoma, each representing a different carcinogenetic model. Malignant transformation is suggested to develop either through the dysplasiacarcinoma sequence [17,18] or the adenoma-carcinoma sequence [19].

Adenomas are uncommon polypoid lesions simply classified as tubular, papillary or tubulopapillary. They usually arise in the background of normal GB mucosa [20]. Based on the morphometrical analysis of both GB adenoma and carcinoma, these lesions were suggested to have malignant potential. Kozuka et al [21] suggested that most carcinomas in the GB arise from preexisting adenomas.

Present study determined 2 adenomas (2/1500-0.13%) . Both were of the tubular adenoma type and associated with gallstones (mixed cholesterol and black

pigment type respectively) as well. We observed severe dysplasia which is reported to frequently exist within these lesions in one of them. Neither was associated with malignancy.

The second and more plausible carcinogenetic model is the dysplasia-carcinoma sequence. In this model of carcinogenesis, mucosal damage caused by a stone and subsequent chronic inflammation is thought to be important in the histogenesis of intestinal metaplasia and dysplasia30 and GB carcinoma as well [22,23] . Although the exact relationship between intestinal differentiation and carcinoma is unknown, it is well known that metaplastic epithelium is more susceptible to malignant transformation than the normal one.

We observed either intestinal or gastric type metaplastic cells in 174 out of 1500 cholecystectomies. Among these, 166/174 (95.40%) were associated with gallstones whereas 8 of them were not. The association of metaplasia with chronic cholecystitis and with gallstones was statistically significant ($p<0.05$; $p<0,05$). We think that the prolonged mucosal damage by stone(s) causes desquamation and regeneration of mucosal epithelium with subsequent metaplastic changes and especially intestinal metaplasia. On the other hand, dysplasia often develops in metaplastic epithelium [24].

The incidence of dysplasia reported in the literature ranges from 0.4 to 33.8% and the difference may be explained by a variety of reasons including extent of sampling, varying definitions of precursor lesions, geographic and racial differences in the incidence of GB carcinoma and its precursors37. We found dysplasia in 24 cases (24/1500-1.60%) in our study. Metaplasia was also observed in 18 out of 24 dysplastic GBs either adjacent to or within the dysplastic epithelium. The association of metaplasia with dysplasia was significant ($p<0,001$) and was in accordance with the previously reported data. This supports the hypothesis that metaplasia could evolve to dysplasia. However, we could not demonstrate the suggested sequence of intestinal metaplasia-dysplasia-carcinoma probably due to the small size of our cancer series.

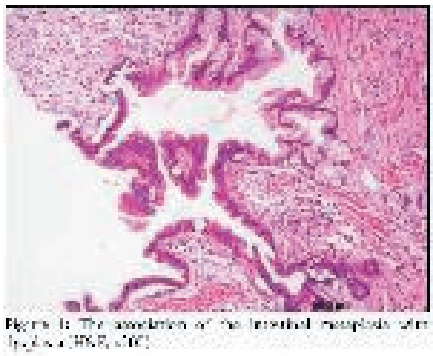

Figure 1: The association of the intestinal metaplasia with dysplasia (H&E; x200).

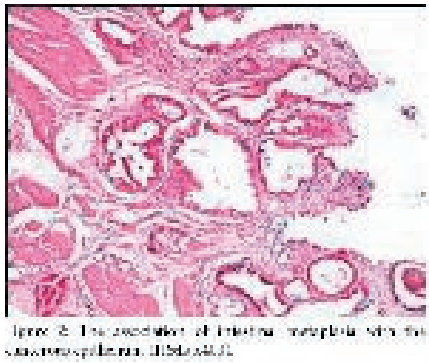

Figure 2: The association of intestinal metaplasia with the cancerous epithelium (H&E; x200).

Figure 3: Mixed cholesterol type gallstones were the most common type of gallstones in our series.

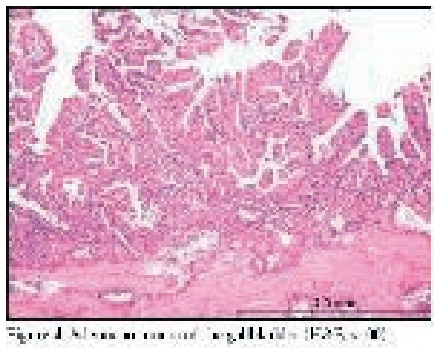

Figure 4: Adenocarcinoma of the gallbladder (H&E; x100).

CONCLUSION

Cholesterol polyps are the most frequent type of

gallbladder polypoid lesions. Mixed cholesterol type gallstones are the most frequent type of gallstones in this region where people consume a large amount of cholesterol and saturated fat. Having demonstrated the association of intestinal metaplasia and GB stones and also of the chronic inflammatory process in the GB, its concludes that women especially older than 60 years with longstanding gallstone disease should undergo elective surgery even when no symptoms are present.

Conflict of Interest: Nil

Source of Funding : Nil

Ethical Clearance: Approval of Institutional ethics committee

REFERENCES

1. Cetta F: The role of bacteria in pigment stone disease. Ann Surg 1991, 213:315-326
2. Owen CC, Bilhartz LE: Gallbladder polyps, cholesterolosis, adenomyomatosis, and acute acalculous cholecystitis. Semin Gastrointest Dis 2003, 14:178-188
3. Roa I, de Aretxabala X, Morgan R, Molian R, Araya JC, Roa J, Ibacahe G: Clinicopathological features of gallbladder polyps and adenomas. Rev Med Chil 2004, 132:673-679
4) Mukada T, Andoh N, Matsushiro T: Precancerous lesions of the gallbladder mucosa. Tohoku J Exp Med 1985, 145:387-394.
5) Rosai J: Gallbladder and extrahepatic bile ducts. In Rosai J (Ed): Ackerman's Surgical Pathology. 9th ed., Edinburg, Mosby, 2004, 1035-1060
6) Albores-Saavedra J, Scoazec J, Wittekind C: Carcinoma of the gall bladder and extrahepatic bile ducts. In: Hamilton SR, Aaltonen LA (Eds): WHO classification of tumours. Pathology and genetics of tumours of the digestive system. IAR C Press: Lyon, 2000, 206- 214
7) Kim MH, Lim BC, Myung SJ, Lee SK, Ohrr HC, Kim YT, Roe IH, Kim JH, Chung JB, Kim CD, Shim CS, Yun YB, Min YI, Yang US, Kang JK: Epidemiological study on Korean gallstone disease: a nationwide cooperative study. Dig Dis Sci 1999, 44:1674-1683
8) Shaffer EA: Gallstone disease: Epidemiology of gallbladder stone disease. Best Prac Res Clin Gastroenterol 2006, 20:981-996
9) Devesa F, Ferrando J, Caldentey M, Borghol A, Moreno MJ, Nolasco A, Moncho J, Berenguer J: Cholelithiasic disease and associated factors in a Spanish population. Dig Dis Sci 2001, 46:1424-1436
10) Tazuma S, Kajiyama G: Carcinogenesis of malignant lesions of the gallbladder. The impact of chronic inflammation and gallstones. Langenbecks Arch Surg 2001, 386:224-229.
11. Terzi C, Sokmen S, Seckin S, Albayrak L, Ugurlu M: Polypoid lesions of the gallbladder: report of 100 cases with special reference to operative indications. Surgery 2000, 127:622-627
12. Kratzer W, Kächele V, Mason RA, Hill V, Hay B, Haug C, Adler G, Beckh K, Muche R: Gallstone prevalence in Germany: the Ulm gallbladder stone study. Dig Dis Sci 1998, 43:1285-1291
13. Terzi C, Sokmen S, Seckin S, Albayrak L, Ugurlu M: Polypoid lesions of the gallbladder: report of 100 cases with special reference to operative indications. Surgery 2000, 127:622-627
14. Jørgensen T, Jensen KH: Polyps in the gallbladder. A prevalence study. Scand J Gastroenterol 1990, 25:281-286.
15. Huang CS, Lien HH, Jeng JY, Huang SH: Role of laparoscopic cholecystectomy in the management of polypoid lesions of the gallbladder. Sur Laparosc Endosc Percutan Tech 2001, 11: 242-247
15. Escalona A, León F, Bellolio F, Pimentel F, Guajardo M, Gennero R, Cruz JP, Viviani P, Ibáñez L: Gallbladder polyps: correlation between ultrasonographic and histopathological findings. Rev Med Chil 2006, 134:1237-1242.
16. Roa I, de Aretxabala X, Araya JC, Roa J: Preneoplastic lesions in gallbladder cancer. J Surg Oncol 2006, 93:615-623.
17. Stancu M, Caruntu ID, Giusca S, Dobrescu G: Hyperplasia, metaplasia, dysplasia and neoplasia lesions in chronic cholecystitis - a morphologic study. Rom J Morphol Embryol 2007, 48: 335-342.
18. Nakajo S, Yamamoto M, Tahara E: Morphometrical analysis of gall-bladder adenoma and adenocarcinoma with reference to

histogenesis and adenoma-carcinoma sequence. Virchows Archiv A Pathol Anat Histopathol 1990, 417:49-56 .

19 . Hansel DE, Maitra A, Argani P: Pathology of the gallbladder: a concise review. Cur Diagn Pathol 2004, 10:304–317.

20. Yanagisawa N, Mikami T, Saegusa M, Okayasu I: More frequent beta-catenin exon-3 mutations in gallbladder adenomas than in carcinomas indicate different lineages. Cancer Res 2001, 61: 19-22 .

21. Kozuka S, Tsubone N, Yasui A, Hachisuka K: Relation of adenoma to carcinoma in the gallbladder. Cancer 1982, 50: 2226- 2234

22. Yanagisawa N, Mikami T, Saegusa M, Okayasu I: More frequent beta-catenin exon-3 mutations in gallbladder adenomas than in carcinomas indicate different lineages. Cancer Res 2001, 61: 19-22 .

23. Martinez-Guzman G, Rosa-Bayon J: Neoplasms and dysplasias of the gallbladder and their relationship with lithiasis. A case control clinicopathological study. Rev Gastroenterol Mex 1998, 63:82-88 .

24. Kanoh K, Shimura T, Tsutsumi S, Suzuki H, Kashiwabara K, Nakajima T, Kuwano H: Significance of contracted cholecystitis lesions as high risk for gallbladder carcinogenesis. Cancer Lett 2001, 169:7-14

DOI Number: 10.5958/2321-1032.2017.00013.4

Effect of Dietary Management on Albuminuria and Renal Markers in Cases of Diabetic Nephropathy

Jyoti Prakash[1], Jiut Ram Keshari[2], Manish Kumar[3], Bhim Ram[4], Guddi Singh[5], Ravi Vishnu Prasad[6] Rekha Kumari[2]

[1]Assistant Professor, Dept. of Medicine, DMCH, Darbhanga, [2]Associate Professor, Dept. of Biochemistry, [3]Assistant Professor, Dept. of Pharmacology, IGIMS, Patna, [4]Consultant Medical officer, Metro City Hospital & Research Centre, Patna, [5]Senior Resident, Dept. of Pathology, [6]Assistant Professor, Dept. of Cardiology, IGIMS, Patna

ABSTRACT

Introduction: Diabetes mellitus (DM) involves cardiovascular, renal, neurological, ocular, gastrointestinal tract, genitourinary, dermatological systems. Diabetic Nephropathy is a persistent proteinuria of >500mg/day with concomitant retinopathy & hypertension. This study was done to assess the effect of dietary protein restriction as a non pharmacological approach on albuminuria and renal markers in patients of diabetic Nephropathy.

Material and method: 200 patients were randomly selected and grouped into A, B, C, and D containing 50 patients in each group. Group A and B had hypertensive patients with low and high protein diet given respectively for 24 weeks. Group C and D had normotensive patients with low and high protein diet given respectively for 24 weeks. 24 hours urinary albumin (mg/day) excretion rate, Blood urea, Serum creatinine, Urine creatinine, Creatinine clearance were estimated initially and at 24 weeks.

Results: In Group A mean albuminuria has decreased from 1702±360.41 (at baseline) to 1169±276.86 (at 24th week) with p value < 0.0001 that decrease was extremely significant. In Group B mean albuminuria has increased from 1706±251.44 (at baseline) to 2023±301.50 (at 24th week) with p value < 0.0001 that increase was extremely significant. In Group C, mean albuminuria has decreased from 1279.80±178.62 (at baseline) to 826.60±186.39 (at 24th week) with p value < 0.0001 that decrease was extremely significant. In Group D mean albuminuria has increased from 1288.6±101.01 (at baseline) to 1484±151.6 (at 24th week) with p value < 0.0001 that increase was extremely significant.

Conclusion: Dietary protein restriction has overall beneficial effect on patients of diabetic nephropathy. The effect is independent of blood glucose and blood pressure changes and is due to improved glomerular permeability and selectivity probably.

Keywords*: Diabetic nephropathy, Low protein diet, High protein diet, Albuminuria, Renal markers*

INTRODUCTION

Diabetes mellitus (DM) is a clinical syndrome characterized by hyperglycemia due to absolute or relative deficiency of insulin, with or without glycosuria resulting from diversity of aetiologies, environmental and genetic acting jointly. It is the commonest endocrinological disorder encountered clinically, which involves kidney also as a part of its chronic complication. The underlying cause of DM is the defective production or action of insulin, a hormone that controls the metabolism of carbohydrate, fat and protein. Chronic complication of DM includes cardiovascular, renal, neurological, ocular, gastrointestinal tract, genitourinary,

Corresponding author:
Dr. Manish Kumar,
Assistant Professor, Dept. of Pharmacology, IGIMS, Patna-800014, Mob: 9304093698,
Email Id: manu072@gmail.com

dermatological systems etc.[1]

Ancient Ayurvedic physicians, Charak and Sushruta (600-400 B.C.) recognized the disease and named as MADHUMEHA. The term diabetes was coined by Areteaus in the first century A.D.[2-4]

Diabetes Nephropathy is the leading cause of ESRD worldwide. It is clinically defined as:-

(a) Progressive in ↑ albuminuria.

(b) Progressive ↑ in BP.

(c) Eventual ↓ in GFR leading to ESRD.

(d) Presence of Diabetes retinopathy.

(e) Accompanied by Progressive increase in cardiovascular risk.

Staging of Diabetes Nephropathy

(1) Increased blood flow and glomerular hyperfiltration.

(2) Early glomerular lesions- thickening of glomerular basement membrane.

(3) Incipient diabetic Nephropathy – the stage of micro albuminia.

(4) Overt diabetic nephropathy

(5) End stage renal disease in diabetes.

Kimmelsteil and Wilson first described diabetic intercapillary glomeruloslerosis in 1936 A.D. most common lesion is diffuse glomeruloslerosis but nodular glomeruloslerosis (Kimmelsteil Wilson nodule) is the pathognomonic of diabetic nephropathy.[5] Diabetic nephropathy manifests as a varying combination of proteinuria, hypoproteinemia, hypertension, oedema & azotemia. The principal clinical manifestation is proteinuiria, which is followed by a decline in renal function after a variable period of time. T1DM carries 30-40% chance of diabetic Nephropathy & T2DM a chance of 15-20% after 20 years.

The first & principal clinical sign of diabetic nephropathy is microalbumiuria defined as albumin excretion/24 hour in the range of 30-300mg or overnight urinary albumin excretion rate 20-200µg/min in at least 2 out of 3 collections over a time period not exceeding 3 months. Other cause of albumin excretion in urine is strenuous physical exercise, Pregnancy, CCF, HTN, UTI, fluid overload, oral Protein challenge etc.

Once proteinuria is established the renal function starts to decline steadily if appropriate treatment is not started immediately. The rate of progression of disease can be reduced by restriction of dietary protein (Low Protein diet), low carbohydrate diet, tight glycemic control and prompt treatment of hypertension & hyperlipidemia.

Dietary protein restriction reduces GFR & retards the progression of Nephropathy.[6] Various studies have shown that protein restriction up to 0.6 g/kg/d retards the progression of Nephropathy. The general consensus is to prescribe a protein intake of 0.8 g/kg/day (~10% of daily calories) in patients with overt nephropathy. However it has been suggested that once GFR begin to fall further restriction to 0.6g/kg/day may prove useful in retarding the progression of nephropathy to avoid malnutrition. The rate of progression of declining renal function can be reduced by dietary protein restriction, prompt glycemic control & management of hypertension.

The treatment of hypertension in patients of diabetic nephropathy is particularly very challenging as many of agents used to lower blood pressure can adversely affect glucose metabolism.

Thus, in short, we can say that dietary protein restriction is quite effective non-pharmacological intervention to retard diabetic nephropathy. This is free from any risk and reduces proteinuria, reduces oedema by improving serum protein level and thus slowing the declining renal functions, when combined with prompt treatment of hyperglycaemic and hypertension.

MATERIAL AND METHOD

The study was carried out on patients of diabetic nephropathy attending diabetic clinic attached to PMCH, general MOPD and also in medical indoor wards, at Patna Medical College & Hospital, Patna.

Sample Size: 200 patients of T1DM of age <40 years

Study Period: - Feb. 2012- Feb. 2013

Selection Criteria:

(a) Inclusion Criteria

(i) Patients of T1DM willing to undergo study.

(ii) Sex – either sex

(iii) Age <40 years

(iv) Presence of retinopathy

(v) Persistent albuminuria

(b) Exclusion Criteria

(i) Patients of T2DM

(ii) UTI

(iii) Congestive cardiac failure

(iv) Malignant hypertension

(v) ESRD

Plan or work: Randomly selected patients were divided into four groups (200)

(i) Group A- Hypertensive patients on low protein diet for 24 weeks(n-50)

(ii) Group B- Hypertensive patients on high protein diet 24 weeks(n-50)

(iii) Group C- Normotensive patients on low protein diet 24 weeks(n-50)

(iv) Group D- Normotensive patients on high protein diet 24 weeks(n-50)

Initially detailed clinical history of randomly selected patients was taken like age of onset, duration of illness, family history of diabetes, thorough physical examination. Following initial investigations were done for this study.

- Blood pressure (BP)
- Complete Blood Count (CBC)
- Blood sugar: Fasting (F) and Post-Prandial (PP)
- Hba_1c (Glycosylated Haemoglobin)
- Lipid profile
- Routine examination (R/E) urine and Urine Culture
- 24 hour urinary albumin excretion rate or Overnight urinary albumin excretion rate or Spot urinary albumin excretion rate (ACR)
- Blood Urea
- Serum creatinine
- Urine creatinine
- Creatinine clearance
- USG – KUB (Kidney Ureter Bladder)
- Echocardiogram (ECG)

Follow up – (After 6 months)-following investigations were done

- BP
- CBC
- Blood sugar: F and PP
- R/E urine and Urine culture
- 24 hours urinary albumin (mg/day) excretion rate.
- Blood Urea
- Serum creatinine
- Urine creatinine
- Creatinine clearance

Statistical analysis: Student's t test was used for the statistical analysis by using Graphpad software.

RESULTS

Table-1-Age, Sex, Duration of diabetes and Retinopathy

Groups in present study	Mean age (in year)	Sex		Mean duration of diabetes (in years)	Retinopathy	
		Male	Female		Simplex	Proliferative
Group-A (n-50)	30	35	15	20	28	22
Group-B (n-50)	30	32	18	20	22	28
Group-C (n-50)	28	24	26	18	30	20
Group-D (n-50)	28	22	28	18	29	21

Table 2- Albuminuria (mg/day)

		At the start (Baseline)	After 24 weeks	p-value
Group-A (n-50)	Mean±SD	1702±360.41	1169±276.86	< 0.0001
	SEM	50.97	39.15	
Group-B (n-50)	Mean±SD	1706±251.44	2023±301.50	< 0.0001
	SEM	35.56	42.64	
Group-C (n-50)	Mean±SD	1279.80±178.62	826.60±186.39	< 0.0001
	SEM	25.26	26.36	
Group-D (n-50)	Mean±SD	1288.6±101.01	1484±151.6	< 0.0001
	SEM	14.29	21.44	

p value < 0.0001 (Extremely Significant)

Table-3- Blood Urea (mg/dl)

		At the start (Baseline)	After 24 weeks	p-value
Group-A (n-50)	Mean±SD	33.4±8.184	32.6±8.096	>0.05
	SEM	1.16	1.15	
Group-B (n-50)	Mean±SD	27.6±6.57	26.9±6.28	>0.05
	SEM	0.93	0.89	
Group-C (n-50)	Mean±SD	28.6±5.63	27.2±4.01	>0.05
	SEM	0.80	0.57	
Group-D (n-50)	Mean±SD	27.2±3.75	26.2±3.22	>0.05
	SEM	0.53	0.46	

p value >0.05 (Not significant)

Table-4 Serum Creatinine

		At the start (Baseline)	After 24 weeks	p-value
Group-A (n-50)	Mean±SD	1.18±0.27	1.11±0.26	>0.05
	SEM	0.037	0.036	
Group-B (n-50)	Mean±SD	1.09±0.245	1.01±0.324	>0.05
	SEM	0.035	0.046	
Group-C (n-50)	Mean±SD	0.73±0.076	0.72±0.073	>0.05
	SEM	0.012	0.01	
Group-D (n-50)	Mean±SD	0.68±0.118	0.64±0.08	>0.05
	SEM	0.017	0.011	

p value >0.05 (Not significant)

Table 5- Creatinine clearance (ml/min)

		At the start (Baseline)	After 24 weeks	p-value
Group-A (n-50)	Mean±SD	94.6±9.58	92.2±9.3	>0.05
	SEM	1.35	1.32	
Group-B (n-50)	Mean±SD	91.0±7.75	89.5±6.914	>0.05
	SEM	1.095	0.978	
Group-C (n-50)	Mean±SD	101±4.781	99.6±3.037	>0.05
	SEM	0.68	0.43	
Group-D (n-50)	Mean±SD	99.8±5.51	95.2±5.76	>0.05
	SEM	0.78	0.815	

p value >0.05 (Not significant)

Table-6-Urinary Creatinine

		At the start (Baseline)	After 24 weeks	p-value
Group-A (n-50)	Mean±SD	88.3±24.07	83±25.96	>0.05
	SEM	3.404	3.672	
Group-B (n-50)	Mean±SD	82.9±9.52	84±7.97	>0.05
	SEM	1.35	1.13	
Group-C (n-50)	Mean±SD	78±4.29	76.8±2.74	>0.05
	SEM	0.61	0.39	
Group-D (n-50)	Mean±SD	68.6±6.312	66.4±6.3	>0.05
	SEM	0.893	0.88	

p value >0.05 (Not significant)

DISCUSSION

Diabetic Nephropathy is clinically defined by presence of persistent proteinuria of >500mg/day in a diabetic patient who has concomitant retinopathy & hypertension and in the absence of clinical or laboratory evidence of other kidney or renal tract disease. The presence of retinopathy is an important pre-requisite because in its absence, albuminuria in a Type 2 diabetic patient may be due to diabetic or non-diabetic glomerulosclerosis and the chances for both are equal.[7-8] The incidence of overt proteinuria peaks after 15 years, therefore one inclusion criterion was that patients must have had a definite history of DM for at least 15 years. T1DM carries a 30-40% chance of diabetic Nephropathy and T2DM carries a 15-20% chance of Nephropathy after 20 years.[1] This explains why no patient of T2DM was available for the study. Other than that it can be attributed to mere a chance.

Table No. 1 shows out of 200 patients selected, only 87 were females explaining the observation that diabetes is more common in males. Also men are more likely to develop proteinuria. This also explains the higher proportion of males in this study.

Table No. 1 shows that out of 200 patients 109 had simplex retinopathy & 91 had proliferative retinopathy. In the hypertensive group, out of 100 patients 55% had proliferative whereas 45% had simplex retinopathy which is comparable to study by Hans-Henrik Parving et al. (1988) – out of 16 patients 14 were hypertensive; 8 (57%) of these 14 patients had proliferative retinopathy.[9]

In the normotensive group, 60% had simplex retinopathy & 40% had proliferative retinopathy which is comparable to study conducted by Parving et al. 1990, on normotensive patients, where 19 (59%) of the 32 patients had simplex retinopathy whereas 13 (41%) had proliferative retinopathy.

Table No. 2 shows the effect of protein diet on patients of diabetic nephropathy with hypertension and without hypertension. In Group A mean albuminuria has decreased from 1702±360.41 (at baseline) to 1169±276.86 (at 24th week) with p value < 0.0001 and decrease was extremely significant. In Group B mean albuminuria has increased from 1706±251.44 (at baseline) to 2023±301.50 (at 24th week) with p value < 0.0001 and increase was extremely significant. In Group C, mean albuminuria has decreased from 1279.80±178.62 (at baseline) to 826.60±186.39 (at 24th week) with p value < 0.0001 and decrease was extremely significant. In Group D mean albuminuria has increased from 1288.6±101.01 (at baseline) to 1484±151.6 (at 24th week) with p value < 0.0001 and increase was extremely significant.

Table 3 shows that the effect of protein diet on blood urea level after 24 weeks in all groups A, B, C and D was not significant (p value >0.05).

Table 4 shows that the effect of protein diet on serum creatinine level after 24 weeks in all groups A, B, C and D was not significant (p value >0.05).

Table 5 shows that the effect of protein diet on creatinine clearance level after 24 weeks in all groups A, B, C and D was not significant (p value >0.05).

Table 6 shows that the effect of protein diet on urinary creatinine level after 24 weeks in all groups A, B, C and D was not significant (p value >0.05).

Comparison between LPD (Low Protein Diet) & HPD (High Protein Diet) on hypertensive group showed that at the start of the study, the difference in the baseline values of albuminuria in the two groups was statistically insignificant. At the end of 24 weeks, albuminuria decreased in patients on low protein diet & increased in those taking high protein diet & the difference was highly significant (P < 0.005) this may be comparable to studies by Ciavarella et al. 1987 carried out on 16 patients of T1DM with overt nephropathy. A significant reduction in albumin excretion rate was found in all LPD patients after dietary protein restriction.[10]

Yue et al. (1988)[11] studied on 7 T1DM patients the effect of restricted protein diet (0.6 g/kg/day) for a period of 3 month. There was about 50% decrement in albumin excretion rate in patients with overt as well as microalbuminuria. In most of these patients, there were no change or least change in GFR, renal plasma flow & plasma albumin excretion rate.

Hansen HP et al. (July 2002)[12] studied the effect of low protein diet on prognosis in patients with diabetic nephropathy and concluded that moderate dietary protein restriction improves prognosis in type 1 diabetic patients with progressive diabetic nephropathy.

Raal FJ et al. (1994-Oct)[13] studied the effect of moderate dietary protein restriction on the progression of overt diabetic nephropathy. Patients consuming the moderately protein restricted diet (0.8 g/kg/day)

showed a marked decrease in the degree of proteinuria (2.1 gm/day to 1.13 gm/day; p=0.036) as compared to those consuming unrestricted protein diet (> 1.6 g/kg/day)> this concluded that moderate dietary protein restriction can ameliorate progression of overt diabetic nephropathy. All the studies in this regard match with the present study.

Thus, the present study & the other comparable studies showed that low protein diet has beneficial effect on patients with diabetic nephropathy (reduces albuminuria) independently of blood glucose and blood pressure charges.

CONCLUSION

Dietary protein restriction has overall beneficial effect on patients of diabetic nephropathy. The effect is independent of blood glucose and blood pressure changes and is due to improved glomerular permeability and selectivity probably.

Source of Funding: Self

Conflict of Interest: None

Ethical Clearance: Taken

Acknowledgment: Nil

REFERENCES

1. Alvin C. Powers, Harrison's Principles of Internal Medicine, 18e. USA: The McGraw-Hill Companies, Inc.; 2012. Page-2968.
2. Tipton MC. Susruta of India, an unrecognized contributor to the history of exercise physiology. J Appl Physiol. 2008;108:1553–6. [PubMed]
3. Frank LL. Diabetes mellitus in the texts of old Hindu medicine (Charaka, Susruta, Vagbhata) Am J Gastroenterol. 1957;27:76–95. [PubMed]
4. Melissa Sattley. The History of Diabetes. From: http://diabeteshealth.com/read/2008/12/17/715/the-history-of-diabetes/ Accessed: May 2013.
5. Graham Poole. Intercapillary Glomerulosclerosis and the Kimmelstiel-Wilson Syndrome. *Postgrad Med J* 1953 29: 137-146. doi: 10.1136/pgmj.29.329.137
6. Nezu U, Kamiyama H, Kondo Y, et al. Effect of low-protein diet on kidney function in diabetic nephropathy: meta-analysis of randomised controlled trials. BMJ Open 2013;3. pii: e002934. [PMC free article][PubMed]
7. Jitendra Singh. Evaluation of Diabetic Nephropathy: Clinical Recommendations. In: R.K. Singal, D.G. Jain, editors. Medicine Update Volume 17, 2007. Mumbai: The Association of Physicians of India; 2007. Chapter 45. Available from: http://www.apiindia.org/pdf/medicine_update_2007/45.pdf
8. Parving HH. Prevalence and cause of Albuminuria in NIDDM. Kidney Int 1992;41(4):758-62.
9. Hans-Henrik Parving, Eva Hommel, Elisabeth Mathiesen, Peter Skøtt, Berit Edsberg, Mogens Bahnsen, Mogens Lauritzen, Philip Hougaard, and Erik Lauritzen. Prevalence of microalbuminuria, arterial hypertension, retinopathy, and neuropathy in patients with insulin dependent diabetes. Br Med J (Clin Res Ed). 1988 Jan 16; 296(6616): 156–160. PMCID: PMC2544895
10. Ciavarella A, Di Mizio G, Stefoni S, Borgnino LC, Vannini P. Reduced albuminuria after dietary protein restriction in insulindependent diabetic patients with clinical nephropathy. Diabetes Care. 1987;10:407–13.
11. Yue DK, O'Dea J, Stewart P, Conigrave AD, Hosking M, Tsang J, Hall B, Dale N, Turtle JR. Proteinuria and renal function in diabetic patients fed a diet moderately restricted in protein. Am J Clin Nutr. 1988 Aug;48(2):230-4. PMID: 3407603
12. Hansen HP, Tauber-Lassen E, Jensen BR, Parving HH. Effect of dietary protein restriction on prognosis in patients with diabetic nephropathy. Kidney Int. 2002 Jul;62(1):220-8. PMID: 12081581; DOI: 10.1046/j.1523-1755.2002.00421.x
13. Raal FJ, Kalk WJ, Lawson M, Esser JD, Buys R, Fourie L, Panz VR. Effect of moderate dietary protein restriction on the progression of overt diabetic nephropathy: a 6-mo prospective study. Am J Clin Nutr. 1994 Oct;60(4):579-85. PMID: 8092094

DOI Number: 10.5958/2321-1032.2017.00014.6

Evaluation of Risk Factors and Clinical Outcome of Infective Endocarditis in a Tertiary Care Hospital of Kerala

Rashmi

Assistant Professor, Department of Medicine, Government T D Medical College, Alappuzha

ABSTRACT

Background: Infective endocarditis is a challenging disease with regional variation of pattern in its presentation

Aim: To explore the factors that could be associated with the outcome of patient diagnosed with infective endocarditis , which could be used for a better guidance in management.

Method : This is a prospective study from January 2013 to December 2015. 50 patients with definite IE based on modified Duke's criteria were recruited into the study. Clinical presentation, risk factors, biochemical markers, echocardiography and outcome were obtained via chart review, clinic data and telephone call. Simple logistic regression was utilised for inferential statistic.

Results: A total of 50 patients, 37 male (74%) and 13 female (26%) were included within the study. The mean age was 42 ± 16.4. Most patients (80.39%) were diagnosed within the first week of admission. *Staphylococcus aureas* was the most common pathogen (38%) and the mitral valve was predominantly affected (68%). Complication were common and in hospital mortality remains high (28%). 20% of the patient who had surgical intervention survived and discharged alive. Presence of complications predicts poor outcome (OR 5.5 p-value 0.02) whereas surgical intervention predicts good outcome (OR 1.56 p-value 0.027).

Conclusions: Mortality remains relatively high in patient with infective endocarditis. Those who presented with complications are at 5.5-fold risk of mortality. Surgical intervention showed association with good outcome within this cohort.

Key-words: *endocarditis, infective endocarditis,outcome.*

INTRODUCTION

Infective endocarditis (IE) continues to be a major challenge in modern medicine. Despite major advances in both diagnostic and therapeutic procedures, mortality rates have not changed in the past 25 years.[1]-6 The current in-hospital mortality for patient with IE is 15-23%, with a 1 year mortality approaching 40%.[7-9]

Address of Correspondence :
Dr. Rashmi
Assistant Professor, Department of Medicine,
Government T D Medical College, Alappuzha
Kerala, Email id : drrashmi.2016@rediffmail.com

In developed countries, IE mainly affects ageing population with comorbidities. It presents acutely with high rates of *Staphylococcus aureus* infection and complications such as cardiogenic shock and embolization.[2]-4 Global registries tend to under report IE patterns from developing nations and identify patterns pertinent to Western medicine.[9] One study from a low middle income region highlighted a high incidence of IE in patients with rheumatic heart disease.[3] Published data from upper middle income countries is lacking. We hereby sought to describe patterns of IE and predictors of outcome from this region.

The main objective was to describe the characteristic of patients admitted with IE from a tertiary care hospital of Kerala

METHOD

All patients admitted to Government T D Medical College Hospital , Alappuzha between January 2013 to December 2015 with definite IE according to modified Duke's criteria were included. This study received ethical approval from the institutional ethics committee.

For each patient, the following information were collected: demographics, comorbidities such as diabetes, end stage renal failure on dialysis, intravenous drug use and HIV infection, clinical presentation, laboratory findings, treatment modality, complications and outcomes. The definition for IE complications such as severe valve dysfunction, heart failure, septic shock and embolization are based on contemporary guideline.[4] The type of echocardiography (transthoracic, transoesophageal or both), valve involved and presence of vegetation were recorded. The valve involved was determined by the presence of vegetation, abscess and fistula on echocardiogram. Outcomes measure were: in-hospital mortality and discharge alive. Good outcome is defined as patient discharged alive and poor outcome is defined as in-hospital mortality.

STATISTICAL ANALYSIS

For descriptive analysis, measurement of mean and standard deviation were calculated for the numerical data. Frequency and proportion were employed for categorical data. Simple logistic regression was utilised in calculating crude odd ratio and the 95% confidence intervals for the predictors with significance value was set at 0.05 ($p< 0.05$). SPSS version 17.0 were utilised for the analysis.

RESULTS

Sixty-four medical records fulfilled the search criteria. Fourteen patients did not fulfill the Duke's criteria for definite IE and were excluded.

In the study group (n=50), the mean age was 42.5 ± 16.4 . The majority were male (74%) and diagnosed with infective endocarditis within the first week of admission to hospital.

The commonest predisposing factor were intravenous drug user (IVDU) which occurred in 13 patients, diabetes mellitus (9) and valvular heart disease (6). Three patients had colonoscopy done prior to symptoms of IE. Seventeen out of 50 patients did not have known predisposing factors .

Forty-nine out of 50 patients (98%) presented with fever. New murmurs and raised inflammatory markers were clues leading to a diagnosis of IE. None of our patients had immunological manifestation of IE such as Osler's node and Janeway lesions

All patients had at least one set of blood culture taken during hospitalisation. Staphylococcus is the predominant microorganism followed by streptococcus. Echocardiography was performed in all patients and vegetation was identified in all. 16% of subjects had concurrent transthoracic and transesophageal echocardiogram. The mitral valve is the commonest affected (N=24, 48%). Most cases had single valve lesions (80%), with multiple valve involvement affecting 10 patients .

Complications of endocarditis in this study includes severe valvular regurgitation (32%), shock (18%), systemic embolization other than stroke (12%) and stroke (10%) (Table 2). Of the 50 patients, ten (20%) were referred for surgical management. All of the surgically treated endocarditis patients were alive on discharge. In patients who were treated with antibiotics only, 25 (50%) were discharged alive. One patient took self-discharge and was lost to follow up.

Mortality occurred in 28% of our cohort. Eleven patients died due to complication of IE and three patients died due to hospital acquired pneumonia. Those cases were not referred for surgical intervention as they were deemed non suitable. Embolization was the commonest complication that was associated with 3.5-fold increase in mortality. Similarly, patient developing shock had a four fold increase in mortality.

Presence of complication predicted poor outcome (OR 5.5. p-value 0.02). Septic or cardiogenic shock has been shown as strongest predictor for poor outcome, followed by embolization (non stroke) and stroke. For predictor of good outcome, surgical intervention showed significant association (OR 1.56, p-value 0.027). Other parameters such as gender, age, clinical presentations, type of organisms and site of vegetation have no association as predictor of outcome.

DISCUSSION

The present study described the first series of patients with infective endocarditis from our teaching hospital . Most of our patients were young with a third having no risk factors. Overall mortality is high at 29%.

Our findings revealed that most patients within this cohort presented without classical signs of infective endocarditis. This is consistent with the findings from The International Collaboration on Endocarditis prospective study in 2009 which showed similar changes in the characteristics of IE.[9] Our study differs from published literature from the period between 1960 to 1980 which documented immunological manifestation in almost 50% of patients with endocarditis [5-8].

IVDU is a significant risk factor to contract IE (26%).[5] Similar findings were observed from the Malaysia and Hong Kong.[6-7] This is in contrast to data from ICE-PCS where the majority of IE from developing countries had degenerative valvular heart disease.[9] Another study from India highlighted the younger age of affected patients along with the presence of rheumatic heart disease as risk of contracting IE.[6] Among the IVDU group, *Staphylococcus aureus* was commonest and right sided valves were mainly affected consistent with previous published study. Urbanisation may be a factor, contributing to a higher rise of alcohol and drug abuse.[7]

Culture negative IE made up 32% of our cohort. This is unusually high in comparison to contemporary data which showed rate of culture negative IE between 14-19%.[8],[9] This trend was last seen in 1980s[10] . The use of antibiotics prior to hospital admission might contribute to this occurrence.

Systemic embolization is the commonest complication, occurring in up to 50% of patients with endocarditis [11]. It is associated with high mortality [12]. In our study, nine patients had embolization with mortality occurring in five (56%).

The indications for surgical intervention in our study include embolic phenomenon, severe acute mitral regurgitation, large vegetation of more than 1cm, fungal IE and endocarditis in the presence of congenital heart defect. The survival rate seen in post-surgical patients is consistent with prior studies, emphasising the need for early intervention when indicated especially when medical intervention has failed [13].

CONCLUSION

Mortality remains relatively high in patient with infective endocarditis. Those who presented with complications are at 5.5-fold risk of mortality. Surgical intervention showed association with good outcome within this cohort.

This study highlights the need for further research into disease patterns amongst different healthcare and population environment to gain maximum yield from resource allocation.

Conflict of Interest: Nil

Source of Funding : Nil

REFERENCES

1 Cabell CH, Jollis JG, Peterson GE, Corey GR, Anderson DJ, Sexton DJ, et al. Changing patient characteristics and the effect on mortality in endocarditis. Arch Intern Med. 2002;162(1):90-94.

2 Murdoch DR, Corey GR, Hoen B, Miró JM, Fowler VG, Bayer AS, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis–Prospective Cohort Study. Archives of internal medicine. 2009;169(5):463-73.

3 Mirabel M, Rattanavong S, Frichitthavong K, Chu V, Kesone P, Thongsith P, et al. Infective endocarditis in the Lao PDR: clinical characteristics and outcomes in a developing country. International journal of cardiology. 2015;180:270-3.

4 Habib G, Hoen B, Tornos P, Thuny F, Prendergast B, Vilacosta I, et al. Guidelines on the prevention, diagnosis, and treatment of infective endocarditis (new version 2009). European heart journal. 2009;30(19):2369-413.

5 Wilson LE, Thomas DL, Astemborski J, Freedman TL, Vlahov D. Prospective study of infective endocarditis among injection drug users. Journal of Infectious Diseases. 2002;185(12):1761-6.

6 Jain SR, Prajapati JS, Phasalkar MA, Roy BH, Jayram AA, Shah SR, et al. Clinical Spectrum of Infective Endocarditis in a Tertiary Care Centre in

Western India: A Prospective Study. International Journal of Clinical Medicine. 2014;2014.

7 Sundquist K, Frank G. Urbanization and hospital admission rates for alcohol and drug abuse: a follow-up study of 4.5 million women and men in Sweden. Addiction. 2004;99(10):1298-305.

8 Hoen B, Selton-Suty C, Lacassin F, Etienne J, Briançon S, Leport C, et al. Infective endocarditis in patients with negative blood cultures: analysis of 88 cases from a one-year nationwide survey in France. Clinical infectious diseases. 1995;20(3): 501-6.

9 Zamorano J, Sanz J, Almeria C, Rodrigo JL, Samedi M, Herrera D, et al. Differences between endocarditis with true negative blood cultures and those with previous antibiotic treatment. The Journal of heart valve disease. 2003;12(2):256-60.

10 Van Scoy RE. Culture-negative endocarditis. In Mayo ClinicProceedings.1982;57:149-154.

11. Hoen B, Alla F, Selton-Suty C, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. JAMA 2002;288:75–81.

12. Mocchegiani R, Nataloni M. Complications of infective endocarditis. Cardiovasc Hematol Disord Drug Targets. 2009 ;9(4):240-8.

13. Aneil Malhotra, Bernard D Prendergast. Evaluating Treatment Options for Patients With Infective Endocarditis. Future Cardiol. 2012;8(6):847-861.

DOI Number: 10.5958/2321-1032.2017.00015.8

To Study the Prevalence of Microalbuminuria among Essential Hypertensives

Vinay Sindhu[1], Sunny Khari[2], Yatish[1], Ankita Sharma[1], Kameshwer Prashad[3]

[1]Post Graduate III[rd] year, [2]Post Graduate I[st] Year, [3]Professor and HOD, Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur, (U.P)

ABSTRACT

Objective- To study the prevalence of microalbuminuria among essential hypertensive patients.

Method: A group of 110 patients with Essential Hypertension formed the sample& investigated. P value was calculated by using analysis of variance test (ANOVA) & P value <0.05 was considered as statistically significant.

Result- Maximum number of patients were in the age group of 51-60 years (28 patients, 25.4%), followed by the age group 41-50 years (26 patients, 23.6%) and least were in the age group < 30 years (1 patients, 0.9%), followed by the age group >80 years (6 patients, 5.4%). It can be seen that maximum number of patients (60 patients, 54.5%) had urinary microalbumin in the normal range. 32 patients or 29% had levels between 30-300 and 18 patients had levels more than 300. Hence, the prevalence of Microalbuminuria among Essential Hypertensives in our study is 29%. It can be seen that more males than females were normoalbuminuric, in terms of absolute numbers (34), and also in terms of percentage(55.7%). Meanwhile, more females were microalbuminuric in terms of percentage (30.6%), but not in absolute numbers(15). However, among the patients who were microalbuminuric, there were more males (17) than females (15).

Conclusion- The prevalence of Microalbuminuria is significant among patients suffering from essential hypertension (29%).Microalbuminuria is an independent risk factor for development / worsening of Hypertensive Nephropathy and endothelial dysfunction, thereby increasing the risk of micro and macrovascular complications. at last we recommended that a large case control study is required to find better understanding of microalbuminuria in essential hypertension.

Keywords- *Coronary heart disease (CHD), Congestive heart failure (CHF)***,** *Essential hypertension (EHT), urinary albumin excretion (UAE)*

INTRODUCTION

Hypertension is one of the leading causes of the global burden of disease. In our country, the prevalence ranges between 17-21 % in all states with marginal rural-urban differences.[1] Hypertension doubles the risk of cardiovascular diseases, including coronary heart disease (CHD), congestive heart failure (CHF), ischemic and hemorrhagic stroke, renal failure, and peripheral arterial disease. Although antihypertensive therapy clearly reduces the risks of cardiovascular and renal disease, large segments of the hypertensive population are either untreated or inadequately treated. Hypertension is present in all populations except for a small number of individuals living in primitive, culturally isolated societies. In industrialized societies, blood pressure increases steadily during the first two decades of life. The probability that a middle-aged or elderly individual will develop hypertension in his or her lifetime is 90%. Both environmental and genetic factors may contribute to regional and racial variations

Corresponding author:
Vinay Sindhu
Post Graduate III[rd] year, Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur (U.P), G-mail: vinaysindhu11@gmail.com
Mobile: 9759148201

in blood pressure and hypertension prevalence. Obesity and weight gain are strong, independent risk factors for hypertension. It has been estimated that 60% of hypertensives are >20% overweight. In twin studies, heritability estimates of blood pressure are ~60% for males and 30–40% for females. High blood pressure before age 55 occurs 3.8 times more frequently among persons with a positive family history of hypertensio n.[2]Hypertension is common, asymptomatic, readily detectable, usuallyeasily treatable and often leads to lethal complications if left untreated. Although the understanding of the pathophysiology of elevated arterial pressure has increased, in 90 to 95% of cases the etiology (and thus potentially the preventive cure) is still largely unknown. As a consequence, in most cases hypertension is treated non-specifically leading to a large number of minor side effects and high non-compliance rate.[3]The conventional methods of detecting renal damage in hypertension which include the measurement of blood urea nitrogen and creatinine, and proteinuria, are relatively insensitive, and only show abnormalities when the disease process is fairly advanced. Essential hypertension (EHT) produces clinical proteinuria and significant reduction in renal function in 5-15% of patients.[4] There has recently been considerable interest in the quantitative measurement of albuminuria to detect the subtle effects of hypertension on the kidneys. The term microalbuminuria was first used to describe the subclinical elevation of urinary albumin in patients with diabetic nephropathy. The advent of more sensitive method to quantitate the urinary albumin excretion (UAE) has unfolded higher frequency (25-100%) of microalbuminuria in patients with hypertension than in normotensive population.[5-9]Microalbuminuria has recently emerged as a marker of wide spread vascular damage in essential hypertension. According to National Kidney Foundation Microalbuminuria is defined as a Urine Albumin Excretion Rate (UAER) of approximately 30-300mg/d in at least two of three consecutive samples of non-ketotic sterile urine.[10]Hypertensives with microalbuminuria were found tohave significantly higher prevalence of coronary artery disease, hypertensive retinopathyand cerebrovascular disease when compared to their normoalbuminuric counter parts.[11,12] Microalbuminuria is an early marker of target organ damage in essential hypertension.[13] The main determinant of albumine excretion rate in subjects with mild hypertension and no cardiovascular complications, seems to be the hemodynamic load, whereas in subjects with more severe hypertension and associated target organ damage, augmented urinary leak is probably the consequence of glomerular damage.[14]It has been clearly demonstrated that microalbuminuria is a risk factor for the development of clinical proteinuria, renal failure and increased cardiovascular mortality in insulin dependent diabetes mellitus. Studies show that microalbuminuria also predicts development of proteinuria and decline in renalfunction in hypertension.[15]

MATERIAL AND METHOD

The study was approved by the Ethical Committee of the Institute. This was a hospital based cross-sectional study conducted between December 2015 to December 2016 in the Department of General Medicine, Saraswathi Institute of Medical Science, Pilkhuwa, Hapur Uttar Pradesh, India. A total of 110 patients were included in the study. All demographic data such as age, sex, height and weight were recorded. A detailed clinical history for all the patients was taken and careful general examinations weredone. Microalbumin estimation was done by immunoturbidimetric assay, which is an in vitro diagnostic assay for quantification of albumin in human urine by means of clinical chemistry analyser. The method is sensitive to very low concentrations of human albumin. It is based on the addition of Trichloroacetic or sulfosalicylic acids to the sample, which results in altered colloid properties and production of turbidity which can be read in a densitometer. The minimum concentration which can be detected is 50 - 100 mg/l.

STATISTICAL ANALYSIS

Data was collected and analyzed using SPSS software. The dichotomous/categorical variables were compared by using Chi-square Exact test. More than two continuous variables were compared by using Kruskall-wallis test with multiple comparison tests. P value was calculated by using Analysis of variance test(ANOVA) and p value <0.05 was considered statistically significant.

RESULT

The study was conducted on 110 newly diagnosed patients of Essential Hypertension.

Table 1: Sex distribution

Males	Females
61 (55.4%)	49 (44.5%)

55.4% of all patients were male compared to 44.5% females in our study.

Table 2: Age distribution

Age group (years)	Frequency	Percentage (%)
<30	1	0.9
31-40	10	9
41-50	26	23.6
51-60	28	25.4
61-70	24	21.8
71-80	15	13.6
>80	6	5.4

Maximum number of patients were in the age group of 51-60 years (28 patients, 25.4%), followed by the age group 41-50 years (26 patients, 23.6%) and least were in the age group < 30 years (1 patients, 0.9%), followed by the age group >80 years (6 patients, 5.4%)

Table 3: Microalbumin levels

Microalbumin (mcg/mg Cr)	Frequency	Percentage (%)
<30	60	54.5
30-300	32	29
>300 (upto frank proteinuria)	18	16.4

It can be seen that maximum number of patients (60 patients, 54.5%) had urinary microalbumin in the normal range. 32 patients or 29% had levels between 30-300 and 18 patients had levels more than 300. Hence, the prevalence of Microalbuminuria among Essential Hypertensives in our study is 29 %.

Table 4: Sex related distribution of Microalbumin levels

Microalbuminuria distribution	Males	Females	Total
<30	34 55.7%	26 53.1%	60 54.5%
30-300	17 27.9%	15 30.6%	32 29.0%
>300	10 16.4%	8 16.3%	18 16.4%
Total	**61** **100%**	**49** **100%**	**110** **100%**

It can be seen that more males than females were normoalbuminuric, in terms of absolute numbers (34), and also in terms of percentage(55.7%). Meanwhile, more females were microalbuminuric in terms of percentage (30.6%), but not in absolute numbers(15). However, in the among the patients who were microalbuminuric, there were more males (17) than females (15).

Table 5: Age related distribution of microalbumin levels

Age distribution	Sex	<30	30-300	>300	Total
<30	Male	1		0	1
	Female	0		0	0
	Total	1		0	1
31-40	Male	4	2	1	7
	Female	2	1	0	3
	Total	6	3	1	10
41-50	Male	5	3	2	10
	Female	10	5	1	16
	Total	15	8	3	26
51-60	Male	12	4	1	17
	Female	5	5	1	11
	Total	17	9	2	28
61-70	Male	7	5	4	16

Cont... Table 5: Age related distribution of microalbumin levels

	Female	5	2	1	8
	Total	12	7	5	24
71-80	Male	5	2	1	8
	Female	3	1	3	7
	Total	8	3	4	15
>80	Male	0	1	1	2
	Female	1	1	2	4
	Total	1	2	3	6

Table 6: Age specific prevalence

Age group (years)	Prevalence (%)
<30	0
31-40	30
41-50	30.7
51-60	32.1
61-70	29.1
71-80	20
>80	33.3

Table 7: Sex specific prevalence among the age groups

Age group (years)	Male prevalence (%)	Female prevalence (%)
<30	0	0
31-40	28.7	33.3
41-50	30	31.2
51-60	57.1	45.4
61-70	31.2	25
71-80	25	14.2
>80	50	25

It can be seen that maximum number of patients with Microalbuminuria were from the age group 51-60 years (9 patients), followed by 41-50 years (8 patients) and minimum were in the age group <30 years (0 patients), followed by >80 years (2 patients).However, maximum prevalence was in the age group of >80 years years (33.3%), followed by 51-60 years (32.1%). Minimum prevalence of 0% was noted in the age group <30 years, followed by 20% in the age group 71-80.Maximum number of male patients with microalbuminuria were 5, in the age group 61-70, minimum were 0, in patients <30 years of age.Similarly, maximum females were 5, again in the age group of 41-50 years and 51 -60 years both and minimum was 0, that too in the age group <30 years.

DISCUSSION

Hyprtension is a leading cause of mortality and morbidity all over the world with prevalence between 17-21% in our country and 30% in the western world. This study assesses the prevalence of Microalbuminuria among patients suffering from essential hypertension. Findings from other important studies which have attempted to find similar conclusions are compared with the findings from our study in the following paragraphs.Prevalence of Microalbuminuria in Essential Hypertension: In our study, the prevalence was 29% out of 110 patients. In a study conducted by Sabharwal et al[16] in 2008 on 174 patients, the prevalence was 33.3%. Pontremolli R et al[17,18] found a prevalence of only 8% in their study. Palatini P et al[19] in 2005 found a prevalence of only 6% among 1041 young hypertensives aged 18-55. Analysis of the population of the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study[20] of 8,029 subjects (aged 55–80 years) with stage II–III essential hypertension results in a prevalence of 26%, not much different from our study. In a study on 130 Hypertensives and 100 Normotensives by Maharajan BR et al[21] in 2012 in Nepal, the prevalence was 17.7% in the Hypertensive arm. In another study in Nepal in 2012 by Bibek Poudel[22] et al on 106 patients revealed a prevalence of 51.88%. Kim YS[23] in 2013 found the prevalence to be 14.1% in his study among 40,473 patients in the Republic of Korea. Mc Kenna MJ[24] in 1991 and Schrader J(8 of 14)[25] in 2006 found a prevalence of 30%. Silva RP[26] in 2008 found a prevalence of 9.5% among 73 Hypertensives. In

a Portuguese study by Jorge Polonia et al(27)[27] in 2007, 1582 hypertensive patients were studied and prevalence of microalbuminuria was 29% was concurred. Pranja Hunse[28] in 2011 found prevalence of 23% among 100 patients. In another study by J Magadheesha[29] in 2006, the prevalence was 48%.The variability in these studies can be explained by different values used to define microalbuminuria, and different methods used to assess the same. Several factors can affect the prevalence of microalbuminuria in hypertension including sex, race, severity of the disease and concomitant risk factors. Sex distribution: In our study, 27.9% of male hypertensive patients and 30.6% of female hypertensive patients have microalbuminuria.Sabharwal et al[16] found prevalence among males to be 34% and among females to be 30.7%. In the study by Pranja Hunse[28] 22.5% male patients and 24.1% female patients had microalbuminuria. In the study by Magadheesha[29], 50% males and 44.4% females had microalbuminuria. Bibek Poudel[22] found 46.67% male and 58.7 female hypertensives to have microalbuminuria. These variations are in part due to regional variations, stages of hypertension among different populations and a minor contribution to raised levels in females of developing countries can be attributed to increased prevalence of asymptomatic bactiuria as found by Bibek Puodel[22].Age distribution: In our study, maximum prevalence of microalbuminuria was in the the age group >80 years (2 out of 6 patients, 33.3%) followed by the age group 51-60 years (9 out of 28 patients, 32%). In the study by Hunse[28], 10 out of 24 patients in the age group 50-59 years (41.7%) had microalbuminuria, the maximum age specific prevalence in that study, closely correlating with ours.

CONCLUSION

The prevalence of Microalbuminuria is significant among patients suffering from essential hypertension (29%). Microalbuminuria is an independent risk factor for development / worsening of Hypertensive Nephropathy and endothelial dysfunction, thereby increasing the risk of micro and macrovascular complications. In last we recommended that a large case control study is required to find better understanding of microalbuminuria in essential hypertension.

Source of Funding- None

Ethical Permission– Taken from ethical committe of Institute

Conflict of Interest- None

REFRENCES

1. Park K. Hypertension Text book of preventive and social medicine 22nd edition. M/s Banarsidas Bhanot, Jabalpur 2014.
2. Harrison's Principles of Internal Medicine, 18th edition, part 10, section 5, chapter 247.
3. Narhare P, Chaitra B, Surender T. A comparative study of cardiovascular autonomic function in hypertensive and normotensive people. Int J Pharm Biomed Res 2011;2(4):223-6.
4. Bigazzi R, Bianchi S, Campese VM, Baldari G. Prevalence of microalbuminuria in a large population of patients with mild to moderate essential hypertension. Nephron. 1992;61:94-7.
5. Jalal S, Sofi FA, Alai MS, Siddiqqi MA, Bhat MA, Khan KA, et al. Prevalence of microalbuminuria in essential hypertension: A study of patients with mild to moderate hypertension. Indian J Nephrol.2001;11:6–11.
6. Parving HH, Mogensen CE, Evrin PE. Increased urinary albumin excretion in benign essential hypertension. Lancet. 1974;1:231–7.
7. Losito A, Fortunati F, Zampi I, Del Favero A. Impaired functional reserve and albuminuria in essential hypertension. Br Med J. 1988;1: 1562–4.
8. Giaconi S, Levanti C, Fommei E, Innocenti F, Seghieri G, Palla L, et al. Microalbuminuria and casual and ambulatory blood pressure monitoring in normotensives and in patients with borderline and mild hypertension. Am J Hypertens. 1989;2: 259–61.
9. Bianchi S, Bigazzi R, Baldari G, Campese VM. Microalbuminuria in patients with essential hypertension: Effects of several antihypertensive drugs. Am J Med. 1992;93:525–8.
10. William B. The prognostic significance of proteinuria. Framingham Heart study.
11. Ravera M, Ratto E, Ventoretti S, Viazzi F, Leoncini G. Microalbuminuria and subclinical cerebrovascular damage in essential hypertension. J Nephrol 2002;15:519-524.
12. Rossignol P, Hosseini K, Tropeano AI, Fay R, Tsatsaris A, Guillemin F, Mounier-Vehier C. Target

organ damage assessment in French hypertensive patients without established cardiovascular or renal disease: results of the PREVENT-A study. J Hypertens. 2013 Jan;31(1):177-85

13. Pontremoli R, Micolella C, Viazzi F, Vettoretti S, Parodi D, Tomolillo C et al. Microalbuminuria is an early marker of target organ damage in essential hypertension. Am J Hypertensive. 1998;11:430-438.
14. Palatini P. Microalbuminuria in hypertension. Curr Hypertens Rep 2003;5(3):208-14.
15. Ljungman S. Microalbuminuria in essential hypertension. Am J Hypertens 1990;3:956-960.
16. Sabharwal R, Singh P, Arora MM, Somani BL, Ambade V. Incidence of microalbuminuria in hypertensive patients. Indian J Clin Biochem. Jan 2008;23(1):71-75.
17. Pontremoli R, Sofia A, Ravera M, Nicolella C, Viazzi F, Tirotta A et al. Prevalence and clinical correlates of microalbuminuria in essential hypertension. The MAGIC study. Hypertension 1997;30:1135–1143
18. Pontremolli R, Leoncini G, Ravera M, Parodi D, Tomolillo C. Microalbuminuria: Cardiovascular and Renal risk in Primary Hypertension. Journal of American Society of Nephrology 2002;13s: 169-172.
19. Palatini P. Microalbuminuria in hypertension. Curr Hypertens Rep. 2003 Jun;5(3):208-14.
20. Wachtell K, Olsen MH, Dahlof B, Devereux RB, Kjeldsen SE, Nieminen MS, Okin PM, Papademetriou V, Mogensen CE, Borch-Johnsen K, Ibsen H: Microalbuminuria in hypertensive patients with electrocardiographic left ventricular hypertrophy: the LIFE study. J Hypertens 20: 405–412, 2002.
21. Mahajan BR, Bhandary S, Sunuwar L, Shrestha A, Ranjitkar N. Association of hypertension with microalbuminuria and lipid profile in the local population of Patan. Nepal Med Coll J. 2012 Jun;14(2):157-62.
22. Poudel B, Yadav BK, Kumar A, Jha B, Raut K. Prevalence and association of microalbuminuria in essential hypertensive patients. N Am J Med Sci.2012 Aug;4(8):331-335.
23. Kim YS, Kim HS, Oh HY, Lee MK, Kim CH, Kim YS et al. Prevalence of microalbuminuria and associated risk factors among adult Korean hypertensive patients in a primary care setting. Hypertens Res. 2013 Sep;36(9);807-23.
24. McKenna MJ, Arias C, Feldkamp CS, Whitehouse FW. Microalnuminuria in clinical practice. Arch Intern Med. 1991;151:1745-7.
25. Schrader J, Lüders S, Kulschewski A, Hammersen F, Züchner C, Venneklaas U, et al. Microalbuminuria and tubular proteinuria as risk predictors of cardiovascular morbidity and mortality in essential hypertension: Final results of a prospective long-term study (MARPLE Study) J Hypertens.2006;24:541–8
26. Silva RP, Cisne K, Oliveira JM, Kubrusly M, Rodrigues Sobrinho CR, Andrade PJ. Determination of microalbuminuria in hypertensive patients and in patients with coronary artery disease. Arg Bras Cardiol. 2008 Feb;90(2):99-103.
27. Polonia J, Carmona J, Mendes E, Pisco L. Prevalence of microalbuminuria in non-diabetic hypertensive patients attended by Portuguese Gps. Rev Port Cardiol 2007;26(6):637-644.
28. Study of Microalbuminuria in patients of Essential Hypertension. Hunse P. 2011. http: //14.139.159.4:8080/jspui/bitstream/123456789/5501/1/Prajna%20Hunse.pdf
29. Significance of microalbuminuria in essential hypertension-one year cross sectional study. Jagadeesha M. 2006. http://hdl.handle.net/123456789/2823.

DOI Number: 10.5958/2321-1032.2017.00016.X

To Study the Association of Coronary Artery Disease with Metabolic Syndrome in Western Uttar Pradesh

Pankaj Kumar[1], Yatish[2], Vinay Sindhu[2], Syed Azizur Rahman[2], Ashish Saran[3], Kameshwar Prasad[4]

[1]Assistant Professor, [2]Post Graduate IIIrd year, [3]Post Graduate Ist year, [4]Professor and Head of Department, Department of General Medicine Saraswathi Institute of Medical Sciences Hapur (U.P)

ABSTRACT

Objective- To Studythe association of coronary artery disease with metabolic syndrome.

Method- A Total 200 patients were included in this study & investigated for coronary artery disease associated with metabolic syndrome or not. A study of presence or absence of metabolic syndrome in coronary artery disease was done. P value was calculated by using analysis of variance test(ANOVA)& P value <0.05 was considered as statistically significant.

Results- Total 200 patients were included in this study in 156 patients(78%) were suffering from metabolic syndrome and 44 patient (22%) were not suffering from metabolic syndrome.Most of the patients suffering from coronary artery disease associated with metabolic syndrome were of older age groups (65.38%)>61 years.Second most common group was (21.79%)51-60 years. Other patients of coronary artery disease not suffering from metabolic syndrome (68.18%) in 51-60 years followed by(18.18%) in > 60 years. Amongst the patients suffering from coronary artery disease and metabolic syndrome males outnumbered females, although this data is not statistically significant p=0.4. Among the CAD patient group prevalence was highest therefore raised fasting blood sugar(n=106) (67.94%) and low HDL values (67.94%), whereas it was lowest for Hypertension(51.28%). In the coronary artery disease group out of total 200 patients 78%(n=156) were suffering from metabolic syndrome and 22%(n=44) were not suffering from metabolic syndrome there is positive correlation between metabolic syndrome and coronary artery disease .Using Test for equality for proportion (z-score) this data is found to be statistically significant .

Conclusion- In coronary artery disease group (total patients =156) 67.5%(n=108) were having 3 risk factors, 50%(n=80) were having 4 risk factors and 11.25%(n=18) were having 5 risk factors of metabolic syndrome among the cases .Among the patients suffering from coronary artery disease (total patients =156) the prevalence of hypertension was 51.28%(n=80),of low HDL was67.94%(n=106),of high TGs was 57.69%(n=90),of raised waist circumference was 56.41%(n=88) and of increased fasting blood sugar was 67.94%(n=106) in the case group.

Keywords- *Lipid level,Coronary artery disease (CAD), Metabolic syndrome(MS), High density lipoprotein (HDL),Low density lipoprotein(LDL),Triglycerides(TGL),NCEP ATP III,NAFLD(Non-alcoholic fatty liver disease)*

INTRODUCTION

Whereas the previous epidemic of coronary heart disease between 1910 and the 1960s was largely attributed to increased intake of saturated fat, it is quite plausible that the current epidemic of obesity and metabolic syndrome will lead the new epidemic of coronary heart disease, throughout the world. Because MS is associated with increased risk of CHD, it has also been called the "Deadly Quartet" or "cardiovascular dysmetabolic syndrome.[1,2] The metabolic syndrome, a concurrence of disturbedglucose and insulin metabolism, overweight and abdominal fatdistribution,

Corresponding author:
Pankaj Kumar
Assistant Professor, Department of General Medicine
Saraswathi Institute Of Medical Sciences,Hapur (U.P)
pankaj19822000@gmail.com, Mob.: 9450136739

mild dyslipidemia and hypertension, is associatedwith subsequent development of type 2 diabetes mellitus andcardiovascular disease (CVD).[3] Metabolic syndrome is a combination of medical disorders that increase the risk of developing cardiovascular disease and diabetes. It affects one in five people, and prevalence increases with age. Some studies estimate the prevalance in the USA to be up to 25% of the population.[4] Metabolic syndrome is also known as metabolic syndrome X, syndrome X, Insulin resistance syndrome, Reaven's syndrome, and CHAOS (Australia). Symptoms and features are:

- Fasting hyperglycemia —diabetes mellitus type2 or impaired fasting glucose, impaired glucose tolerance, or insulin resistance.
- High blood pressure
- Central obesity (also known as visceral, male-pattern or apple-shaped adiposity), overweight with fat deposits mainly around the waist; Decreased HDL cholesterol; Elevated Triglyceride; Associated diseases and signs are:hyperuricemia, fatty liver (especially in concurrent obesity) progressing to non-alcoholic fatty liver disease, polycystic ovarian disease (in women) and Acnathosis nigricans.According to Scott Grundy, University of Texas Southwestern Medical School, Dallas,Texas, the intent was just to update the NCEP ATP III definition and not create a new definition.[3,5]:Elevated waist circumference: Men — Equal to or greater than 40 inches (102 cm) ,Women — Equal to or greater than 35 inches (88 cm) Elevated triglycerides: Equal to or greater than 150 mg/dL Reduced HDL ("good") cholesterol: Men — Less than 40 mg/dL ,Women — Less than 50 mg/dL Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension .Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia.

MATERIAL AND METHOD

The study was approved by the Ethical Committee of the Institute. This was a hospital based cross-sectional study conducted between Oct 2015 to 0ct 2016 in the Department of General Medicine, Saraswathi Institute of Medical Science, Pilkhuwa, Hapur Uttar Pradesh, India. A total of 200patients were included in the study. All patients of age more than 40yrs, who admitted in ICU for coronary artery disease. All Demographic data such as age, sex, height and weight were recorded. A detailed clinical history for all the patients was taken and careful general examinations were done. The Exclusion criteria are patient on lipid lowering drugs, When Alcohol consumption is>30gm/d and >20gm/d in male and female respectively, Diabetes mellitusand very low and high Body Mass Index (BMI). BMI was calculated by using the formula [weight (kg)/height (meter^2)]. Lipid profile such as total cholesterol, serum triglycerides, serum high-density lipoprotein (HDL), serum low-density lipoprotein (LDL) and serum very low-density lipoprotein (VLDL) was measured. ECG,TMT,Troponin-T or Echocardiography proven of all the patients was done for diagnosing and proven ischemic heart disease. Case selection- Patients in above mentioned groups must fulfill the criterion for metabolic syndrome, which were as following ;(1)Elevated waist circumference: Men — Equal to or greater than 40 inches (102 cm) ,Women — Equal to or greater than 35 inches (88 cm),(2)Elevated triglycerides: Equal to or greater than 150 mg/dL ,(3)Reduced HDL ("good") cholesterol: Men-Less than 40 mg/dL ,Women — Less than 50 mg/dL, (4)Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension, (5)Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia. (3 out of 5 must be present).Control Selection- (1)Control subjects were selected from the patients who were admitted in our hospital due to coronary artery disease but were not suffering from metabolic syndrome .(2)Control subjects were matched according to age and sex group.Informed consent was taken from each of the patients before including them in this study.

STATISTICAL ANALYSIS

Data was collected and analyzed using SPSS software. The dichotomous/categorical variables were compared by using Chi-square Exact test. More than two continuous variables were compared by using Kruskall-wallis test with multiple comparison tests. P value was calculated by using Analysis of variance test(ANOVA) , Z score Test for equality for proportion (z-score) and p value <0.05 was considered statistically significant.

RESULT

Table -1: Sample selection-case and control groups

Patients of coronary artery disease suffering from metabolic syndrome	156	78%
Patients of coronary artery disease not suffering from metabolic syndrome	44	22%

156 Patients (78%) suffering from coronary artery disease with metabolic syndrome and 44 Patients (22%) suffering from coronary artery disease without metabolic syndrome.

Table-2: Frequency distribution of cases and controls in different age groups

Variable	**Patients of CAD suffering from metabolic syndrome**	**Patients of CAD not suffering from metabolic syndrome**	
Age (in years)			
41-50	20(12.82%)	6(13.63%)	26
51-60	34(21.79%)	30(68.18%)	64
>60	102(65.38%)	8(18.18%)	110
Total	156	44	200

Most of the patients suffering from coronary artery diseases with metabolic syndrome were of older age groups(>61years). Second most common group was 51-60years. Most of the patients suffering from coronary artery disease without metabolic syndrome were of older age groups(>61years) followed by 51-60years.

Table-3: Distribution among Gender wise

VARIABLE	**Patients of CAD suffering from metabolic syndrome**	**Patients of CAD not suffering from metabolic syndrome**	**Significance**	**P value**
MALE	112(71.79%)	36(81.81%)	X^2=0.640 df=1	0.4237
FEMALE	44(28.21%)	8(18.19%)		

Among the patients suffering from coronary artery disease & metabolic syndrome males outnumber females, although this data is not statistically significant.

Table-4: Frequency of Metabolic Syndrome in coronary artery disease

Patient groups	**Metabolic syndrome present**	**Metabolic syndrome absent**	**Significance**
Type of vascular disease			***Z-score***
Coronary artery disease	156(78%)	44(22%)	**3.961421**

In the coronary artery disease group out of total 200 patients 156 patients (78%) are suffering from metabolic syndrome.Using **Test for equality for proportion (z-score)** this data is found to be statistically significant **(Z score=3.961421)**

Table 5: Frequency distribution of components of Metabolic Syndrome

Patient groups	patients with IHD& Metabolic syndrome	patients of IHD without Metabolic syndrome
Risk factors		
1.hypertension	80(51.28%)	8(18.18%)
2.FBS>100	106(67.94%)	8(18.18%)
3.raised waist circumference	88(56.41%)	6(13.63%)
4.low HDL values	106(67.94%)	30(68.18%)
5.high TGs values	90(57.69%)	4(9.09%)

Among the coronary artery disease patients group prevalence was highest that for raised Fasting blood sugar(n=106)(67.94%) &low HDL values (n=106)(67.94%) whereas it was lowest that for hyperten sion(n=80)(51.28%).the low prevalence of hypertension may be due to reduced LV contractile function secondary to ischemic myocardial dysfunction . Among the *female patients* maximum were suffering from raised fasting blood sugar values 86.95%(n=44) followed by raised waist circumference 82.60%(n=40) and least with low HDL values 73.91% (n=36) ,high TGs values 73.91%(n=36) and hypertension 73.91%(n=36). Among the patients suffering from coronary artery disease (total patients =44) the prevalence of hypertension was 18.18% (n=8),of low HDL was 68.18% (n=30),of high TGs was 9.09% (n=4),of raised waist circumference was 13.63%(n=6) and of increased fasting blood sugar was 18.18% (n=8) *in the control group*.Case control study is recommended to find better understanding of association of metabolic syndrome in patients of coronary artery disease.

DISCUSSION

The present study was undertaken with the aim: To study the association of coronary artery disease with metabolic syndrome.The sample for patient group was drawn from the patients admitted in the medicine and cardiology department . A total number of 200 patients of coronary artery disease were screened for metabolic syndrome who fulfilled the selection criteria as case group. The patients who were not suffering from metabolic syndrome are taken as control group. National Cholesterol Education Program adult treatment panel-III (ATP-III*)* was taken as a criterion to define metabolic syndrome. Which is as following; (1)Elevated waist circumference: (A)Men — Equal to or greater than 40 inches (102 cm) ,(B)Women — Equal to or greater than 35 inches (88 cm) .(2)Elevated triglycerides: Equal to or greater than 150 mg/dL.(3)Reduced HDL ("good") cholesterol: (A)Men — Less than 40 mg/dL ,(B)Women — Less than 50 mg/dL.(4)Elevated blood pressure: Equal to or greater than 130/85 mm Hg or use of medication for hypertension .(5)Elevated fasting glucose: Equal to or greater than 100 mg/dL (5.6 mmol/L) or use of medication for hyperglycemia. (3 out of 5 must be present) .In the present study, the overall prevalence of metabolic syndrome was found 78% in patient groups. The prevalence was 72% in *coronary artery disease* group. No subject of control group could complete the criteria for the metabolic syndrome. The data shows that there is a positive correlation of coronary artery disease with metabolic syndrome.Ninomiya et al[19] have evaluated the association between Metabolic syndrome and history of myocardial infarction and/or stroke among the participants in the *Third National Health and Nutrition Examination Survey (NHANES III)*. On the basis of participants self-reported histories, they found that the presence of metabolic syndrome was associated with increased risk of myocardial infarction and stroke.[6] These findings give further credence to the prevailing thinking that the presence of Metabolic syndrome identifies a cohort of the population that is at substantial risk of cardiovascular disease .There are only limited previous data showing the association of Metabolic syndrome with cardiovascular disease.[7,8] The study by Lakka et al[7] prospectively examined the relationship between Metabolic syndrome and cardiovascular disease and overall mortality rate in middle-aged men participating in the population-based Kuopio Ischemic Heart Disease Risk Factor Study, who were followed up for 11.4 years. Using both the ATP III (Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults [Adult Treatment Panel III]) and World Health

Organization definitions, Lakka et al[7]demonstrated that even in the absence of diabetes or prior cardiovascular disease, the presence of Metabolic syndrome was associated with significant increase in the risk of cardiovascular disease and all-cause mortality.According to Northern Manhattan Study[9], The metabolic syndrome was associated with increasedrisk of cardiovascular eventsafter adjustment for socio-demographicand risk factors. The effect of the metabolic syndrome on coronary artery diseases,risk was greater among women thanmen and among Hispanics compared with blacks and whites. The conclusion is that the metabolic syndrome is an important riskfactor for coronary artery disease, with differential effects by sexand race/ ethnicity.According to American Stroke Association meeting report[10] (07 Feb 2004) The Metabolic syndrome - the simultaneous occurrence of multiple cardiovascular risk factors - may almost double the risk of stroke, researchers reported today at the American Stroke Association's 29th International Stroke Conference. The findings suggest that treating the risk-factor components of metabolic syndrome might reduce stroke risk before the onset of Type 2 diabetes.In the present study the prevalence of metabolic syndrome and associated diseases (coronary artery disease) increases with age. In the study maximum numbers of patients were more than 61 years of age, next more common age group was 51 to 60 years. According to study by Alberti KG et al[11,18] the prevalence of metabolic syndrome increases with age , with nearly 60% of women ages 45-49 and 45% of men ages 45-49 meeting National Cholesterol Education Program adult treatment panel-III criterion. Greater industrialization worldwide is associated with rising rates of obesity, which is anticipated to dramatically increase prevalence of the metabolic syndrome, especially as the population ages. In the present study, among the male patients of metabolic syndrome, frequency of hypertension was highest and that for waist circumference was lowest among the different components of metabolic syndrome. Among the female patients of metabolic syndrome , frequency of raised fasting blood sugar was highest followed by raised waist circumference and that for Low HDL values, High TGs values & Hypertension were lowest among the different components of metabolic syndrome. According to National Health and Nutrition Examination Survey (NHANES) III[12]Increases in waist circumference predominate in women whereas fasting triglycerides >150 mg/dL and hypertension are more likely in men.In the present study the frequency of coronary artery disease were higher among individuals with sedentary working habits. The frequency of cases in the sedentary working habits group was almost double than that of active labourers group. It suggests that sedentary life style is a risk factor to develop atherosclerotic vascular diseases secondary to increased incidence of metabolic syndrome in this population groups. Although this data was not found to be statistically significant.According to International Journal of Epidemiology[13]lack of physical activity is a modifiable risk factor for both total stroke and stroke subtypes. Moderately intense physical activity is sufficient to achieve risk reduction.According to The Framingham Study[14]overall mortality and mortality due to cardiovascular and ischemic heart disease were inversely related to the level of physical activity for men. The effect of being sedentary on mortality is rather modest compared to the effects of other risk factors but, in mortality due to ischemic heart disease, it persists when these factors are taken into account. For women, the effect is negligible. In occlusive peripheral arterial disease, and cardiac failure, an inverse relationship is noted, but does not reach statistical significance. There is a statistically significant association with incidence of ischemic heart disease and with incidence of all forms of cardiovascular disease when they are taken together. Little correlation was noted between physical activity level (at the generally low level found) and the level of major risk factors. In the present study the frequency of coronary artery disease were higher among individuals residing in urban or relatively industrialized areas of state. In the coronary artery disease group 69.43% cases were residing in urban areas whereas only 30.57% cases were residing in rural areas, although this data is not statistically significant. It may be due to the difference in the approachability of these two population groups attending the hospital. Frenk, et al[15] have argued that many of the non communicable diseases like heart disease , stroke and cancer are a result of defective process of industrialization that has placed more value on economic growth rather than on human welfare. In developing countries the unequal distribution of wealth and health service coverage results in the widening of the gap in the health status among social classes and geographical regions. Omran[16,17] noticed as a general pattern ,irrespective of the epidemiological transition model, that mortality decline due to non communicable diseases like heart disease, stroke and cancer starts among the

higher social classes with the lower classes eventually catching up.

CONCLUSION

In this study we have found that coronary artery disease with metabolic syndrome are common in Indian society & is in increasing trend. Apart from this other causes of coronary artery disease with metabolic syndrome is sedentary life style & less work by Indian society especially in urban area. We found abnormal lipid profile levels amongst patients with fatty liver. In last we recommended that a large case control study is required to find better understanding of coronary artery disease with metabolic syndrome.

Source of Funding- None

Ethical Permission –Taken from ethical committee of Institute

Conflict of Interest- None

REFRENCES

1. Deedwania PC. The deadly quartet revisited. Am J Med. 1998;105(1A):1S–3S.
2. Fagan TC, Deedwania PC. The cardiovascular dysmetabolic syndrome.Am J Med. 1998;105(1A): 77S–82S.
3. Hanna-Maaria Lakka; David E. Laaksonen; Timo A. Lakka; Leo K. Niskanen; Esko Kumpusalo; Jaakko Tuomilehto; Jukka T. Salonen;JAMA. 2002;288: 2709-2716 .
4. Ford ES, Giles WH, Dietz WH (2002). Prevalence of metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 2002 jan 16, 287(3): 356-359.
5. Grundy SM, Brewer HB, Cleeman JI, Smith SC, Lenfant D, for the Conference Participants.Definition of metabolic syndrome: report of the National, Heart, Lung And Blood Institute/American Heart Association conference on scientific issues related to definition.Circulatio n2004;109:433-438.
6. American Heart Association's description of Syndrome X.
7. Lakka HM, Laaksonen DE, Lakka TA, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men . JAMA.2002; 288:2709–2716.
8. Klein BE, Klein R, Lee KE. Components of the metabolic syndrome and risk of cardiovascular disease and diabetes in Beaver Dam. Diabetes Care. 2002;25:1790–1974.
9. Bernadette Boden-Albala, MPH, DrPH; Ralph L. Sacco, MD, MS; Hye-Sueng Lee, MS; Cairistine Grahame-Clarke, MRCP, PhD; Tanja Rundek, MD, PhD; Mitchell V. Elkind, MD, MS; Clinton Wright, MD, MS; Elsa-Grace V. Giardina, MD; Marco R. DiTullio, MD; Shunichi Homma, MD Myunghee C. Paik, PhD,Stroke. 2008;39:30-35; 2008 American Heart Association.
10. Najarian et al; American Stroke Association meeting report. 07 Feb 2004 - 0:00 PDT.
11. Alberti KG et al: The IDF Epidemiology Task Force Consensus Group. The metabolic syndrome—a new worldwide definition. Lancet 366:1059, 2005.
12. ES Ford et al ;NHANES, National Health and Nutrition Examination Survey; JAMA 287:356, 2002.
13. International Journal of Epidemiology 2004 33(4): 787-798.
14. William B. Kannel, MD; Paul Sorlie, MS ;The Framingham Study; Arch Intern Med. 1979;139(8): 857-861.
15. frenk J.Bobadilla JL,Sepulveda J ,Cervantes LM. Health transition in middle income countries : new challenges for health care . health policy and planning 1989;4(1):29-39.
16. Omran A. The epidemiologic transition : A theory of the epidemiology of population change .Milbank memorial fund quarterly 1971;49:509-538.
17. Omran AR . The epidemiologic transition theory : A preliminary update . J Trop Pediatr 1983;29:305-316.
18. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome-a new world-wide definition. A Consensus Statement from the International Diabetes Federation. DiabetMed 2006 May;23(5): 469-80.
19. Ninomiya JK, L'Italien G, Criqui MH, et al. Association of the metabolic syndrome with history of myocardial infarction and stroke in the Third National Health and Nutrition Examination Survey. Circulation. 2003; 109:42–46.

DOI Number: 10.5958/2321-1032.2017.00017.1

A Study of Microalbuminuria Levels among Patients with Type 2 Diabetic Complications in Western U.P

Ankita Sharma[1], Richa Sharma[2], Ankur[3], Jaison Paul[3], Ankit Tyagi[4], Sunny Khari[4], Kameshwar Prasad[5]

[1]Post Graduate III[rd] Year., [2]Assistant Professor, [3]Post Graduate II[rd] Year, [4]Post Graduate I[nd] Year, [5]Prof & HOD, Department of General Medicine Saraswathi Institute of Medical Sciences Hapur (U.P)

ABSTRACT

Objective- To study the levels of microalbuminuria among patients with type 2 diabetes and its complications in western UP.

Method- The study included 110 patients with Type 2 diabetes mellitus visiting the diabetic out-patient department. Patients with complications, such as hypertension, retinopathy and neuropathy were diagnosed based on history, clinical examination and related investigations. Microalbuminuria levels were compared in patients with complications (subjects) of Type 2 diabetes mellitus and patients without complications(control).

Results- The study revealed that microalbumin levels are at a significantly higher range in patients with complications ($p<0.05$) mainly with diabetic retinopathy, When compared to patients with other complications.

Conclusion-The study supports that microalbuminuria is significant among patients with diabetic complications and strict glycemic control can prevent microalbuminuria and thereby prevent progress on to diabetic nephropathy in patients with Type 2 diabetes mellitus.

Keywords- *Microalbuminuria, Diabetes mellitus, Diabetic Retinopathy, Hypertension, Diabetic Neuropathy.*

INTRODUCTION

Diabetes mellitus is the most common metabolic disorder characterized by chronic hyperglycemia and disturbances of carbohydrate, fat, and protein metabolism due to absolute or relative deficiency of insulin secretion or action [1]. Diabetes Mellitus (DM) is increasing globally particularly in developing countries. About 347 Million people worldwide have diabetes. In 2014, the global prevalence of DM was estimated to be 9% among the adults aged >18 years [2]. In 2012, an estimated 1.5 million deaths were directly caused by diabetes. More than 80% of diabetic death occurs in low and middle income countries[3]. WHO projects that diabetes will be 7th leading cause of death by 2030[4]. There is an emerging epidemic of diabetes in India with more than 62 million diabetics with diagnosed disease [5,6] It is predicted that by 2030 diabetes may affect 79.4 million individuals in India[7]

People with diabetes are at increased risk of chronic complications which affect many organ systems and are responsible for the majority of morbidity associated with the disease. The risk of chronic complications increases with the duration of hyperglycemia[8]. Chronic complication includes vascular complications microvascular (retinopathy, neuropathy, and nephropathy) macrovascular (coronary artery disease and cerebral vascular disease) [9].

Diabetic retinopathy (DR) is one of the leading causes of blindness in the world[10]. It is one of the most

Corresponding author:
Ankita Sharma
Post Graduate III[rd] Year, Department of General Medicine, Saraswathi Institute of Medical Sciences, Hapur (U.P), E-mail: drankita12475@gmail.com
Mob.: 7060375067

common microvascular complications, affecting 80% of patients over 20 years duration of diabetes[11]. Patients with DR have a higher chance of losing vision about 25 times compared to the normal population. The risk of developing DR or other microvascular complications of diabetes depends on both the duration and the severity of hyperglycemia[10]. In a clinical-based study, the overall prevalence of DR was 33.4% in Type 2 diabetic patients[12].

Interestingly, another study showed that 7% of Type 2 diabetic patients had DR even at the time of diagnosis of diabetes[13]. The prevalence of DR among the known and newly diagnosed diabetes was 23.1% and 10.9%, respectively. DR is detected clinically by the presence of visible ophthalmoscopic retinal microvascular lesions[14].

A link between renal and retinal angiopathy in diabetes has been long recognized, an effect that may be mediated through an increases in blood pressure, fibrinogen levels, and lipoproteins[15].

Diabetic neuropathy a heterogeneous disease affecting different parts of the nervous system that present with diverse clinical manifestations. They may be focal or diffuse. Most common among the neuropathies are chronic sensorimotor distal symmetric polyneuropathy and the autonomic neuropathies[16].

While a cross-sectional study of 6487 patients found a 28.5% prevalence of neuropathy (young *et al*. 1993), other series reported a range of 5-100%. Using comprehensive evaluation methods, neuropathy was present in 66% of diabetic patients in one series (Dyck *et al*. 1993) 8% have neuropathy at the time of diagnosis of diabetes mellitus, 50% after 25 years. The most common neuropathy was polyneuropathy, with a prevalence of 54% in insulin dependent diabetes mellitus and 45% in non-insulin dependent diabetes mellitus, while focal forms account for 25%. The prevalence increases with the duration of diabetes mellitus[17]. The diagnosis of diabetic peripheral neuropathy can only be made after a careful clinical examination, and all patients with diabetes should be screened annually for diabetic peripheral neuropathy by examining pinprick, temperature and vibration perception (using a 128-HZ tuning fork)[18].

Microalbuminuria has become a prognostic marker for cardiovascular disease (CVD), and the presence of microalbuminuria is an indication for the screening of possible vascular disease and aggressive intervention to reduce all cardiovascular risk factors [14,15]. Hypertension in patients with diabetes is a well-recognized cardiovascular risk factor[19].

Insulin resistance and hyperglycemia combine to make hypertension more prevalent in Type 2 diabetic patients[20]. Approximately 15% of hypertensive patients are diabetic and approximately 75% of Type 2 diabetic patients are hypertensive[21].

When urinary albumin excretion is 30-300 mg/24 hrs is known as microalbuminuria and referred to as having incipient nephropathy**.** In India, the prevalence of microalbuminuria varies from 19.7% to 28.5% of unselected Type 2 diabetic patients, whereas the prevalence of diabetic nephropathy in Type 2 diabetic is reported to be 5-9% from various Indian studies[22].

HbA1c could be used as an objective measure of glycemic control. It establishes a validated relationship between HbA1c and average glucose across a range of diabetes types and patients populations[23].

Diabetic nephropathy patients with Type 2 diabetes has a cumulative prevalence of 30-40% and is currently the leading cause of end-stage renal disease (ESRD)[24,25].

We tried to evaluate the level of urinary microalbumin among various complications of type 2 diabetes and to find out the risk of nephropathy in patients with various diabetes complications and whether there is any association between glycemic control, duration of diabetes, and microalbumin levels.

MATERIAL AND METHOD

The study was approved by the Ethical Committee of the Institute. This was a hospital based cross-sectional study conducted between May 2015 to May 2016 in the Department of General Medicine, Saraswathi Institute of Medical Science, Pilkhuwa, Hapur Uttar Pradesh, India. A total 110 patients were included 90 patients diagnosed with Type 2 diabetes mellitus and associated complications such as retinopathy, neuropathy, and hypertension as subjects and 20 patients with Type 2 diabetes mellitus as a control. Complications were diagnosed based on history, and clinical examination and related investigation were done.

Sample collection-Fasting blood samples were collected for estimation of blood glucose, creatinine,

HbA1c, and lipid profile and urine sample for microalbuminuria of subjects and control. Biochemical evaluations include fasting plasma glucose, postprandial glucose, HbA1c, lipid profile, serum creatinine, and urine microalbumin were analyzed. Plasma glucose was measured in auto analyzer OLYMPUS AU 400 based on enzymatic method (glucose oxidase and peroxidase) fasting lipid profile - total cholesterol (cholesterol-oxidase), triglyceride (glycerol-oxidase-peroxidase), high-density lipoprotein (enzymatic assay), low-density lipoprotein, very low-density lipoprotein, (Friedewald's calculation Method), and HbA1C (immunoturbidity method) was estimated using commercially available kit on the same day of collection

Statistical analysis- Data was collected and analyzed using SPSS software. The statistical significance was analyzed in the subjects and controls using the paired Student's t-test. Significance was considered for all tests ($p<0.05$).

RESULT

In our study, we tried to evaluate the levels of urine microalbumin in diabetics with complications and in diabetic patients without any complications who are considered as controls. Total 110 patients enrolled in the study, 62 male and 48 female.

90 patients had complications(cases) and 20 were without complications(control).

The study showed that urine microalbumin level in diabetics with peripheral neuropathy was found to be 89.4±75.5 compared to 15.6±14.2 in controls ($p<0.00$).

In diabetics with hypertension urine microalbumin level was 59.6±25.8 and in controls 15.6±14.2 ($p<0.00$).

In Diabetics with retinopathy urine microalbumin levels was 120.3±95.2 compared to 15.6±14.2 in controls ($p<0.00$).

It was also seen that the patients with diabetic retinopathy showed poor glycemic control with HbA1C levels being highest in them, HbA1c being 10.5±2.3 where as controls had good glycemic control with HbA1c being 5.4±0.7 ($p<0.00$)]

Table 1. Shows the level of Microalbuminuria among various complications of T2DM

Patients with T2DM	Microalbuminuria	p-value
Neuropathy	89.4±75.5	p<0.00
Hypertension	59.6±25.8	p<0.00
Diabetic Retinopathy	120.3±95.2	p<0.00
Diabetics without complication	15.6±14.2	p<0.00

DISCUSSION

Diabetes is a risk factor for various microvascular complications such as retinopathy, neuropathy, cardiovascular disease, and nephropathy. We conducted a study to evaluate the risk of nephropathy in patients with various complications associated with diabetes such as neuropathy, retinopathy, and hypertension. For this, we analyzed microalbuminuria levels in all these 3 complication groups and tried to assess the group which are at earliest risk of nephropathy.

Our study showed a significant increase in urine microalbumin levels and poor glycemic control in the study group when compared to control group.

The association between microalbuminuria DR, diabetic peripheral neuropathy, and hypertension in the present study could be explained by the view that microalbuminuria might represent a state of generalized vascular dysfunction.

Mohan *et al*. reported that the prevalence of DR was significantly higher in Type 2 diabetic patients with macroproteinuria (35%). Renal involvement only identifies a group of the diabetic patient at higher risk of developing complications. Some studies have reported that duration of diabetes, male sex, and pre-existing retinopathy as major risk factors for microalbuminuria[26].John *et al*. reported poor glycemic control and raised blood pressure as a risk factor of microalbuminuria[27].Some studies have reported that duration of diabetes, male sex, and pre-existing retinopathy as major risk factors for microalbuminuria[28,29].In the present study, duration of diabetes and lipid profile was not statically significant when compared with control.

In diabetic neuropathy study group, our result showed a significance increase in microalbuminuria levels when compared to control groups.

Florakowski *et al*. reported an association of microalbuminuria and neuropathy in the absence of retinopathy and suggested that this provides support for a microalbuminuria element in the pathogenesis of diabetic neuropathy[30].

Parving *et al*. also reported increased prevalence of peripheral neuropathy in patients with microalbuminuria and non-insulin dependent diabetes mellitus[31].

Young *et al.* reported an association between the advancement of motor, sensory, and autonomic neuropathy that was independent of glycemic control[32].

When compared to controls, there was no significant association between HbA1c and Urine microalbuminuria and duration of diabetes, even though it was reported in several studies. Urine microalbuminuria levels are significantly higher in retinopathy cases when compared to neuropathy and hypertension.

Retinopathy is easy to detect clinically,and typically precedes the onset of overt nephropathy in these patients.

The relationship between diabetic nephropathy and retinopathy is less predictable in type 2 diabetes. Based upon the correlation between retinopathy and nephropathy, the 2007 K/DOQI Guidelines for diabetes and chronic kidney disease suggest that chronic kidney disease should be attributed to diabetes in most patients with diabetes if microalbuminuria or proteinuria and diabetic retinopathy are both present[33]. By comparison, other causes of CKD should be entertained if diabetic retinopathy is absent.

Screening for microalbuminuria should be done in all type 2 diabetic patients at time of diagnosis. Annual screening should be done in patients who had not demonstrated microalbuminuria on first time examination. Glycemic and blood pressure control, particularly with angiotensin converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs), may reduce both microalbuminuria and progression to macroalbuminuria[34]. Clinical trials have also demonstrated efficacy of ACE inhibitors and ARBs and of glycemic control for the primary prevention of microalbuminuria and subsequent overt nephropathy in patients with type 2 diabetes

CONCLUSION

The presence of microalbuminuria is a powerful predictor of renal and cardiovascular risk in patients with Type 2 diabetes mellitus. Patients with Type 2 diabetes mellitus and associated complications such as retinopathy, neuropathy, and hypertension are at risk of developing diabetic nephropathy. Since Type 2 diabetes mellitus is slow onset disease and most of the Type 2 patients are unaware of the symptoms of diabetes mainly in rural population. Therefore, Screening for microalbuminuria is important for early detection and prevention of diabetic nephropathy.

Source of Funding-none

Ethical Permission –Taken from ethical committee of Institute

Conflict of Interest- None

REFERENCES

1. Prasad KD, Rajaseker P. Study of micro albuminuria as a cardiovascular risk factor in type diabetes mellitus. Iran J Kidney Dis 2012;3(1):12-6.
2. Global status report on noncommunicable diseases 2014. Geneva, World Healh Organization, 2012.
3. World Health Organization. Global Health Estimates: Deaths by Cause, Age, Sex and Country, 2000-2012. Geneva, WHO, 2014.
4. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med, 2006, 3(11):e442.
5. Joshi SR, Parikh RM. India - diabetes capital of the world: now heading towards hypertension. J Assoc Physicians India. 2007;55:323–4.
6. Kumar A, Goel MK, Jain RB, Khanna P, Chaudhary V. India towards diabetes control: Key issues.Australia Med J. 2013;6(10):524–31.
7. Whiting Dr, Guariguata L, Weil C, Shawj. IDF Diabetes atlas: Global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract. 2011;94:311–21.
8. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR, et al. Meta-analysis: Glycosylated hemoglobin and cardiovascular

disease in diabetes mellitus. Ann Intern Med 2004;141(6):421-31.

9. Powers AC. Diabetes mellitus. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Harrison's Principles of Internal Medicine. 16th ed. USA: The McGraw Hill Companies Inc.; 2005. p. 2152-80.
10. Taylor R. Practical community screening for diabetic retinopathy using the mobile retinal camera: Report of a 12 centre study. British diabetic association mobile retinal screening group. Diabet Med 1996;13(11):946-52.
11. Balasubramanyam M, Rema M, Premanand C. Biochemical and molecular mechanism of diabetic retinopathy. Curr Sci 2002;83:1507-13.
12. Rema M, Ponnaiya M, Mohan V. Prevalence of retinopathy in non-insulin dependent diabetes mellitus at a diabetes centre in southern India. Diabetes Res Clin Pract 1996;34(4):29-36.
13. Rema M, Deepa R, Mohan V. Prevalence of retinopathy at diagnosis among Type 2 diabetic patients attending a diabetic centre in South India. Br J Ophthalmol 2000;84(9):1058-60.
14. Gardner TW, Aiello P. Biochemical and molecular mechanism of diadetic. Am Acad Opthalmol Monogr 2000;14:1-18.
15 Root HF, Pote WH Jr, Frehner H. Triopathy of diabetes; sequence of neuropathy, retinopathy, and nephropathy in one hundred fifty-five patients. AMA Arch Intern Med 1954;94(6):931-41.
16. Boulton AJ, Vinik AI, Arezzo JC, Bril V, Feldman EL, Freeman R, et al. Diabetic neuropathies: A statement by the American Diabetes Association. Diabetes Care 2005;28(4):956-62.
17. Thomas FP. The spectrum of diabetic neuropathy. Phys Med Rehabil Clin N Am 2008;19(1):1-5. type-2 diabetes mellitus. Liver Int. 2009; 29(1): 113-119.
18. Abbott CA, Carrington AL, Ashe H, Bath S, Every LC, Griffiths J, et al. The North-West diabetes foot care study: Incidence of, and risk factors for, new diabetic foot ulceration in a community-based patient cohort. Diabet Med 2002;19(5):377-84.
19. Turner RC, Millns H, Neil HA, Stratton IM, Manley SE, Matthews DR, et al. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). BMJ 1998;316(7134):823-8.
20. Bell DS. Treatment of diabetic hypertension. Diabetes Obes Metab 2009;11(5):433-44.
21. Sever PS, Poulter NR, Dahlof B, Wedel H, Beevers G, Caulfield M, et al. The Anglo-Scandinavian cardiac outcomes trial lipid lowering arm: Extended observations 2 years after trial closure. Eur Heart J 2008;29(4):499-508.
22. Bouhanick B, Berrut G, Chameau AM, Hallar M, Bled F, Chevet B, et al. Predictive value of testing random urine sample to detect micro albuminuria in diabetic subjects during outpatient visit. Diabete Metab 1992;18(1):54-8.
23. Nathan DM, Kuenen J, Borg R, Zheng H, Schoenfeld D, Heine RJ; Ac-Derived Average Glucose Study Group. Translating the A1C assay into estimated average glucose values. Diabetes Care 2008;31(8):1473-8.
24. American Diabetes Association. Cardiovascular risk factor and disease management in Type 2 diabetes with diabetes nephropathy. Diabetes Care 2006;29(3):498-503.
25. Parving HH, Lewis JB, Ravid M, Remuzzi G, Hunsicker LG; DEMAND Investigators. Prevalence and risk factors for micro albuminuria in a referred cohort of Type 2 diabetic patients: A global perspective. Kidney Int 2006;69(11):2057-63
26. Mohan V, Meera R, Premalatha G, Deepa R, Miranda P, Rema M. Frequency of proteinuria in Type 2 diabetes mellitus seen at a diabetes centre in Southern India. Postgrad Med J 2000;76(899): 569-73.
27. John L, Rao PS, Kanagasabapathy AS. Prevalence of diabetic nephropathy in non-insulin dependent diabetics. Indian J Med Res 1991;94:24-9.
28. Klein R, Klein BE, Moss SE. Prevalence of micro albuminuria in older-onset diabetes. Diabetes Care 1993;16(10):1325-30.
29. Haffner SM, Morales PA, Gruber MK, Hazuda HP, Stern MP. Cardiovascular risk factors in non-insulin-dependent diabetic subjects with micro albuminuria. Arterioscler Thromb 1993;13(2): 205-10.
30. Florkowski CM, Jennings PE, Rowe B, Lawson

N, Nightingale S, Barnett AH. Micro albuminuria in diabetic subjects with chronic peripheral neuropathy. Diabetes Res Clin Pract 1988;5(1): 45-8.

31. Parving HH, Hommel E, Mathiesen E, Skøtt P, Edsberg B, Bahnsen M, et al. Prevalence of micro albuminuria, arterial hypertension, retinopathy and neuropathy in patients with insulin dependent diabetes. Br Med J (Clin Res Ed) 1988;296(6616): 156-60.
32. Young RJ, Maclntyre CC, Martyn CN, Prescott RJ, Ewing DJ, Smith AF, et al. Progression subclinical polyneuropathy in young patients with - Type 1 (insulin-dependent) diabetes: Associations with glycemic control and microangiopathy (microvascular complications). Diabetologia 1969;29:156-61.
33. KDOQI. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. Am J Kidney Dis 2007; 49:S12.
34. Arake S,Haneda M,Sugimoto T et al.Factors associated with frequent remission of microalbuminuria in patients with type 2 diabetes.Diabetes 2005;54:2983

DOI Number: 10.5958/2321-1032.2017.00018.3

Role of FNAC to Diagnose Cervical Tuberculosis

Ajay Kansal

Associate Prof. Pathology Sarasvati Institute of Medical Sciences, Hapur (U.P)

Introduction: Cervical Lymph Nodes (LN) are the second most common primary site of Tubercular infection after Lungs. For the diagnosis of Cervical Lymph-adenitis, clinicians often face challenges, since they have no easily accessible tools like X ray and Sputum exam. Fine Needle Aspiration Cytology (FNAC) offers an easy, effective and affordable option; this study was conducted to evaluate the efficacy of FNAC to diagnose the infection of Tuberculosis in cervical LN.

Methodology: The study involved 520 patients of cervical lymph-adenitis of all age group. FNAC of their enlarged Lymph Nodes were performed by 20 Gauge needle and 20 Millilitres syringe. After the result, the patients with Positive reports for TB were observed while taking ATT. And the patients with a Negative report were followed up for the progression of LN and the FNAC was repeated each month.

Result: Out of total 520 patients 443 were diagnosed Tubercular, 68 had reactive hyperplasia, 04 had malignancy and the rest 05 cases could not be diagnosed.

Conclusion: Almost all positive cases were proved to have TB; however, only a few per cent of negative cases were false negative and came out to have TB later. Thus, the combination of FNAC and follow-up may provide cent per cent results. This is enough to establish the efficacy of FNAC to diagnose cervical TB.

Keywords: *TB, Cervical Lymph-adenopathy, Cervical TB, FNAC, SIMS Hapur*

INTRODUCTION

Since time immemorial, Tuberculosis (TB) has been a very common infectious disease caused by various strains of Mycobacterium, the commonest being Mycobacterium Tuberculosis. TB infection primarily attacks human lungs, and cervical Lymph Nodes are the next common target; however it may infect and spread to almost all human organs.

Despite enough advancement in the anti-tubercular therapy, TB is still one of the biggest causes of morbidity and mortality, especially in developing countries.[1] One third of the world's population is thought to have been infected with M. tuberculosis. However, only one in ten develop clinical symptoms.[2] In 2007, there were an estimated 13.7 million chronic active cases all over the globe; in 2010, 8.8 million new cases were added and caused 1.5 million deaths, mostly in developing countries.[3] The development of multi-drug resistant cases has further worsened the devastating impact of this disease.

HISTORY

Modern microbiologists believe that this infection was not prevalent among our nomadic ancestors before domestication. However, after domestication of cattle, humans began to drink their milk without boiling, which had an almost similar bacterium as commensal. Consequently, the bacteria reached human intestine and their genetic transformation gave birth to different strains of MTB.[4] The oldest evidence of tubercular infection has been discovered in prehistoric human remains belonging to some 9,000 years ago. The most convincing evidence of TB infection was detected in the vertebra of a mummy in Egypt buried around 5,000 years ago.[5]

It is said that the great Egyptian king Akhenaten and his wife both died from TB; during his period, as early as 3500 years ago, hospitals for the disease existed in Egypt. The term Phthisis for this disease first appeared in Greek literature around 460 BC. Hippocrates has mentioned the illness as the most common cause of morbidity in his time. The first reference to tuberculosis in Asian civilization is found in the oldest surviving

text Rig Veda (1500 BC); it has named the disease as Yaksma.

During the last three thousand years, history mentions that TB killed countless people including famous kings, philosophers, scientists, writers and other dignitaries. Most people of that time believed that certain demons or vampires are responsible for the disease and they often used divine remedies to cure the patients. Famous German scientist Robert Koch's, in 1882, discovered the deadly killer behind the disease and was awarded Noble Prize for this ground breaking work.[6] Fifty years after this invention, Streptomycin, the first drug for TB was discovered.

Pathogenesis

The main cause of TB is Mycobacterium Tuberculosis (MTB), which is a small, aerobic, non-motile bacillus. The high lipid content of this pathogen accounts for most of its unique clinical characteristics. It divides every 16 to 20 hours, which is an extremely slow rate compared with other bacteria, which usually divide in less than an hour.[7] MTB can withstand weak disinfectants and survive in a dry state for weeks. The bacterium can grow only within the cells of an organism, but it can be cultured in the laboratory.

The mode of transmission of TB to a healthy person is inhalation of the droplets released into the air by coughing, sneezing or shouting of a patient.[8] These particles are between 1 to 5 micron in size and invisible to naked eyes; these may remain suspended in room air for a long time. Most infections are asymptomatic and latent; however, approximately one in ten infections eventually progresses to active disease, which depends upon the immune status of the person.

Diagnosis

The infection of TB instigates diverse symptoms according to the involved organs; therefore, different diagnostic tools are designed for each organ. In the cases of pulmonary tuberculosis, X ray chest offers a cheap, non-invasive and reliable tool to diagnose pulmonary TB cases. The bacterium may be identified in sputum under light microscope, after staining the smear by Ziehl Neelsen stain. The stain provides a bright red colour to the bacteria against a blue background. The positivity of this test is almost diagnostic. This examination carries the big chances of False Negative reporting.

However, sputum exam for MTB by PCR method offers an almost absolute tool to detect MTB. Furthermore, AFB culture is another very sensitive tool. Surprisingly, many Indian clinicians have not yet adopted both these very reliable tests as a routine. Apart from diagnosis, in the light of present day drug resistance cases, each affording TB patient must be advised for AFB culture and sensitivity.

In contrast to pulmonary TB, to diagnose the cases of cervical lymph node infections, only two invasive methods are available: FNAC and Histopathology. Histopathology requires surgical excision of the lymph node; however, FNAC is relatively less invasive and offers enough sensitivity and specificity. The material obtained by FNAC may be further examined to see the presence of MTB by PCR or AFB culture.

Investigations such as ESR, Montoux Test and ELISA for anti-Tubercular antibody are much popular, but they offer only a relative and ambiguous conclusion.

Apart from the above, recently, Interferon-gamma release assay (IGRA) or the TB Gold test, has gained popularity to diagnose tubercular infections anywhere in the body.[9] This test evaluates the cellular immune response of the patient to the bacteria in vitro, and reflects the presence of MTB inside. However, IGRA cannot distinguish between latent infection and active tuberculosis (TB) disease, and therefore cannot diagnose active infection, which is a microbiological diagnosis. In other words, a positive TB Gold result does not necessarily indicate the active TB; at the same time, a negative result may not rule out either the latent or the active infection.

Clinical Presentation

Tuberculosis may infect any part of the body, and the symptoms of active TB infection depend largely upon the involved organ. For instance, the infection of lungs cause chronic cough with sputum and that of cervical lymph nodes comes out with a lump in neck. However, all tubercular patients suffer from classic triad of fever, loss of appetite and loss of weight (this gave rise to the famous name 'consumption'). Infection of other organs causes a wide range of symptoms e.g. sterility in cases of female genital tract involvement. However, several patients remain asymptomatic for a long period and eventually develop some symptoms. TB has a special

affinity for the patients of HIV, since this reduces their resistance power.

MATERIAL AND METHOD

The study analysed a total 520 patients between January 2014 and October 2016. These patients arrived for FNAC at Ajay Pathology Clinic Hapur. The patients were attending the Medicine and Pediatric OPD of Saraswati Institute of Medicine Hapur U.P India. These all patients have cervical lymph-adenitis and belonged to all age group. Their clinical history and examination often revealed mild fever, loss of weight and appetite; all these indicated high possibility of TB. FNAC of their enlarged Lymph Nodes were performed with 20 Gauge needle and 20 Ml syringe; for this, the largest LN was preferred. The aspirated material was finely spread over glass slides, Giemsa Staining was done and these slides were studied under light microscope.

A smear of normal LN shows Lymphocytes and its precursors; however, smear of TB LN shows Lymphocytes, epitheliod cells, plasma cells and giant cells. Apart from these, the smear of TB LN shows very scanty cells. The slide has amorphous, granular, eosinophilic necrotic material, which is caseous material—the pathognomic feature of TB. The necrotic material often comes out as thick grayish yellow pus and its abundance helps facilitate the diagnosis, but it is not diagnostic. The cases of malignancy may also have similar necrotic material.

If we recollect the cut section of a TB LN, this often shows big round areas of caseation occupying almost ninety per cent of the area; this high ratio increases the success rate of aspiration. In order to further increase the success rate, we repeated the FNAC, with thicker needles, of the cases where we could not aspirate enough material. Apart from this, in cases we still found inadequate material, we washed the inner bore of the thick needle to procure even a trace of tissue of the LN.

Furthermore, we followed up the cases with a negative report and repeated their FNAC if they complained that their LNs were increasing or continuing some symptoms like fever.

OBSERVATION

After the study the data was compiled and that provided excellent insight about the efficacy of FNAC. Overall 443 patients were diagnosed Tubercular, 68 had reactive hyperplasia, four had malignancy and the rest 05 could not be diagnosed.

After the diagnosis, the physicians advised adequate ATT to the patients who had evidence of TB (443), and began to observe them. After three months, physicians evaluated their four parameters: occurrence of fever, appetite, weight and size of LNs. They were happy to see that almost all responded the ATT; however duration of their response was much variable. Their fever subsided, weight and appetite improved and the LN size regressed. We drew a conclusion that their diagnosis was invariably correct.

There were three unique patients who did not respond, rather their general condition deteriorated. They developed pulmonary TB, and they were either immuno-compromised or had multi drug resistance.

SUMMARY OF CLINICAL FEATURES

Table 1: Age distribution:

Age	No of Patients	Percentage
05-10 years	57	11 %
11-20 years	102	19.6 %
21-30 years	132	25.4 %
31-40 years	98	18.8 %
41-50 years	88	16.9 %
Above 51	43	8.2 %
Total	**520**	

Table 2: Summary of Presenting Symptoms

Symptom	No of Patients	Percentage
Cervical LN Enlargement	520	100%
Fever	460	88.4 %
Loss of Appetite	445	85.5 %
Loss of weight	390	75 %
Sputum	60	11.5 %
Weakness	495	95.2 %
Anemia	82	15.7 %

Table 3: Summary of the results of FNAC

Diagnosis	No of Cases	Percentage
Total	520	100
Tuberculosis	443	
False Positive	00	
Reactive Hyperplasia	68	
Group A (No Symptoms)	59	
Group B (Deteriorated)	09	Later Came out Tubercular
Malignancy	04	
Undiagnosed	05	

Table 4: Summary of Improvement in Symptoms

Symptom	Improvement after First Month	Second	Third	Forth
LN Enlargement	12 %	43%	62%	89%
Fever	34%	85%	100%	
Appetite better	45%	84%	100%	
Improvement of weight	28%	68%	100%	
Weakness	63%	92%	100%	
Anemia	33%	54%	78%	100%

DISCUSSION

Cervical Lymph Nodes are the second common site of Tubercular attack after lungs. This may further complicate with extension of infection to lungs, if patient is not diagnosed in time and does not take adequate ATT. The diagnosis of pulmonary TB is easy and efficient due to X ray and identification of TB bacterium in Sputum; however, for cervical TB, we have fever tools to diagnose. The blood tests such as TB Gold are also not much useful, since they provide ambiguous results more in extra-pulmonary cases. FNAC of cervical LNs is safe, easy and minimally invasive tool to diagnose TB and malignancy both.

The above study diagnosed 443 cases as Tubercular and they later proved to have TB with the help of follow up after ATT. However, the 09 False Negative cases out of total 68 negative cases were caught in the follow up FNACs, within two months.

The above study indicates that FNAC is a great tool that carries negligible False Positive reporting; however there are 1.7 % False Negative cases. This fallacy may be reduced to a certain extent by follow up FNAC and other measures those we took during this study.

CONCLUSION

The study proves that FNAC is an excellent tool that is much sensitive and specific. All the positive cases were proved to have TB; this indicates that positive case were diagnosed 100 % correctly. And only 1.7 per cent of the negative cases came out to have TB later. This is enough to establish the efficacy, both sensitivity and specificity, of FNAC to diagnose cervical TB. During the last two decades, FNAC has gained popularity in the view of its efficacy.

Ethical Clearance- No need

Source of Funding- Self

Conflict of Interest – Nil

REFERENCES

1. World Health Organization (2011). “The sixteenth global report on tuberculosis
2. “Tuberculosis Fact sheet N°104”. World Health Organization. November 2010. Retrieved 26 July 2011.
3. http://www.medicalnewstoday.com/articles/241155.php

4. Comas, I; Gagneux, S (2009 Oct). "The past and future of tuberculosis research". In Manchester, Marianne. PLoS Pathogens 5 (10): e1000600. doi: 10.1371/journal.ppat.1000600. PMC 2745564. PMID 19855821.

5. Zink A, Sola C, Reischl U, Grabner W, Rastogi N, Wolf H, Nerlich A (2003). "Characterization of Mycobacterium tuberculosis Complex DNAs from Egyptian Mummies by Spoligotyping". J Clin Microbiol 41 (1): 359–67. doi:10.1128/ JCM.41.1.359-367.2003. PMC 149558. PMID 12517873

6. Nobel Foundation. The Nobel Prize in Physiology or Medicine 1905. Accessed 7 October 2006.

7. Jindal, editor-in-chief SK (2011). Textbook of pulmonary and critical care medicine. New Delhi: Jaypee Brothers Medical Publishers. 525. ISBN 978-93-5025-073-0.

8. Konstantinos A (2010). "Testing for tuberculosis". Australian Prescriber 33 (1): 12–18

9. Ferrara G et al. (2006). "Use in routine clinical practice of two commercial blood tests for diagnosis of infection with Mycobacterium tuberculosis: a prospective study" (abstract). Lancet 367 (9519): 1328–1334. doi:10.1016/S0140-6736(06)68579-6. PMID 16631911.

DOI Number: 10.5958/2321-1032.2017.00019.5

Sero-prevalence and Co-infection of Hepatitis A & E Virus in Patients with Acute Viral Hepatitis at a Tertiary Care Hospital

Swati Salila[1], Suman Kumar[1], Kumar Vikram[1], Rakesh Kumar[2], Shailesh Kumar[3], Anima Xess[4], S K Shahi[4]

[1]JR, [2]Asst. Professor, [3]Assoc. Professor, [4]Professor, Department of Microbiology, IGIMS, Patna, Bihar, India

ABSTRACT

Introduction - Viral Hepatitis is a global public health problem. India is hyperendemic for Hepatitis A virus (HAV) and Hepatitis E virus (HEV) Enterically transmitted viral hepatitis is common in resource limited countries with limited access to essential water sanitation, hygiene and health services. This study was conducted to determine the prevalence of HAV and HEV in patients presenting with acute viral hepatitis(AVH) and co-infection of HAV and HEV in these patients. **Objective** - Prevalence of HAV, HEV and co-infection in patients with AVH . **Materials And Method**- Serum samples of 748 patients with symptoms of AVH were analysed for IgM anti-HAV and IgM anti-HEV for detection of HAV & HEV using ELISA kits. **Results** - Seroprevalence of HAV &HEV was 12.7% and 10.02% respectively.The sero-prevalence of both HAV & HEV was 3.07%. The males(88.23%) were affected more than females(11.76%). There was a slight increase in number during the month of August and September. **Conclusion** - The increase in prevalence during the monsoon suggests water contamination during these months hence, better water sanitation is recommended. Increased prevalence in males suggest more exposure to outside contaminated food as they travel more for job or business.

Keywords – *Acute viral hepatitis, HAV, HEV, coinfection.*

INTRODUCTION

Viral Hepatitis is a global public health problem. India is hyperendemic for Hepatitis A virus (HAV) and Hepatitis E virus (HEV)[1,2] . HAV and HEV are both enterically transmitted, resulting in acute viral hepatitis (AVH) in developing countries[3,4]. They pose major health problems in our country. HEV is also the major cause of sporadic adult acute viral hepatitis and acute liver failure (ALF). Pregnant women and patients with chronic liver disease constitute the high risk groups to contract HEV infection, and HEV-induced mortality among them is substantial, which underlines the need for preventive measures for such groups. Children with HAV and HEV coinfection are prone to develop ALF[2].

Corresponding author:-
Dr. Swati Salila
Junior Resident, Department of Microbioloy
IGIMS, Patna-800014, (M)-8521637372
Email:-dr.swatisalila@gmail.com

The disease may occur as outbreak or sporadic, both due to faecal contamination of drinking water[4]. The outbreaks frequently follow heavy rainfall and floods, which create conditions that favour mixing of human excreta with sources of drinking water, or in hot and dry summer months, possibly due to diminished water flow in rivers leading to an increased concentration of fecal contaminants[5]. Enterically transmitted viral hepatitis is common in resource limited countries with limited access to essential water sanitation, hygiene and health services[6].

HAV is a non-enveloped 27-nm, heat-, acid-, and ether-resistant ribonucleic acid (RNA) virus in the genus *Hepatovirus* of the family *Picornaviridae*[7].

HEV is a non-enveloped virus with a single-stranded positive-sense RNA in the genus *Hepevirus* of the family *Hepeviridae*[8].

HAV and HEV never progress to chronic hepatitis, either clinically or histologically. The vast majority of

hepatitis A patients make a full recovery, and the case fatality rate is low[9]. Current trend shows an increase in the prevalence of HAV and HEV co-infection, hence this study was conducted to determine the prevalence of HAV and HEV and their co-infection in patients presenting with AVH at IGIMS, a tertiary care hospital in Bihar.

MATERIALS & METHOD

The study was conducted from July 2015 to June 2016 in the Department of Microbiology. It is a cross sectional study done over a period of one year in patients with history of acute viral hepatitis attending OPD. Patients presenting with typical symptoms of acute hepatitis for several weeks i.e. fatigue, dyspepsia, anorexia, nausea, vomiting, jaundice and elevated amino-transferase levels[10] were selected. Samples with request of both HAV IgM and HEV IgM were included and their serum was tested by commercially available ELISA kit.

A total of 748 serum samples were analysed for IgM anti-HAV and IgM anti-HEV for detection of HAV & HEV using ELISA kits as per the guidelines provided by the commercial kit. The positive samples were tested again twice and then included in the study.

RESULTS

A total of 748 serum samples were processed for HAV and HEV IgM. Among 748 serum samples processed, 194 were tested positive for HAV and/or HEV. The sero-prevalence of co-infection was 3.07%.

Prevalance of mono-infection of HAV & HEV was 12.7% and 10.02% respectively. The males (76.47%) were affected more than females (23.52%). There was a slight increase in number of cases and percentage of positive individuals during the month of August and September.

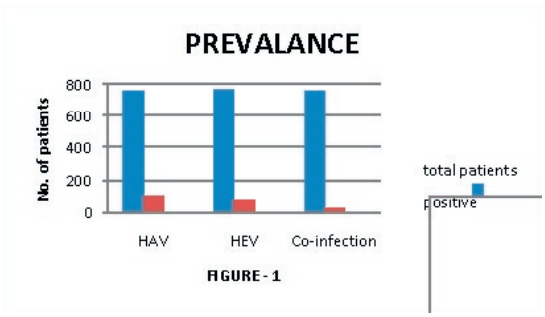

Figure 1 – Overall prevalence of HAV, HEV and co-infection

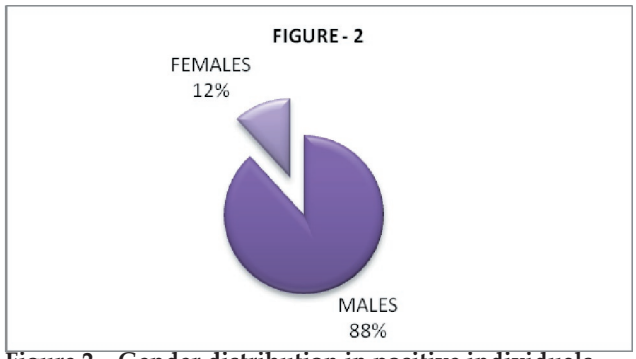

Figure 2 – Gender distribution in positive individuals

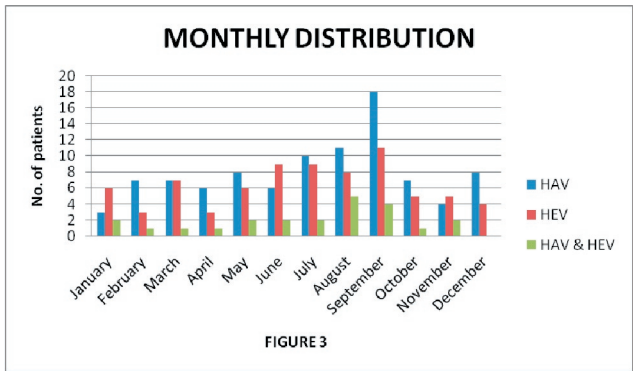

Figure 3 – Seasonal variation of positivity

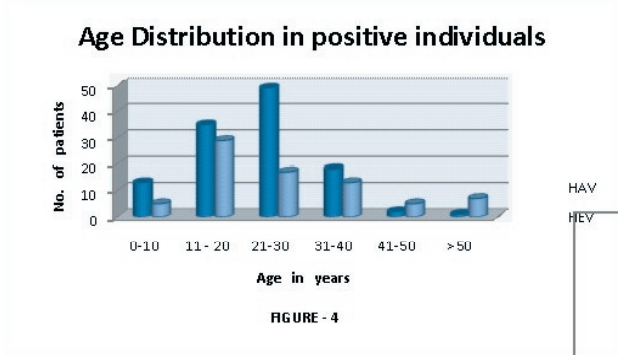

Figure 4 – Distribution of age among sero-positive individuals

DISCUSSION

Globally, HAV is found as the common cause of viral hepatitis[4,11]. Our study was conducted mainly to determine the prevalence of HAV and HEV and their co-infection in this region. In the present study, only 25.9% of the suspected cases had a positive viral marker. This was comparatively lower than the 49% as seen in another study[13]. A prevalence of 3.07% cases with co-infection of HAV and HEV was noted in our study. Other studies showed 11.5% (33 cases)[6],8.61% (23 cases)[4], 5.31%[13], 5.2% (25 cases)[1]. Co-infection with HEV and HAV did not affect the prognosis as these cases improved after symptomatic treatment. Acute hepatitis

A is usually improved by conservative management, but in another case report it was found that co-infection of HAV and HEV may lead to severe forms of disease such as hepatic encephalopathy[14]. This study shows a slightly higher percentage of HAV positive (12.7%) than HEV positive (10.02%) which correlates with the study results of *Jain et al*[4] and the same scenario is seen globally[11]. Generally, the incidence of Hepatitis A is closely related to the socioeconomic conditions of sanitation and hygiene. In India the vaccine against hepatitis A is available for the people who can afford it, but the government of India does not include it in the national immunization schedule hence, the economically deprived section of people are more susceptible to infection[15].

We found that prevalence of HAV was more than HEV with respect to age specificity HAV and HEV were predominantly seen among young adults, the risk and severity increases with age in HEV infection. The low prevalence of anti-HEV in children is attributable to lack of exposure to HEV in children [16] . The HEV infection preferentially reaches teenagers and young adults. In the same study, Hepatitis E was more common in young adults (15-44 years). This seems paradoxical for an enteral infection transmission, in which exposure is theoretically the same for all people subject to the terms of hygiene (Pawlotsky, 2001). It is possible that HEV infection is usually anicteric and goes unnoticed in children. These findings also agree with the results found in some other studies too[17,18]. Even in the adult population, the prevalence of HEV infection was markedly lower than that of HAV infection. The age-specific sero-prevalence of antibody to HEV was studied in Pune, India. Antibodies to HEV were uncommon in children and reached a peak prevalence of 33-40% in early adulthood. Prevalence of both HAV and HEV were higher in males than in females which has correlated with other studies[1,4,6] . It could be explained by a greater exposure of men in their professional and social activities.

Considering the seasonal variations, HAV and HEV were seen to be prevalent all around the year with predominance seen towards the end of monsoons and beginning of winters and also a peak rise of HEV during beginning of rainy season. Hepatitis E is mainly transmitted by cross contamination of drinking water with sewage. Hepatitis A was more common in late winter and Hepatitis E was more common in summer[1,6].

CONCLUSION

All the cases of AVH should be confirmed by serology for viral aetiology as a significant number of cases were positive(25.9%). Co-infection sometimes have poor prognosis so an initial screening is recommended. There is increased prevalence during the monsoon which suggests water contamination during these months hence, better water sanitation self hygine should be practiced.

Increased prevalence in males, suggest more exposure to outside contaminated food as they travel more for job or business therefore precaution should be taken while consuming outside food.

Hence, timely diagnosis by serology along with clinical suspicion may help in the proper management and prevention from complications.

Source of Funding: Self

Conflict of Interest: None

Ethical Clearance: Taken

REFERENCES

1. Monika Agrawal, Kapoor Ruchi, Bajaj Ashish, Saharia Pallab. Hepatitis A and E co-infection and seroprevalence. J of Med Sci and Health. 2016; 2(3).
2. Acharya SK, Madan K, Dattagupta S, Panda SK. Viral hepatitis in India. Natl Med J India. 2006 Jul-Aug;19(4):203-17.
3. Irshad M, Singh S, Ansari MA, Joshi YK. Viral hepatitis in India: A report from Delhi. Glob J Health Sci 2010; 2:96-103.
4. P Jain, S Prakash, S Gupta, KP Singh, S Shrivastava, DD Singh, J Singh, A Jain. Prevalence of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus and hepatitis E virus as causes of acute viral hepatitis in North India: A hospital based study. Ind J of Med Microbiol. 2010; 31(3):261-265
5. World Health Organisation, The Global Prevalence of Hepatitis E Virus Infection and Susceptibility: A Systematic Review; 2010.
6. Joon A, Rao P, Shenoy SM, Baliga S. Prevalence

of Hepatitis A virus (HAV) and Hepatitis E virus (HEV) in the patients presenting with acute viral hepatitis. Indian J Med Microbiol. 2015;33Suppl: 102-5.

7. WHO Hepatitis A Fact Sheet Updated 2015. http: //www.who.int/mediacentre/factsheets/fs328/en/.
8. WHO Hepatitis E Fact Sheet Updated 2015. http: //www.who.int/mediacentre/factsheets/fs280/en/.
9. World Health Organisation, The Global Prevalence of Hepatitis A Virus Infection and Susceptibility: A Systematic Review; 2010.
10. Braunwald E, Fauci AS, Kasper DL, Hauser SL, Longo DL,Jameson JL. Harrison's Principles of Internal Medicine. 18th ed.
11. Fischer GE, Thompson N, Chaves SS, Bower W, Goldstein S, Armstrong G, et al. The epidemiology of hepatitis A virus infections in four Pacific Island nations, 1995-2008. Trans R Soc Trop Med Hyg 2009;103:906-10.
12. Al-Naaimi AS, Turky AM, Khaleel HA, Jalil RW, Mekhlef OA, Kareem SA, et al. Predicting acute viral hepatitis serum markers (A and E) in patients with suspected acute viral hepatitis attending primary health care centers in Baghdad: A one year cross-sectional study. Glob J Health Sci 2012;4:172-83.
13. Das AK, Ahmed S, Medhi S, Kar P. Changing patterns of aetiology of acute sporadic viral hepatitis in India – Newer insights from North-East India. Int J Curr Res Rev 2014;6:14-20.
14. Park JH, Kim BS, Lee CH, Kim SY, Seo JH, Hur CJ. A case of co infection of Hepatitis A and E virus with hepatic encephalopathy. Korean J Med 2011;80 Suppl 2:S101-5.
15. Ramesh Verma, Pardeep Khanna. Hepatitis A vaccine should receive priority in National Immunization Schedule in India. Hum Vaccin Immunother 2012 Aug 1; 8(8): 1132–1134.
16. Takahashi M, Nishizawa T, Gotanda Y, Tsuda F, Komatsu F, Kawabata T, et al. High prevalence of antibodies to hepatitis A and E viruses and viremia of hepatitis B, C, and D viruses among apparently healthy populations in Mongolia. Clin Diagn Lab Immunol 2004;11:392-8.
17. Kamal SM, Mahmoud S, Hafez T, El-Fouly R. Viral Hepatitis A to E in South Mediterranean Countries. Mediterr J Hematol Infect Dis 2010;2: e2010001.
18. Pelosi E, Clarke I. Hepatitis E: A complex and global disease. Emerg Health Threats J 2008;1: e8.

DOI Number: 10.5958/2321-1032.2017.00020.1

Insulin Resistance in Polycystic Ovarian Syndrome

Ajay Kansal[1], Pawan Singhal[2]

[1]Associate Prof. Pathology SIMS, Hapur, U.P, [2]Prof. & Head Radiology, Rama Medical College, Hapur, U.P

ABSTRACT

Introduction: Polycystic ovary syndrome (PCOS) is a hormonal and metabolic disorder, which affects around 3 to 10 per cent women of child bearing age. Its diagnosis is not straight forward but depends upon clinical, ultra-sonological and pathological findings.

Methodology: The study involved 204 patients of Irregular menstrual cycle, Hirsutism and or Weight gain. Ultrasound examination was done and 28 patients fulfilling the sonological criteria of PCOS were selected; these were followed up by Glucose Tolerance Test and Hormonal Assessment. Out of total 28 cases of PCOS, 18 cases had high Insulin levels and Impaired Glucose Tolerance.

Result: Around 64 % cases of PCOS had Insulin Resistance

Conclusion: Insulin Resistance is very common in cases of PCOS

Keywords: *PCOS, Obesity in females, Hirsutism, Infertility, SIMS Hapur*

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a heterogeneous disorder, which affects around three to ten per cent women of child bearing age.[1] PCOS was first reported by Stein and Leventhal in 1935. Women with PCOS have a hormonal imbalance and metabolism problem that may affect both health and cosmetic appearance. This is a common cause of infertility. More than half of the patients of PCOS are obese.

Symptoms of PCOS

Patients of PCOS presents with varying degree of symptoms. Several patients are having very mild problem of menstrual irregularity and they do not bother to consult until they marry and notice infertility. Several patients consult just after they watch hairs on their face. Irregular menstrual cycle, excessive body and facial hairs, acne, weight gain and Infertility are the prominent symptoms of PCOS.[2] More than 80% of women presenting with symptoms of androgen excess like hirsutism and acne have PCOS.

Pathogenesis:-

- Modern Life style changes such as sedentary schedule and high calorie food facilitate obesity and PCOS in young females. The exact cause of polycystic ovary syndrome is unknown. However, PCOS supposed to be caused by a combination of genetic and environmental factors.[3]

- **High level of insulin**– Many women with PCOS have insulin resistance especially those who are obese.[4] They have unhealthy eating habits, do not do enough physical activity and may have family history of diabetes. Insulin resistance reduces utilization of glucose into the cells. Consequently blood glucose increases, and glucose inside the cells is reduced. Cells start starving and that triggers pancreas to produce more Insulin: the level of Insulin increases in blood. Thus, despite high levels of Insulin in blood, patients have high blood glucose levels.

- **High level of androgens**- Hyper-insulinemia increases androgen production by theca cells of ovaries. Apart from this, high Insulin reduces hepatic production of sex hormone binding globulin; this results in higher concentration of free androgen.[5] The prevalence of insulin resistance in PCOS is 50 to 70% and is independent of obesity.[6] The effect of obesity on insulin resistance is additive of that of PCOS.

- Women with PCOS have more androgens

than oestrogens, which prevents ovulation and causes hirsutism and acne.[7] The follicles growth is arrested after follicles reach a diameter of 4 to 8 mm. Thus several small and un-ruptured follicles are formed in each ovary. The size of ovaries increases from 10 ml to more. Since dominant follicles do not rupture, ovulation does not occur.[8]

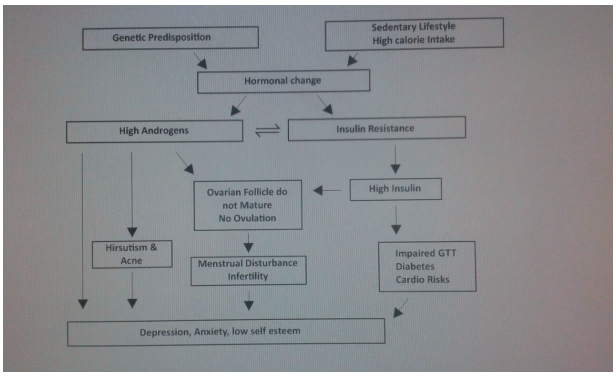

Illustration 1: Pathogenesis of PCOS and its Symptoms

• PCOS seems a benign condition; however, some untreated patient may develop diabetes and Ischemic Heart Disease.[9] Some patients may develop endometrial Hyperplasia and that may increase their chances of Endometrial Carcinoma.[10] Some studies state that the patients of PCOS are at higher risk of Ovarian and Breast carcinoma; however. These are not yet well established. Early diagnosis, control of weight gain and other treatments may reduce the risk of these long-term complications.

• Valproic acid, an antiepileptic drug widely used to treat epilepsy is associated with development of the features of PCOS when used to treat women with epilepsy.

Clinical Criteria of PCOS:- Patient must have at-least two of the following symptoms:

o Irregular periods i.e. oligo-menorrhoea, amenorrhoea and menorrhagia.

o Signs of excess androgens such as hirsutism & acne.

o High levels of androgen in blood.

o Multiple cysts in both ovaries (PCOM).

Sonological criteria of PCOS:-

o Presence of 12 or more follicles of less than 10 mm.

o Increased ovarian volume of more than 10 cc.

o Maximum dimension of at least one ovary is more than 3.5 cm.

This presentation in one ovary is enough to diagnose the polycystic ovary; however, 30% patients with clinical presentation of PCOS have normal ovaries.

Exclusion diagnosis of PCOS:-

The diagnosis of PCOS requires exclusion of all other disorders that can result in menstrual irregularity and hyper-androgens. We must exclude adrenal or ovarian tumours, thyroid dysfunction, congenital adrenal hyperplasia, hyper-prolactinemia, acromegaly and Cushing syndrome.

Lab test to rule out other conditions with similar signs and symptoms:-

• TSH – to rule out thyroid dysfunction.

• Cortisol – to rule out Cushing syndrome.

• Prolactin – to rule out hyper-prolactinemia.

• 17 – hydroxyprogesterone - to rule out congenital adrenal hyperplasia.

Hormone Levels in PCOS:-

• Serum Insulin is high in many cases

• FSH – will be normal or low with PCOS.

• LH – will be elevated, resulting in reversal of LH / FSH ratio.

• Testosterone – usually elevated.

• Oestrogen – may be normal or elevated.

• Sex hormone binding globulin – may be reduced.

Patients of PCOS may have higher rates of

• Miscarriage.

• Gestational diabetes.

• Preeclampsia.

• Dyslipidemia & hypertension.

• Mental disorder like depression, bipolar

disorder, anxiety & eating disorder.

PCOS is the most common cause of infertility. In addition, spontaneous abortion occurs more frequently in PCOS with incidences ranging from 40 to 70%.

Management of PCOS:-

Weight loss is recommended as first line therapy for the management of PCOS especially for overweight women. Metformin is a very useful drug that decreases carbohydrate absorption and reduces weight. It improves insulin sensitivity; thus reduces insulin concentration in blood. Insulin normalization reduces androgen levels. Apart from drug, adequate diet and exercise are the more effective measures; they manage the core pathology of Insulin Resistance.

Obese patients with anovulation do not respond well to fertility treatments including clomiphene and gonadotropins. Weight loss of 5 to 10% can increase ovulation & pregnancy rate. After weight loss, the role of clomiphene, gonadotropins & laparoscopic ovarian drilling start. Letrozole and metformin may play an important role in ovulation induced menstrual disturbances; however, 30% of women with PCOS may have normal cycle.

Clomiphene increases the release of FSH from pituitary gland. The starting dose is 50 mg per day for 5 days starting on days 2-5. If ovulation does not ensue dose is increased by 50 mg per cycle to maximum dose of 150 mg per day. The maximum number of cycles is limited to 6 ovulatory cycles. If ovulation is not induced at doses of 150 mg per day, the patient is considered as clomiphene resistant.

The role of metformin for ovulation induction in PCOS is limited but metformin plays important role in improving conception when administered 3 months prior to & concurrent with infertility treatment.

PCOS management also includes oral contraceptive for menstrual irregularities and hirsutism. Women often use laser hair removal because pharmacologic treatment do not produce desired results. They may wait at least 6 months of treatment to see a response due to growth cycle of hair. Anti-androgen can be added, if there has been no improvement after 6 months of treatment. OCPs and anti-androgens have both been effective in treatment of acne.

MATERIAL AND METHOD

The study analysed a total 204 patients between March 2015 and November 2016 in Hapur. These patients arrived in gynaecology OPD to consult for their menstrual irregularity, Facial hairs and or Obesity. The study involved these 204 young females from 15 to 30 years of age having at least two or more symptoms of PCOS viz. Irregular menstrual cycle, Facial Hairs and Weight gain.

SUMMARY OF CLINICAL FEATURES

Table 1: Age distribution:

Age	No of Patients	Percentage
15-20 years	59	29 %
20-25 years	123	60 %
25-30 years	22	11 %
Total	**204**	

Table 2: Summary of Presenting Symptoms

Symptom	No of Patients	Percentage
Menstrual Irregularity	204	100%
Obesity	154	75 %
Hairs on Face	21	10 %
All the three	19	09 %

Ultrasound examination was done and the patients fulfilling the sonological criteria of PCOS were selected. Most of patients had 12 or more follicles of less than 10 mm diameter. These follicles increased the ovarian volume more than 10 cc.

Out of total 204 patients only 28 fulfilled the sonological criteria of PCOS. These were followed up by Glucose Tolerance Test and Serum Insulin levels.

Glucose tolerance test includes taking sample of fasting serum glucose. After the sample, patient ingests 75 gm. Glucose. After glucose, blood samples are taken at each half hour interval until two and a half hour. That means half hour sample, one hour and so on. Serum glucose levels of all these six samples are estimated.

Fasting Serum Glucose level must be less than 115 mg/ dl. And the post Glucose samples must be below 140 mg/ dl. Any fasting sample above the normal indicates Impaired Glucose Tolerance Test. Any post Glucose

sample above 140 mg/ dl indicates Impaired Glucose Tolerance Test. However, fasting sample above 140 and any Post Glucose sample above 200 indicates Diabetes.

Out of 28 PCOS cases, 18 showed increase level of serum Insulin. These all 18 cases had Impaired Glucose Tolerance Test. However, only 4 cases had overt diabetes that is Fasting Glucose level more than 140 mg/ dl and one of the Post Glucose sample had glucose levels more than 200 mg/ dl.

Table 3: Summary of the results

Diagnosis	No of Cases
Total	204
PCOS by Ultrasound	28
High Insulin	18
Impaired GTT	14
Diabetic	04

DISCUSSION

The study establishes that most women with PCOS had high insulin levels. This points to Insulin resistance. This was more common in obese females. They have unhealthy eating habits, do not do enough physical activity and may have family history of diabetes. In this study the prevalence of insulin resistance in PCOS is 64%. Obesity increases the magnitude of insulin resistance.

As already stated that the Insulin resistance reduces entry of glucose into the cells. Consequently, blood glucose inside the cells is reduced. Less glucose in cells triggers pancreas to produce more Insulin. Thus level of Insulin increases in blood. High Insulin level increases androgen production by theca cells of ovaries. Apart from this, high Insulin reduces hepatic production of sex hormone binding globulin; this results in higher concentration of free androgen. Thus high insulin is responsible for high androgen.

High androgens than oestrogens causes hirsutism and acne. This prevents ovulation and thus follicle growth is arrested when they reach a diameter of 4 to 8 mm. Thus several small and un-ruptured follicles are collected in each ovary. The size of ovaries increases from 10 ml to more. Since dominant follicles do not rupture to produce ovum that causes infertility. Insulin resistance seems to be the core factor behind PCOD.

RESULT

The study indicates that around 64 % cases of PCOS had Insulin Resistance

CONCLUSION

Insulin Resistance is very common in cases of PCOS

Ethical Clearance- No need

Source of Funding- Self

Conflict of Interest – Nil

REFERENCES

1. http://www.nichd.nih.gov/health/topics/PCOS/conditioninfo/Pages/risk.aspx
2. http://www.nichd.nih.gov/health/topics/PCOS/conditioninfo/Pages/symptoms.aspx
3. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4947298
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909929
5. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2859983
6. https://www.ncbi.nlm.nih.gov/pubmed/14752302/
7. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909929/#B21
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909929/#B30
9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2909929/#B34
10. https://en.wikipedia.org/wiki/Polycystic_ovary_syndrome#cite_note-BarryAzizia2014-96

DOI Number: 10.5958/2321-1032.2017.00021.3

A Study of Prognostic Value of Glycosylated Hemoglobin in Acute Coronary Syndrome

S Ramkumar[1], S Dharmalingam[2]

[1] Associate Professor, [2]Assistant Professor, Department of Medicine , Karpagam Faculty of Medical Sciences and Research, Othakkalmandapam, Coimbatore, Tamil Nadu. India

ABSTRACT

Background: The role of HbA1c (Glycosylated Hemoglobin) in predicting the outcome of acute coronary syndrome remains largely controversial .

Objective: To determine the impact of HbA1c levels on the severity and complications of acute coronary syndrome in non-diabetics.

Method: This prospective study included 80 patients without diabetes mellitus who were admitted to the ICCU with ACS. The diagnosis of ACS was made on the basis of troponin T value , ECG and echocardiograph . Patients were classified according to their HbA1c into two groups: Group 1 HbA1c <5.6, group 2 HbA1c between 5.7 and 6.4 . Main outcome measures were ECG changes , trop T value , echo changes, along with the complications .

Results: The mean age of patients was 56.67 years out of which 69% were males and 31% females. Of total, 27% were smokers, 33% were hypertensive, 30% had dyslipidemia and BMI was ≥ 25 kg/ m2 in 10 % of the subjects. The findings of this study found that increased levels of HbA1c were associated with poorer result in the non-diabetics.

Conclusion: HbA1c is an index of major adverse outcomes in acute coronary syndrome in patients with non diabetics. Assessment of HbA1c levels might progress the risk assessment in patients with ACS.

Keywords: *acute coronary syndrome, HbA1c ,non-diabetics*

INTRODUCTION

In recent years, much attention has been paid to the glycometabolism in patients with coronary artery disease (CAD). Numerous prior studies have shown that elevated

HbA1C increases the risk of death and in-hospital complications in patients with acute coronary syndrome (ACS) and in patients undergoing coronary revascularization[1,2]. Epidemiological evidence now suggests that HbA1c level is an independent risk factor for cardiovascular events in primary and secondary populations [3,4]. However, the prognostic value of HbA1c level in patients with coronary atherosclerotic disease has not been well established , and the studies that examined this relationship have reported conflicting results [5,6]. Diabetes is considered a highly 'vascular disease' with both microvascular and macrovascular complications .Macrovascular complications start taking place long before the patient develops overt diabetes.This could reflect blood testing being performed during the hospitalization in patients with previously unrecognized diabetes. In addition, stress of MI unmasks or worsens the tendency toward hyperglycemia. Hyperglycemia is an independent risk factor for cardiovascular disease.

Corresponding author:
Dr. S Ramkumar
Associate Professor, Department of Medicine
Karpagam Faculty of Medical Sciences and Research
Othakkalmandapam, Coimbatore - 641 032.
Tamil Nadu. India.

Coronary tissue from diabetics contained a greater amount of lipid-rich atheroma and more macrophage infiltration, both of which are associated with a greater risk for plaque rupture, and a higher incidence of CHD[7,8].Hyperglycemia accelerates the process of atherosclerosis by the formation of glycated proteins and advanced glycation end products, which act by increasing the endothelial dysfunction.In patients with acute coronary syndrome, up to 40% have impaired blood glucose levels on admission [7,8].This has been associated with increased mortality, irrespective of diabetic status .In non-diabetic patients, the at-admission plasma glucose level predicts both long term morbidity (for example, re-infarction, hospitalization with heart failure, adverse ventricular remodeling) and mortality [9]. Recent evidence has shown that chronic glucose dysregulation, assessed by HbA1c levels, is also of prognostic value with regard to future CVD and congestive heart failure .To comprehensively analyze these data, we performed a systematic review to examine whether an association exists between elevated HbA1c (Glycosylated Hemoglobin) and cause of mortality in patients hospitalized with ACS.

METHOD

This is a prospective study at conducted at Karpagam Medical College Hospital, Othakkalmandapam, Coimbatore , during the period (May 2015 – June 2016). 80 patients who were admitted to the CCU with ACS were selected; with mean age of 58.67 years . Patients' data of age, sex, body mass index, history of diabetes mellitus, hypertension, smoking and hyperlipidemia was obtained. Serum levels of the following parameters were tabulated: Glycosylated haemoglobin (HbA1c), fasting total serum cholesterol, low density lipoprotein (LDL),cholesterol and high density lipoprotein (HDL). Patients were excluded if they had history of Fasting blood sugar ≥126 (7 mmol/L),postprandial blood sugar ≥200 (11.1 mmol/L) after a 75g oral glucose,HbA1c level >6 ,CKD on maintenence dialysis and uremia , CLD, Sepsis, Hypothryoidism, those who donated blood recently or Acute & chronic blood loss, Gestational DM, Excessive alcohol intake, Haemoglobinopathy (Sickle cell anemia, Thalassemia, G-6 PD deficiency), Treatment of anemia with iron or erythropoietin, Autoimmune hemolytic anemia . Patients were stratified according to their HbA1c level into two groups; group 1: <5.6(n = 36) and group 2: 5.7-6.4 (n=64).

Left Ventricular Ejection Fraction was measured by Simpson's method using 2-dimentional echocardiography. BMI was measured as weight (kg)/ height (m2) and obesity was defined as BMI ≥ 30kg/ m2 (27). By using SPSS (statistical package for social sciences) software all data of different variables were entered and analyzed with appropriate statistical tests and procedures.Level of significance (p-value) was set at $P \leq 0.05$.

RESULTS

In this study 80 ACS patients were enrolled with mean age of 56.67 years. The number of male patients was 69 as compared to 31 females with a sex ratio of approx 2 : 1 . Most of the patients were in the age group of 40 to 60 years.

In our study 54 out of 80 patient were of high normal HbA1c , and 26 belonged to normal HbA1c. The mean value of HbA1c in patients with normal HbA1c was 5.2± 0.14 and in patients with high normal HbA1c were 6.17± 0.16 (table 1).

There were 72.27%(39out of 54 patients) cases of ST segment elevation MI in high normal HbA1c level patients as compared to 57.65%(15 out of 26 patients) in normal HbA1c level patients(table 2).

In all 80 patients, Trop T values were estimated. Patients with high normal HbA1c levels had mean Trop T value 2179.3±252.1 as compared to patients with normal HbA1c level with mean Trop T value 1915.9±244.7 with p value <0.0001 which is statistically significant ,which means these two groups are significantly different.

In our study, 61 cases out of 80 were positive for presence of RWMA on ECHO. Out of these, 49(80.66%) patients had high normal HAb1C and 12(19.33%) patients had normal HAb1C.

In all 80 patients, LVEF was estimated by ECHO and mean LVEF was 43.64%. Patients with high normal HbA1c level had lower LVEF with mean EF of 38.22 ± 11.54 as compared to patients with normal HbA1c level with mean 47.64 ± 8.32 with p value <0.0001.

Patients were assessed clinically for signs of heart failure and were then grouped according to their HbA1c levels. It was found that the percentage of heart failure in high normal HbA1c level patients were 65.75% (12 out of 16 patients) as compared to 32.25%(6 out of 16

patients) in normal HbA1c level patients (table3).

Electrocardiogram was obtained in all the patients included in this study and the patients were divided on basis of arrhythmia on presentation. The percentage of arrhythmia in high normal HbA1c level patients was 68.23% (9 out of 12 patients) as compared to 29.77% (4 out of 12 patients) in normal HbA1c level.

TABLE 1: NUMBER OF PATIENTS AND THEIR HbA1c LEVELS

	NUMBER	MEAN	SD
NORMAL HbA1c (< 5.6)	26	5.2	0.14
HIGH NORMAL HbA1c (5.7- 6.4)	54	6.12	0.16
Total	**80**	**5.9**	**0.15**

TABLE 2 ECG CHANGES OF ACS IN RELATION TO HbA1c

	NSTEMI	STEMI	TOTAL
NORMAL HbA1c	11(30.55%)	15(69.45%)	26
HIGH NORMAL HbA1c	15(23.43%)	39(76.57%)	54

TABLE 3 HEART FAILURE IN ACS PATIENTS IN RELATION TO HbA1c

	HEART FAILURE +	HEART FAILURE -	TOTAL
NORMAL HbA1c	6(31.25%)	20(36.90%)	26
HIGH NORMAL HbA1c	12(68.75%)	42(63.09%)	54

DISCUSSION

The objective of this study to evaluate the prognostic value of HbA1c in non diabetic patients presenting with Acute coronary syndrome. 80 patients (diagnosed as per clinical symptoms , ECG changes, Trop T values), who were above 30 years of age and gave consent, were enrolled in this study. Different metabolic parameters, ECG, Echo criteria were evaluated in them. The results were analyzed in terms of demographic profile (age and sex), metabolic parameters (blood sugar- both fasting and postprandial, HbA1c, lipid profile, Trop T , BMI), ECG and Echo criteria, severity (Trop T quantitative levels , EF, RWMA, ECG) and complications (LVF, arrhythmia). In the current study we found a relation between HbA1c and poor outcome among patients of ACS without known diabetes. Elevated HbA1c level was a strong and independent predictor of severity and complication in ACS patients even in non- diabetics. Khaw KT, et al. showed that an elevated HbA1c is associated with increased cardiovascular risk in patients with and without diabetes [10] . Increasing HbA1c levels were clearly associated with adverse baseline characteristics such as a higher cardiovascular risk profile, explaining in part the poorer outcome of ACS. In a systematic review of 15 studies (1966–1998) on AMI, the association of hyperglycaemia with increased in-hospital mortality was stronger in non-diabetic patients than in diabetic patients [11]. In a study conducted in Asian Indians with normal glucose tolerance (NGT), a strong correlation of HbA1c and cardiovascular risk factors was found. NGT subjects with three or more metabolic abnormalities had the highest HbA1c levels and an HbA1c cut off point of ≥ 6.5% was found to have the highest accuracy in predicting both metabolic syndrome and coronary artery disease [12]. Elevated glucose is not only a feature of glucose dysregulation , but also of stress and a more high-risk patient population. Stress hyperglycemia is a common occurrence in patients admitted to the intensive care units with acute coronary syndrome. Hence , elevated HbA1c levels can be predictive for cardiovascular disease and mortality in patients without diabetes mellitus, regardless of fasting glucose levels, a finding that was suggested in a recent cohort study [13] .In addition to the effect of associated insulin resistance, excess glucose may be directly detrimental during ACS, offering a target for treatment. The molecular mechanisms for this adverse effect include the promotion of oxidative stress, non-enzymatic glycation of platelet glycoproteins with abrupt changes in aggregability, amplification of inflammation, and suppression of immunity [14].

In fact, some studies have shown even higher cardiovascular mortality and morbidity in patients with hyperglycemia in previously undiagnosed diabetes than in patients with known diabetes or normoglycemic subjects [15] .In addition, part of the association between longterm abnormalities in glucose control and outcome is due to the same complex mechanisms responsible for

the adverse association between overt diabetes mellitus and cardiovascular outcome.

Our study found that the ST segment elevated ACS is more common in high normal HbA1c group as compared to normal HbA1c group.

Also, we found that most of the patients with high normal HbA1c have higher Trop T values as compared to most of the patients with normal HbA1c.

Even RWMA on echocardiography was more common in high normal HbA1c group (66.66%) as compared to normal HbA1c group (33.33%).

In our study,we found that most of the patients having high normal HbA1c had lower LVEF (mean 38.22% ±11.54) as compared to most of the patients with normal HbA1c,who had higher LVEF (47.64% ±8.32).

Manal Khudhur Abdul Razzaq et al, showed that the mean EF was significantly lower in group HbA1c 6.5-8.5 and in group HbA1c >8.5 as compared with that group <6.5. A linear decrease in EF was found with rising HbA1c levels in patients with unstable angina (p value =0.0043), with STEMI (p value=0.0290) and NSTEMI(p value=0.0015) [16]. Patients were assessed clinically for signs of heart failure and were then grouped according to their HbA1c levels. It was found that the percentage of heart failure in high normal HbA1c level patients were 65.75% (12 out of 16 patients) as compared to 32.25%(6 out of 16 patients) in normal HbA1c level patients.

CONCLUSION

This study shows that ACS patients without known diabetes mellitus are associated with poorer outcomes if they have higher levels of HbA1c. High normal HbA1c is associated with more complications like LVF and Arrhythmia. High normal HbA1c is also associated with more severe ACS in terms of higher levels of Trop T ,lower EF, presence of RWMA on ECHO, Presence of ST elevation on ECG as compared to normal HbA1c patients.

Source of Funding – Nil

Conflict of Interest - Nil

Ethical Clearance – Taken

REFERENCES

1. ADA Position Statement; Standards of Medical Care in Diabetes - 2010. Diabetes Care 2010; 33(Suppl-1): S11-61
2. Sato K K , Hayashi T, Nobuko H , Younda T, Nakamora Y, Endo G, et al, Combined measurement of fasting plasma glucose and A1C is effective for the prediction of type 2 Diabetes; The Kansai Healthcare Study. Diabetes Care 2009; 32: 644-6.
3. Shechter M, Merz CN, Paul-Labrador MJ, Kaul S .Blood glucose and platelet dependent thrombosis in patients with coronary artery disease. J Am Coll Cardiol2000; 35:300-7.
4. Coisne D, Mauco G, et al. Prognostic value of admission plasma glucose and HbA1c in acute myocardial infarction. Diabet Med 2004;21:305-10.
5. Bauters C, Ennezat PV, Tricot O, et al. Stress hyperglycemia is an independent predictor of left ventricular remodeling after first anterior myocardial infarction in non diabetic patients. Eur Heart J2007;28:546 52
6. O'Sullivan CJ, Hynes N, Mahendran B, Andrews EJ, Avalos G, Tawfik S, Lowery A, Sultan S. Haemoglobin A1c (HbA1C) in non-diabetic and diabetic vascular patients. Is HbA1C an independent risk factor and predictor of adverse outcome? Eur J Vasc Endovasc Surg. 2006 Aug;32(2):188-97. Epub 2006 Mar 31.
7. Cao JJ, Hudson M, Jankowski M, Whitehouse F, Weaver WD. Relation of chronic and acute glycemic control on mortality in acute myocardial infarction with diabetes mellitus. Am J Cardiol 2005; 96:183-86.
8. Capes S, Hunt D, Malmberg K, et al. Stress hyperglycemia and increased risk of death after myocardial infarction in patients with and without diabetes: a systematic overview. Lancet 2000; 355: 773–78
9. Dilley J, Ganesan A, Deepa R, et al. Association of A1c with cardiovascular disease and metabolic syndrome in Asian Indians with normal glucose tolerance. Diabetes Care 2007; 30:1527-32.
10. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of haemoglobin A1c with cardiovascular disease and mortality in adults:

the European prospective investigation into cancer in Norfolk. Ann Intern Med 2004; 141: 413-20.

10. UKPDS group. Intensive blood-glucose control with sulphonylureas or insulincompared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837-53.
11. Stratton IM, Adler AI , Andrew WN, Mathews DR, Manley SE, Cull CA, et al. Association of glycaemia with macro vascular and micro vascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ 2000;321: 405-11.
12. The DCCT Research Group, Effect of Intensive diabetes management on macro vascular events and risk factors in the diabetes control and complication trial. Am J Cardiol 1995; 75: 894- 903.
13. Nathan DM, Cleary PA, Backlund JY, Genuth SM, Lachin JM, Orchard TJ, Raskin P, Zinman B. Intensive diabetes treatment and cardiovascular disease in patients with type1 diabetes. (DCCT/ EDIC) study research group. N Eng J Med 2005; 353:2643-53.
14. Gerstein HC, Swedberg K, Carlsson J, Mcmurray JJV, Michelson EL, OlofssonB, et al. The haemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure. Arch Intern Med 2008; 168: 1699 704
15. Goode KM, John J, Rigby AS, Kilpatrick ES, Atkin SL, Bragadeesh T, et al.Elevated glycated haemoglobin is a strong predictor of mortality in patients with left ventricular systolic dysfunction who are not receiving treatment for diabetes mellitus. Heart 2009; 95: 917-23.
16. Manal Khudhur Abdul Razzaq, Jawad Ibrahim Rasheed,Haider Shaheed Mohmmad . The Value of Admission Glucose and Glycosylated Hemoglobin in Patients With acute Coronary Syndrome. The Iraqi Postgraduate Medical Journal 2013:12(1):75-84

DOI Number: 10.5958/2321-1032.2017.00022.5

A Study of Risk Factor Profile for Coronary Artery Disease among Patients

S Dharmalingam[1], S Ramkumar[2]

[1]Assistant Professor, [2]Associate Professor, Department of Medicine , Karpagam Faculty of Medical Sciences and Research, Othakkalmandapam, Coimbatore, Tamil Nadu. India

ABSTRACT

Background: Coronary artery disease (CAD) is a worldwide health epidemic. Acute coronary syndrome is a potentially life-threatening condition and patient may die or become disabled in the prime of life.

Objective: To access the risk factors of CAD in young & elderly aged patients.

Method: total 110 CAD patients admitted in ICU at Karpagam Medical College Hospital, Coimbatore were selected for the study . Among them , 30 were aged between 18 – 45 years, and 80 were more than 45 years of age. These patients were evaluated for conventional risk factors contributing to occurrence of CAD.

Results: The hypertension (22%) , smoking (25%), diabetes mellitus(13%) and dyslipidemia (7%) were the commonest risk factors in young patients . Overall risk factors were more likely in males compared to females (18 to <45 years, 79%; ≥65 years, 69.1%). Regarding elderly patients, diabetes mellitus (25%), hypertension (15%) smoker (15%), kidney disease (11%) and dyslipidemia (10%) were the commonest risk factors.

Conclusion: Young patients had a different risk factor profile when compared with older patients. Hypertension and smoking were the commonest risk factors in young patients of coronary artery disease. While diabetes mellitus , kidney disease and smoking were found in elderly patients.

Keywords : *Coronary artery disease, Smoking, Hypertension.*

INTRODUCTION

Coronary artery disease is an emerging health problem in India, various risk factors contributing to increase prevalence of coronary artery disease in different age groups. Hypertension, diabetes mellitus, smokers & dyslipidemia are the most common cause of coronary artery disease [1,2].

The high incidence of risk factor for coronary disease in young individuals is hypertension, where as diabetes is in with the elderly patients. In elderly patients aging is associated with changes in beta cell function and insulin resistance that predisposes to diabetes [3,4].

In the last few decades it has been in upsurge in the epidemiological study by World Health Organization population-based MONICA study[5], INTERHEART [6], Euroheart ACS epidemiologic studies [7], and India Heart Watch Study (2012) [8] along with other randomized controlled trials have shown that certain risk factors and baseline characteristics, such as family history, obesity, dyslipidemia, and use of tobacco products, are more potent predictors of outcomes in the young than in their older counterparts. CAD has a multi-factorial etiology, with many of the risk factors being influenced by lifestyle. Rapid change in dietary habits coupled with decreased physical activity in India as a consequence of urbanization may partly explain the escalation of CAD. India is at present experiencing an epidemiological

Corresponding author
Dr. S. Dharmalingam
Assistant Professor, Department of Medicine
Karpagam Faculty of Medical Sciences and Research
Othakkalmandapam, Coimbatore - 641 032
Tamil Nadu. India.

transition with high rates of urbanization. Thus, effective CAD control is necessary for the prevention of cardiac mortality and morbidity. Currently, there are very limited data available on prevalence of risk factors for CAD from Tamil Nadu. Keeping in view the facts, this study was conducted to assess the risk factors in young and elderly patients of acute MI .

METHOD

This is a hospital based study of 110 patients of acute MI admitted in ICCU, Department of Medicine, during the period January 2015 to August 2016. The Institution Ethics committee approval was taken prior to the study. Proforma was prepared that incorporated information name, age, sex, detail history of risk factor, and investigations. 110 patients were divided in two groups; Group 1: 20 - 45 years of age and Group 2 : more than 45 years of age (elderly patients). Complete detail history and examination were performed at bed side . At the time of admission and on the following day. Hypertension was classified based on the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) classification for hypertension [9]. All patients were subjected for complete hematological and biochemical investigations including Troponin T, ECG to confirm acute MI. Among these patients coronary risk factors like smoking, Diabetes Mellitus, hypertension, dyslipidaemia, gender, kidney disease, alcohol history and also prior MI, heart failure and angina class were studied. The significance of each risk factor between the groups was calculated by employing the chi-square test, and $p<0.05$ was taken as significant.

RESULTS

The patient characteristics of group 1 and group 2 are displayed in table 1. Mean age of patients enrolled in this study was about 40.5 ± 4.1 for younger group and 56.4 ± 6 for elderly patients. Significant differences observed for different risk factors in both groups are shown in table 2. In this study , younger patients were considerably more likely to suffer from hypertension (22%) , smoker (25%), dyslipidemia (7%), obesity (4%) ,diabetes mellitus (13%), and kidney disease(5%) detected at the time of acute coronary events. Regarding age group more than 45 years, observed risk factors were diabetics mellitus (25%), hypertension (15%) and smoker (15%), dyslipidemia (7%), Obesity (8%) , kidney disease (11%) and alcohol intake (7%) (table 2). In addition, younger patients were more likely to be male; none of them were taking lipid-lowering drugs before infarction. At the time of MI, younger patients were less likely to be aware of their dyslipidemia, diabetes. Similarly 2.5% of younger patients who were previously not known to have diabetes were diagnosed with diabetes during presentation. Younger patients were having anterior infarction which was characterized by ST-segment elevation and were treated acutely with the thrombolytic and medical therapy.

DISCUSSION

Hypertension, smoking, and dyslipedimia were leading cause of deaths and other major hazardous outcome mainly attributed to smokers and dyslipdemia.

Reviews of epidemiological studies suggest that all the major cardiovascular risk factors are increasing in India. In this study, most of young patients had risk factors like smoking, hypertension and dyslipidemia. Obesity noted to double the prevalence of cardiovascular disease in men and women under the age of 50 years, has been reported between 30% to 58% of younger patients [10]. Interestingly, a much higher percentage of young patients (almost 20%) were unaware of their hypertension, dyslipedmic status before the index MI and, thus, were not able to benefit from prior therapeutic interventions.

Younger patients were more likely to have an MI as their first event (70.5%), whereas heart failure was a more common first event in older patients (60.5%). Importantly, the relative proportion of sudden death events was similar across age groups. We observed an age-dependent variation in hazard associated with smoking and hypertension, with greater relative hazard in the youngest cohort of patients. However Diabetes Mellitus and kidney disease were more prevalent in elderly patients in this study.

The declining effect of individual risk factors with advancing age is likely because of the influence of competing risk factors. In contrast to their younger counterparts, elderly patients often presented with a more complex cardiovascular risk profile. The individual risk factors contribute disproportionately to risk in younger patients underscores the importance of addressing modifiable risk factors in younger patients, as those risk factors present in younger patients appear

to be associated with differentially greater risk [11-14].

Additionally, this study also showed that most of the patients had multiplicity of risk factor. As many risk factor are synergetic to each other were shown in various studies [15]. In our study, the common risk factors were smoking, hypertension, diabetes followed by dyslipidemia in both groups.

This male preponderance is remarkably consistent across 52 countries with hugely divergent rates of CAD mortality and lifestyles[16]. This study concur with previous finding that overall risk factors are more likely in males compared to females.

Our study showed that smoking is a major risk factor for CAD in both groups. The effect of cigarette smoking on coronary risk factors is pervasive. Unfavorable effects include enhancement of platelet function. Platelet activation by cigarette smoking is linked to thrombosis formation, including onset of myocardial infarction[17]. This study also supports the claim that smoking rate is highly prevalent in central Indian subjects.

High Prevalence of hypertension noted in 20% and 14% of young and elderly patients, respectively was seen among the both study population. This agrees with the previous studies by Sofia and EUROSPIRE , hypertension has been seen as a major risk factor for CAD [18] . The prevalence of hypertension has increased in both urban and rural subjects and presently is 25%-40% in urban adults and 10%-15% among rural adult[19].

A high incidence of diabetes were seen among the elderly population. Indians are genetically prone to develop type II diabetes mellitus due to insulin resistance. The hyperinsulinimia in these patients accelerates the atherosclerotic process in the coronary arteries. Diabetes is second only to CAD as a health burden in India. During the past decade, the number of people with diabetes in India increased from 32 million to 50 million, and the projected Figure may reach 87 million by 2030 [20] . Hyperinsulinemia, insulin resistance, and the higher rate of prevalence of metabolic syndrome in people with type 2 diabetes were attributed to high coronary risk in south Asians [21] . Although there are large regional variations in the prevalence of diabetes it has more than quadrupled in the last 20 years from < 1%-3% to 10%-15% in urban areas and 3%-5% in rural areas [22].

In this study , the fasting lipid profile tests revealed evidence of dyslipidemia in 8% of the young patients and 9% of the elderly subjects . In another study from a north Indian city reported increasing mean levels of total, low density lipoprotein and non-high density lipoprotein (HDL) cholesterol and triglycerides, and decreasing HDL cholesterol [23].

In view of obesity as the risk factor for CAD, based on the BMI, only 4% of the young patients had a BMI higher than 30, whereas 8% of the elderly had a BMI higher than 30. Although most of the co morbidities relating obesity to CAD increase as BMI increases, they also relate to body fat distribution. It might indicate that obesity as such not only relates to but independently predicts coronary atherosclerosis. Additionally, studies have reported increasing obesity as well as truncal obesity due to sedentary lifestyles, and psychosocial stress in the country [24]. Prevalence of overweight and obesity was the highest in southern and northern Indian states and the lowest in central Indian states .

Our study also had showed that elderly patients with chronic kidney disease (CKD) had a 11% prevalence of coronary artery disease (CAD). In 1998, the U.S.National Kidney Foundation Task Force on Cardiovascular Disease in Chronic Renal Disease recommended that patients with CKD be considered to belong to the highest risk group for the development of cardiovascular events [25]. These patients present unique challenges to physicians attempting manage concomitant ischemic heart and CKD .

On the other hand, reviews of CVD risk factor epidemiological studies from India showed significant regional variations in the prevalence of the important CVD risk factors of smoking, obesity, hypertension, diabetes and lipid abnormalities .

Based on the earlier studies conducted in India and also there are limited data pertaining to central Indian population , this preliminary study was planned and focused on conventional risk factors . This was one of the pioneer studies conducted in central Indian population . Thus, the current study is broadly consonant with the INTERHEART study .However, this study was confined to a small population in central India and had several limitations. It is widely believed that the association of these risk factors with CAD in

different populations needs to be ascertained, and there is speculation that differences might range from the frequency of presence of classical risk factors to their total absence or irrelevance in these populations

However, careful scrutiny of available scientific evidence for modifiable CAD risk factors (elevated serum total and low-density lipoprotein cholesterol [LDL-C], low high-density lipoprotein cholesterol [HDL-C], smoking, diabetes, hypertension, low level of physical activity, and obesity) in this population may be helpful in formulating a more immediate CAD prevention strategy.

Table 1. Baseline Characteristics of patients

Characteristics	Age group (Years)	
	18 to <45 years (n = 30)	>45 years (n = 80)
Age (y)	39.5 ± 4.1	54.4 ± 6
Female sex (n)	15	35
Male sex(n)	16	45
BMI (kg/m^2)	26.2 ± 6.3	28.5 ± 5.2
Systolic blood pressure (mm Hg)	118.8 ± 13.4	122.1 ± 15.9
Heart rate (beat/min)	76.5 ± 12.2	86.4 ± 10.5
Hypertension (n)	16	14
Known diabetes before MI(n)	8	21
Dyslipidemia (n)	8	9
Smoking (n)	18	17
Obesity (n)	4	8
Anterior MI (n)	48	54

Table 2. Risk factors for coronary artery disease among young & elderly patients

Risk factor	Age 18 to <45 (n = 30) years	Age ≥45 (n = 80) years	P value
Diabetes mellitus	13%	25%	p<0.05
Hypertension	22%	15%	
Chronic Kidney Disease (CKD)	4%	11%	
Physical inactivity	4%	12%	
Smoking	25%	15%	p>0.05
Dyslipidemia Elevated triglycerides Reduced HDL Elevated LDL	7%	10%	
Obesity (based on BMI)	3%	8%	
Alcohol consumption	5%	6%	

CONCLUSION

The study highlighted that conventional factors like hypertension, smoking , diabetes mellitus, obesity, and dyslipidemia as potential targets. Younger patients had a different risk factor profile in comparison with older patients These risk factors were highly prevalent in the community.

Conflict of Interest: We declare that there is no conflict of interest

Source of Funding: None

REFERENCES

1. Jalowiec DA, Hill JA. Myocardial infarction in the young and in women. Cardiovasc Clin. 1989; 20: 197–206.
2. Yusuf S, Ounpuu S. Tracking the growing epidemic of cardiovascular disease in South Asia. J Am Coll Cardiol 2001; 38:688-9.
3. Choudhury L, Marsh JD. Myocardial infarction in young patients. Am J Med. 1999;107:254-261.
4. Fullhaas J, Rickenbacher P, Pfisterer M, et al. Long-term prognosis of young patients after myocardial infarction in the thrombolytic era. Clin Cardiol. 1997;20:993-998.
5. Mahonen MS, McEldruff P, Dobson AJ, et al. Current smoking and the risk of non-fatal myocardial infarction in the WHO MONICA project populations. Tob Control. 2004;13:244-250.
6. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. Lancet 2004; 364: 937-952
7. Rosengren A, Wallentin L, Simoons M, et al. Age, clinical presentation, and outcome of acute coronary syndromes in the Euroheart acute coronary syndrome survey. Eur Heart J. 2006;27: 789-795.
8. Gupta R, Guptha S, Sharma KK, Gupta A, Deedwania P. Regional variations in cardiovascular risk factors in India: India heart watch. Worl Cardiol 2012; 4(4): 112-120
9. National High Blood Pressure Education Program Coordinating Committee. The seventh report

of the Joint National Committee on Prevention, Detection, Evaluation,and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003; 289:2560–2571.

10. Gupta R, Joshi P, Mohan V, Reddy KS, Yusuf S. Epidemiology and causation of coronary heart disease and stroke in India. Heart 2008; 94: 16-26.
11. Jörgensen S, Köber L, Ottesen M, et al. The prognostic importance of smoking status at the time of acute myocardial infarction in 6676 patients. J Cardiovasc Risk. 1999;6:23-27.
12. Pfeffer M, McMurray J, Leizorovicz A, et al.. Valsartan in Acute Myocardial Infarction Trial (VALIANT): rationale and design. Am Heart J. 2000;140:727-750.
13. Lipscombe LL, Hux JE. Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995-2005: a population-based study. Lancet 2007;369:750-6.
14. Statistics Canada. Portrait of the Canadian population in 2006, by age and sex. July 17, 2007. www12.statcan.ca/english/census06/release/release_agesex.cfm Accessed September 12, 2015.
15. Beckett NS, Peters R, Fletcher AE, et al. Treatment of hypertension in patients 80 years of age or older. N Engl J Med 2008;358:1887-98.
16. Shepard J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomized controlled trial. Lancet 2002;360:1623-30. .
17. Khan N. Epidemiology of coronary heart disease in Peshawar. Pakistan Heart J. 1973;6:64-69.
18. Kalin MF, Zumoff B . Sex hormones and coronary disease: a review of the clinical studies. Steroids 1990; 55:330–352.
19. Teruo Inoue. Cigarette Smoking as a Risk Factor of Coronary Artery Disease and its Effects on Platelet Function. Tob Induc Dis. 2004; 2: 2
20. Gupta R, Gupta VP, Sarna M, Prakash H, Rastogi S, Gupta KD. Serial epidemiological surveys in an urban Indian population demonstrate increasing coronary risk factors among the lower socioeconomic strata. J Assoc Physicians India 2003;51: 470-477.
21. Kotseva K, Jennings C, De Backer G, De Bacquer D, Amouyel P, Gaita D, Keil U, Pajak A, Reiner Z, Wood D. Euroaspire III: lifestyle, risk factor and therapeutic management in people at high risk of developing cardiovascular disease from 12 European regions. Heart 2009;95:4.
22. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004; 18: 73-78.
23. Mohan V, Radhika G, Vijayalakshmi P, Sudha V. Can the diabetes/cardiovascular disease epidemic in India be explained, at least in part, by excess refined grain (rice) intake? India J Med Res 2010;131:369-72.
24. McKeigue PM, Ferrie JE, Pierpoint T, Marmot MG. Association of early-onset coronary heart disease in South Asian men with glucose intolerance and hyperinsulinemia. Circulation 1993;87:152-61.
25. Levey AS, Beto JA, Coronado BE, et al. Controlling the epidemic of cardiovascular disease in chronic renal disease: What do we know? What do we need to learn? Where do we go from here? National Kidney Foundation Task Force on Cardiovascular Disease. Am J Kidney Dis 1998;32:853–906.

DOI Number: 10.5958/2321-1032.2017.00023.7

Assessment of Artesunate on Electrocardiographic QT Interval in Patients with Plasmodium Falciparum Malaria

S Vijay Babu[1] , S Siva Prasad[1]

[1]Assistant Professor, Department of Medicine, Santhiram Medical College & General Hospital, NH-18, Nandyal, Kurnool (Dist), Andhra Pradesh. India

ABSTRACT

Background: Several anti-malarial drugs are associated with adverse cardiovascular effects. There are a few reports available on the potential cardiac effects (QTc interval) of artesunate, which includes an increased risk of potentially ventricular arrhythmia. This study aimed to evaluate the electrocardiographic (ECG) Changes (QTc interval) in malaria patients treated with artesunate.

Method: Total 35 (19 male & 16 female) patients with severe Falciparum malaria enrolled in medical ward at Santhiram Medical College & General Hospital, Nandyal, were selected. Electrocardiogram was recorded, and QTc interval was calculated before and after administration of three doses of artesunate (2.4 mg/kg body weight on admission, followed by 2.4 mg/kg at 12 and 24 hours)given by intravenous injection in all patients who were positive for Falciparum malaria.

Results: The mean QTc interval was not affected by three doses of intravenous artesunate given at different time intervals($p>0.05$). There was no significant effect observed on the JTc or PR interval, QRS width, blood pressure and heart rate. Intravenous artesunate does not have significant on other cardiovascular effects in patients with severe Falciparum malaria.

Conclusion: Intravenous artesunate does not have significant cardiovascular effects in patients with *falciparum* malaria.

***Keyword**s : QT Interval, Plasmodium Falciparum, Artesunate.*

INTRODUCTION

Artemisinin-based therapy are currently recommended worldwide as the first-line treatment for severe patients with Falciparum malaria recommended by the World Health Organization [1](WHO). Intravenous artesunate is the recommended first choice for the treatment of severe Falciparum malaria in areas of low to moderate malaria transmission, as it has been shown to be superior to quinine in that setup [2,3]. Other antimalarial drugs, notably quinidine and halofantrine produce clinically significant delays in ventricular repolarization, resulting in a prolongation of the electrocardiographic QT interval on the electrocardiogram (ECG)[4]. Heterogeneous prolongation of ventricular repolarization predisposes to potentially lethal polymorphic malignant ventricular tachyarrhythmias (torsades de pointes) . The antimalarial halofantrine causes marked QT prolongation and sudden death. After its registration by several regulatory authorities, it has focused attention on the potential cardiotoxicity of the antimalarial drugs.The artemisinins are remarkably well tolerated. High intramuscular doses of the oil-based artemether are associated with significant QT prolongation. The electrocardiographic effects of the artemisinin derivatives in humans is limited. In clinical studies reporting modest QT interval prolongation with the artemisinins, the contributions of drug and disease cannot be disentangled, because

Address of Correspondence :
Dr. S Vijay Babu
Assistant Professor, Department of Medicine,
Santhiram Medical College & General Hospital,
NH-18,Nandyal, Kurnool(Dist),
Andhra Pradesh, INDIA

recovery from malaria itself is associated with significant lengthening of the QT interval [5-9] . Previous studies do not suggest a significant cardiovascular effect. Therefore , this study was conducted to evaluate the effects of intravenous artesunate at different time intervals on the electrocardiographic intervals in patients with severe malaria.

METHOD

This study was conducted between June 2014 –July 2015 in the Department of Medicine at Santhiram Medical College & General Hospital ,Nandyal . This prospective study have been taken permission from ethical committee before doing study. Malaria transmission is seasonal and high prevalence zone specially Plasmodium Falciparum malaria. patients who had been admitted in the hospital with the complaints of fever, headache, altered sensorium , vomiting with a slide test –confirmed the diagnosis of malaria according to modified WHO criteria [10] .Criteria on admission for severe malaria included one or more of the following: cerebral malaria (Glasgow Coma Scale [GCS] < 11), severe anemia (hematocrit < 20% with parasite count > 100,000/μL), jaundice (bilirubin > 1.5 mg/dL with parasite count > 100,000/μL), renal failure (serum creatinine > 1.4 mg/ dL), hypoglycemia (blood glucose < 40 mg/dL), shock (systolic blood pressure < 80 mm of Hg with cool extremities) . 35 patients (19 males and 16 females) were enrolled for this study.

Exclusion criteria

Pregnant or breast-feeding women and any patient who had received any cardioactive drugs within 1 week before the start of artesunate and having cardiovascular disease were excluded from the study. Patients with abnormal ECG before starting artesunate are also excluded.

Study design

On admission, a full history and examination were carried out. Blood samples were obtained for hemoglobin, hematocrit, parasitemia, platelet count, white cell count, glucose levels, and biochemical tests. Patients were followed up a minimum of twice daily until discharge, including a neurologic examination where clinically indicated. Antimalarial drug artesunate (2.4 mg/kg body weight on admission, followed by 2.4 mg/kg at 12 and 24 hours)was given and ECG taken before starting the first dose of artesunate and after each doses. Serial 12 lead electrocardiograms were performed (electrocardiograph model Schiller AT - 1 with a paper speed of 25 mm/s and sensitivity of 10 mm/Mv). Time points for recording ECGs were before artesunate administration and after first hour , second dose (12 hour), last dose (24 hours) of administration. At each time blood pressure, heart rate, were measured. The QTc interval was calculated using the mean QT interval, as measured manually over 10 complexes, corrected for heart rate using Bazett's [11]. The JTc interval was calculated as QTc (Bazett's correction) minus QRS duration. The primary outcome measure of the study was a change in QTc interval before and after artesunate. Secondary outcome measures were other significant changes in the ECG including JTc interval and arrhythmias, change in heart rate, and change in systolic blood pressure. Two-sided 95% confidence intervals (CIs) were calculated for mean QTc intervals and changes in QTc. Means were compared using a paired t test. We calculated that a minimum of five patients were needed to show an increase in mean QTc of 25% from baseline, with significance level (a) of 0.05 and a power (1 − b) of 0.90.

RESULTS

35 patients (19 males and 16 females) were enrolled, of whom ECGs were recorded first, second and after last dose of artesunate. The median number of doses of artesunate received intravenously was three. Baseline characteristics and clinical outcome are summarized in Table 1.

Five patients (14.28%) were already in hemodynamic shock on admission, but only 3 patient required vasopressor drugs. Other complications during admission included acute renal failure (9/32), and aspiration pneumonia (5/32). Ten patients received a blood transfusion, and 7 patients were treated for suspected concomitant septicemia.

The mean QTc (Bazett) and change before and after administration of the first hour, 12 hours and 24 hours of intravenous artesunate were tabulated in Table 2 . No significant change in the mean QTc was observed during the 1 hour observation period (P > 0.05), independent of the correction method used. No patient had an increase of QTc from baseline of > 25% after first bolus dose. The mean maximum increase in mean QTc (Bazett) after the first dose of artesunate was 5.8 ms (95% CI: 10.4–22.0

ms) at 1 hour. In addition to artesunate, the patient also received antibiotic coverage as twice daily like intravenous ceftriaxone (1 g) Piperacillin tazobactum, levofloxacin, ofloxacin and other supportive measure as per patient symptomatology . The next dose of intravenous artesunate was given on 12 hours after admission. The QTc (Bazett) was borderline at 0.499 seconds before receiving the first dose of artesunate and increased 6% to 0.531 seconds by 24 hours after administration of 2.4 mg/kg intravenous artesunate There were no arrhythmias or changes in axis and no significant changes in JT interval, PR interval, or QRS duration after administration of either the first or last dose of artesunate.. There was no significant change in mean heart rate or blood pressure after administration of either the first or last dose of artesunate. Mean heart rate was significantly lower in patients receiving their last dose (89.0 beats/minute; 95% CI, 85.2–92.7 versus 113 beats/minute ; 95% CI, 109–118; $P < 0.0001$), but mean systolic blood pressure was the same throughout (108 mm of Hg; 95% CI, 104–112 versus 111 mm of Hg; 95% CI, 108–115; $P = 0.1$).

DISCUSSION

The importance of evaluating potential cardiotoxic effects of newly introduced anti-malarial drugs has been highlighted with discovery of the cardiotoxicity of new anti-malarial drugs like artesunate after its registration and introduction into clinical practice [12]. Although Plasmodium falciparum sequesters in the myocardial microvasculature, significant myocardial dysfunction or arrhythmias caused by the disease are unusual in severe malaria. The quinoline antimalarials all have potent cardiovascular effects, but the effects of the artemisinin derivatives have been unclear [13,14]. This study evaluated the cardiovascular effects of intravenous artesunate and its effects on ECG changes (QT interval) in patients of falciparum malaria. Artesunate is given as a bolus injection as per guideline, so high blood levels of drug artesunate occur at the end of the injection and its effects on cardiac conduction times can be assessed over a short time period, relatively independent of the changes in disease state. Even these very high plasma concentrations would be expected to be associated with the greatest cardiovascular effects. However, there were no consistent cardiovascular or electrocardiographic effects after first dose of artesunate injection.

In the acute phase of malaria, the QTc is commonly short because of increased sympathetic tone from arousal, stress, discomfort, anxiety, and usually fasting and elongates with recovery when the patient is relaxed, comfortable, supine in bed, and has often resumed eating. All studies of antimalarial drugs (including sul fadoxinepyrimethamine, which has no cardiac activity at all) report some prolongation of the QT interval in the days after the start of treatment with artesunate [15-19] . In this study, the QTc interval was not significantly affected by high doses of intravenous artesunate given at different time intervals. Apart from this, no significant effect was observed on the JTc or PR interval, QRS width, blood pressure, or heart rate.

There are many reasons underlying fluctuation in the QT interval in the acute phase of managing a life-threatening disease. It has been noted that administration of the last dose of artesunate to one patient increase the QTc time (10 ms) and in some other patients, QT not changes immediately after artesunate injection. Of the antimalarial drugs, the quinolines, quinine, quinidine, chloroquine, and halofantrine, can cause significant prolongation of the QT interval [20,21].

QT prolongation by 25% occurs in ~10% of patients given high-dose intravenous quinine. Halofantrine induces consistent dose-dependent prolongation of the QTc interval, and its use in patients with malaria has been associated with arrhythmias and sudden death . There were no arrhythmias or adverse cardiovascular effects in this study. The effects of recovery from severe malaria and any drug activity on ventricular repolarization could not be distinguished. Studies on oral administration of artemether, including in combination with lumefantrine, to both malaria patients and healthy volunteers did not show any significant electrocardiographic abnormalities including evidence of QTc prolongation [22–24] . Compared with artesunate and artemether, artesunate has a more favorable toxicity profile, even though plasma concentrations of the parent compound and the common metabolite DHA after intravenous injection are an order of magnitude higher. Considerably higher doses of artesunate are needed to produce neurotoxicity in animals [22,23]. No effects on the ECG in dogs receiving the equivalent of the standard human dose of 2.4 mg/kg intravenous artesunate was observed and in other studies , doses several orders of magnitude higher than those used to treat malaria were required to cause negative inotropy in isolated guinea pig heart and hypotension in rabbits [24], all suggesting

a very wide therapeutic ratio, and this is in line with the negative findings in this study.

This study had limitations. The sample size was small and only three ECGs per patient were performed. Performing several ECGs at each time point to reduce the intra individual variation would have been more informative. We were not able to perform 24 hour Holter monitoring which would have yielded more data. Pharmacokinetics studies are also needed.

Table 1: Particulars of Patients with Falciparum malaria

Variable	Mean ± SD	
Age, mean years	37.5 (17.9- 50.34)	
Number of Male/ Female		16/16
Blood pressure	Systolic (mmHg)	110 (97.4- 129)
	Diastolic (mmHg)	60 (54-68)
Heart rate, mean beats/min		102 (96-118)
Haemoglobin, mean g/dL		7.78 +3.26
Total WBC count ,mean cells/mm		8966.25+717.34
Serum creatinine level, geometric mean mg/dL		1.38+0.117
Serum urea level, geometric mean mg/dL		54.25+10.3
Serum sodium level,mean mmol/L		134.5+7.616
Serum potassium level,mean mmol/L		3.9+0.801
Serum glucose, geometric mean mg/dL		122.94+7.165

Table 2: Mean (95% CI) QTc (Bazett) and change from baseline after artesunate administration.

Time post dose(hrs)	QTc (ms)	Change QTc from base line
0 hours (Baseline)	422 (406-452)	0 NA
1 hour	423 (408–441)	1
12 hours	426 (408-488)	4
24 hours	432 (414-474)	10

CONCLUSION

This study showed that intravenous artesunate does not have significant cardiovascular effects (QTc interval) in patients with severe falciparum malaria. The artesunate regimen appears to be relatively safe patients in this limited study, but further studies in a larger cohort are warranted for conclusive evidence on safety.

Ethical Clearance : Obtained from Institutional ethics committee

Conflict of Interest: Nil

Source of Funding: None

REFERENCES

1. World Health Organization Global Malaria Programme. WHO Guidelines for the Treatment of Malaria. 2008. http://www.who.int/malaria/docs/TreatmentGuidelines2006.pdf . Accessed April 15 2016.
2. Dondorp A, Nosten F, Stepniewska K, Day N. White N et al. South East Asian Quinine Artesunate Malaria Trial (SEAQUAMAT). Artesunate versus quinine for treatment of severe falciparum malaria: a randomised trial.Lancet. 2005;366:717–725.
3. White NJ. Cardiotoxicity of antimalarial drugs. Lancet. 2007;7:549–558.
4. Nosten F, ter Kuile FO, Luxemburger C, Woodrow C, Kyle DE, Chongsuphajaisiddhi T, White NJ. Cardiac effects of antimalarial treatment with halofantrine. Lancet. 1993;341:1054–1056.
5. Sanguinetti MC, Jurkioewicz NK. Two components of cardiac delayed rectifier K+ current. Differential sensitivity to block by class III antiarrhythmic agents. J Gen Physiol. 1990;96:195–215.
6. International Conference on Harmonization The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Nonantiarrhythmic Drugs. ICH Harmonized Tripartite Guideline. 2008. http://www.ich.org/LOB/media/MEDIA1476.pdf . Accessed June 15 2016 .
7. Shah RR. Drugs, QTc interval prolongation and final ICH E14 guideline: an important milestone with challenges ahead. Drug Saf. 2005;28:1009–1028.
8. Owens RC, Jr, Nolin TD. Antimicrobial-associated QT interval prolongation: pointes of interest. Clin Infect Dis. 2006;43:1603–1611.

9. Classen W, Altmann B, Gretener P, Souppart C, Skelton-Stroud P, Krinke G. Differential effects of orally versus parenterally administered qinghaosu derivative artemether in dogs. Exp Toxicol Pathol.1999;51:507–516.

10. Tran TH, Day NP, Nguyen HP, Nguyen TH, Tran TH, Pham PL, Dinh XS, Ly VC, Ha V, Waller D, Peto TE, White NJ. A controlled trial of artemether or quinine in Vietnamese adults with severe falciparum malaria. N Engl J Med. 1996;335: 76–83.

11. Bazett HC. An analysis of the time-relations electr ocardiograms. Heart. 1920;7:353–370.

12. George OA, Collins OB, Onike P R, Lotte C H, Michael A, Jorgen A K , Bamenla QG. Electrocardiographic study in Ghanaian children with uncomplicated malaria, treated with artesunate amodiaquine or artemether-lumefantrine. Malaria Journal 2012 11:420.

13. Priori SG, Schwartz PJ, Napolitano C, Bloise R, Ronchetti E, Grillo M, Vicentini A, Spazzolini C, Nastoli J, Bottelli G, Folli R, Cappelletti D. Risk stratification in the long-QT syndrome. N Engl J Med.2003;348:1866–1874.

14. van Vugt M, Ezzet F, Nosten F, Gathmann I, Wilairatna P, Looareesuwan S, White NJ. No evidence of cardiotoxicity during antimalarial treatment with artemether-lumefantrine. Am J Trop Med Hyg.1999;61:964–967.

15. White NJ, Looareesuwan S, Warrell DA, Warrell MJ, Bunnag D, Harinasuta T. Quinine pharmacokinetics and toxicity in cerebral and uncomplicated falciparum malaria. Am J Med. 1982;73:564–572.

16. Brewer TG, Grate SJ, Peggins JO, Weina PJ, Petras JM, Levine BS, Heiffer MH, Schuster BG. Fatal neurotoxicity of arteether and artemether. Am J Trop Med Hyg. 1994;51:251–259.

17. Makanga M, Premji Z, Falade C, Karbwang J, Mueller EA, Andriano K, Hunt P, De Palacios PI. Efficacy and safety of the six-dose regimen of artemether-lumefantrine in pediatrics with uncomplicatedPlasmodium falciparum malaria: a pooled analysis of individual patient data. Am J Trop Med Hyg.2006;74:991–998.

18. van Agtmael MA, Gupta V, van der Wosten TH, Rutten JP, van Boxtel CJ. Grapefruit juice increases the bioavailability of artemether. Eur J Clin Pharmacol. 1999;55:405–410.

19. Kshirsagar NA, Gogtay NJ, Moorthy NS, Garg MR, Dalvi SS, Chogle AR, Sorabjee JS, Marathe SN, Tilve GH, Bhatt AD, Sane SP, Mull R, Gathmann I. A randomized, double-blind, parallel-group, comparative safety, and efficacy trial of oral coartemether versus oral chloroquine in the treatment of acute uncomplicated Plasmodium falciparum malaria in adults in India. Am J Trop Med Hyg. 2000;62:402–408.

20. Karunajeewa H, Lim C, Hung TY, Ilett KF, Denis MB, Socheat D, Davis TM. Safetly evaluation of fixed combination piperaquine plus dihydroartemisinin (Artekin) in Cambodian children and adults with malaria.Br J Clin Pharmacol. 2004;57:93–99.

21. Nontprasert A, Nosten-Bertrand M, Pukrittayakamee S, Vanijanonta S, White NJ. Assessment of the neurotoxicity of parenteral artemisinin derivatives in mice. Am J Trop Med Hyg. 1998;59:519–522.

22. Nontprasert A, Pukrittayakamee S, Nosten-Bertrand M, Vanijanonta S, White NJ. Studies of the neurotoxicity of oral artemisinin derivatives in mice. Am J Trop Med Hyg. 2000;62:409–412.

23. Zhao Y. Studies on systemic pharmacological effects of artesunate. Am J Trop Med Hyg. 1985;88: 391–396.

24. Qichao Y, Weizhi S, Rei L, Jun G. The antimalarial and toxic effect of artesunate in animal models. J Tradit Chin Med. 1982;2:99–103.

DOI Number: 10.5958/2321-1032.2017.00024.9

A Comparative Study of Effect of Yoga on Blood Sugar Levels and Lipid Profile between Diabetic Smokers and Non Smokers

S Siva Prasad[1], S Vijay Babu[2]

[1]Assistant Professor, Department of Medicine, Santhiram Medical College & General Hospital, NH-18, Nandyal, Kurnool(Dist), Andhra Pradesh, India

ABSTRACT

Background: Diabetes is a global epidemic and it has been posing a biggest threat ever witnessed with devastating human, social and economic consequences.

Objective: To evaluate the beneficial effects of pranayama on glycemic control, hypertension and dyslipidemia between smoker diabetic and non-smoker diabetic patients

Method: The study was conducted on 48 male patients suffering from diabetes mellitus Type-II between the age group of 35-60 years, for a period of 1 year . These patients were attending the medical OPD of Santhiram Medical College and general Hospital, Nanadyal. Subject will be practicing yoga or simple pranayama (breathing exercise) for approximately 5 min for a period of 6 months. The effect of yoga practice on various parameters (blood glucose, lipid profile and BP) were recorded and statistically analyzed by paired t-test for evaluation

Results: This result showed that after 6 months of yogic exercises there is a significant decline in fasting blood sugar level of subjects who were non smokers, but lipid profile and blood pressure do not show any significant change either on smoker or non-smoker diabetes patients. The effect of yoga practice on various parameters were recorded and statistically analyzed by paired t-test for evaluation.

Conclusion: The term diabetes mellitus comprises a large number of diseases resulting in hyperglycemia. So yoga can be used an alternate therapy , but not a replacement for tested and tried medical management of diabetes mellitus Type II.

Keywords: *smoking , diabetes, Pranayam*

INTRODUCTION

Main culprit for the development of diabetes mellitus Type II now days are increased sedentary lifestyle. Smoking is known to negatively impact human health. Carcinogenic processes, vasomotor dysfunction, impaired endothelial- dependent vasodilatation, and the modification of lipid profiles are included in this adverse effects.[1] A healthy lifestyle, which includes exercise, is important in the fight against diabetes. Yoga can complement such a lifestyle and help to keep diabetes under control. Smoking has also been shown to be associated with insulin resistance in both non-diabetic and Type II diabetic subjects. The acute effects of cigarette smoking in smokers include dyslipidemia and impaired insulin action that leads to abnormal glucose metabolism. Both dyslipidemia and insulin resistance are well-established major risk factor for cardiovascular disease.[2] However, there is limited information available regarding the effect of smoking cessation on blood glucose control and lipid profiles.So

Address of Correspondence :
Dr. S Siva Prasad
Assistant Professor, Department of Medicine,
Santhiram Medical College & General Hospital,
NH-18, Nandyal, Kurnool(Dist), Andhra Pradesh,
INDIA

this study was aimed to evaluate the beneficial effects of pranayama on glycemic control, hypertension and dyslipidemia between smoker diabetic and non-smoker diabetic patients

METHOD

The study comprised of 48 known diabetic patients aged 35-65 years at Santhiram Medical College & General Hospital, Nandyal , between June 2015- July 2016 (1 year). The study population was subjected to practice "Yoga", Anulom vilom Pranayama and Kapalbhati 5 min each daily for a total period of 6 months under observation of a yoga instructor. 23 out of 48 diabetic patients are addicted to smoking or tobacco chewing and remaining 25 diabetic patients are non smokers.

The subjects were informed of aims and objectives of the study:

- Prior to and during the course of study they will be on their regular course of medication.
- Subject will act their own control; a separate control group will not be incorporated.
- Subject will be practicing yoga for a period of 6 months.

Inclusion Criteria

1. Patient is a known case of Type-II diabetes.
2. Subjects not doing any type of physical exercise or yoga.

Exclusion Criteria

1. Subjects having history of complications associated with

diabetes or suffering from other disease.

2. Subjects with age <30 years or above 60 years.
3. Female subjects suffering from gestational diabetes.
4. Patient suffering from Type-I diabetes.

Parameters assessed

1. Fasting blood sugar
2. Blood lipid profile (Low-density lipoprotein [LDL], High- density lipoprotein [HDL], cholesterol)
3. Blood pressure

A. Blood glucose measurement in diabetics:-

- The "gold standard" for diagnozing diabetes is an elevated blood sugar level after an overnight fast (not eating anything after midnight).
- Fasting blood glucose sample was taken.
- Estimation of blood glucose was done in the central lab. The "glucose oxidase-peroxidase" method was used for determining serum glucose.

B. Interpretation of fasting blood sugar (FBS): - According to the 2013 Recommendation of the American diabetes association, fasting blood sugar interpretation is done as:

- FBS < 100 mg/dl (5.6 mmol/l) = normal fasting

blood sugar

- FBS 100–125 mg/dl (5.6-6.9 mmol/l) = IFG (impaired fasting glucose)
- FBS ≥ 126 mg/dl (7.0 mmol/l) = provisional

diagnosis of diabetes[3]

C. Serum lipid measurement in patients:-

- Serum lipid profile was determined by "automated randox machine."

The effect of yoga practice on various parameters were recorded and statistically analyzed by paired *t*-test for evaluation. A *P* lower than 0.05 was considered significant.

RESULT

The effect of yoga on fasting blood sugar, lipid profile and blood pressure in smoker diabetic patient and non-smoker diabetic patients is shown in Table 1.

DISCUSSION

The science of Yoga is an ancient one. Several works has been done on the role of yoga in diabetes. In the present study, an attempt was made to evaluate the beneficial effects of Pranayama on Diabetic patients. Here we tried to assess the role of Pranayama on glycemic control and various co-morbidities such as hypertension and dyslipidemia. Known diabetic patients were taken. Patients with complications such as retinopathy, nephropathy were not included in the study, patients selected were explained the outline and aim of the studies and their consent taken. Those on treatment were advised to continue on the same drugs.

The result of this study suggests that no significant changes was observed in fasting blood glucose level and other blood lipid profile level including blood pressure in subjects who were addicted to those who were not. A study by Dr Vipin Mishra (cited by srivastava 2007)[4] reported that; Yoga is a complementary therapy

for patient with diabetes, although Yoga cannot take care of every aspect of the disease but regular practice of yoga does reduce blood sugar levels.

Sahay[5] reported the useful role of yoga in the control of diabetes mellitus. Twenty-eight Type II diabetics and four Type I diabetics were studied for 1 month. They practiced four types of Pranayama for 30 min, followed by Shavasana for 15 min. Patients developed a sense of well-being within 7-10 days and showed a significant fall in fasting and post- prandial blood glucose values. For 4 in 17 patients the requirement of drugs came down significantly.

A study by Bijlani *et al*. (2005 cited Poole 2006),[6] reported that there was a significant fall in fasting glucose level, however, total cholesterol, LDL cholesterol, VLDL cholesterol, total cholesterol/HDL ratio, and triglycerides, HDL cholesterol do not show significant change in diabetic patients after a 10 day integrated program of yoga (pranayama).

Mercuri *et al*.[7] evaluated the clinical and metabolic changes, observed immediately and 3 months after daily Yoga practices in a group of people with Type II DM. Blood pressure (BP), heart rate (HR), and glycaemia also were recorded at the beginning and end of 13 alternate sessions. There were no overall significant differences (beginning vs. end of the study) in body mass index, HbA1, lipid profile, the dietary plan, habitual physical activity practice, BP, and treatment schedule. Conversely, there was a significant decrease in HR (8 sessions; $P < 0.03$) and glycaemia (10 sessions; $P < 0.03$) immediately after the Yoga sessions. The immediate positive effect of Yoga practices on glycaemia and HR suggests that such practices would be beneficial for the treatment of people with DM.

Badr *et al*.[8] assessed the effect of practicing yoga for management of Type II Diabetes. The study results show improvement in outcomes among patients with Diabetes Type II. These improvements were mainly among short- term or immediate outcomes and not all were statistically significant. The results were inconclusive and not significant for the long-term outcomes. Further research is needed in this area. A definition recommendation for physicians to encourage their patients to practice yoga cannot be reached at present.

Since the present study was conducted taking all precautions to maintain standardization of yoga procedure and lab investigation for all these subjects. However, as planned in the study they were on their regular medication and dietary regime. No subject could achieve normal fasting blood sugar. It also appears that these subjects were happy about their blood sugar and other values achieved with medication regime they were following. They did not want to switch to insulin or go on a stricter diet-medication-exercise regime like so many diabetics all over world they want to avoid medicine and go for looking after some miraculous cure that according to them or general belief can help them cure their diabetes mellitus.

Yoga it appears does help them to lower their blood sugar level but in no way is helpful in achieving control of their diabetes mellitus. On the other hand, they seem to be learned into the belief that yoga is helping cure their diabetes and neglect or do not resort to more effective treatment regime by way of diet, medicine and regular aerobic exercises like brisk walk. These programs appear cumbersome to them.

Table 1: Effect of yoga on fasting blood sugar, lipid profile and blood pressure in smoker diabetic patient and non-smoker diabetic patients

Parameters	Smoker diabetic patient (n=23)	Non smoker diabetic patient (n=25)	t- value	P value and significance
FBS	152.826±21.543	152.623±27.602	t=0.024	P=0.88 Insignificant
Serum cholesterol	179.01±24.889	183.234±21.951	t=1.027	P=0.346 Insignificant
Serum HDL	44.445±5.272	45.354±6.357	t=−0.970	P=0.421 Insignificant
Serum LDL-C	121.549±13.260	112.391±12.362	t=1.903	P=0.069 Insignificant
Triglycerides	154.269±38.621	135.440±39.891	t=1.106	P=0.275 Insignificant
Serum cholesterol/HDL ratio	4.728±0.991	4.189±0.884	t=1.20	P=0.260 Insignificant
Systolic blood pressure	154.50±14.793	152.00±14.72	t=1.635	P=0.162 Insignificant
Diastolic blood pressure	93.89±6.34	93.223±5.62	t=1.099	P=0.277 Insignificant
HDL: High-density lipoprotein, LDL-C: Low-density lipoprotein-cholesterol, FBS: Fasting blood sugar				

CONCLUSION

We can conclude from this study that the people need to know more about diabetes mellitus Type II and rationale of its management. They are to be made aware that alternative easy way outs are not helping them but as diabetes mellitus silently progress it compromises the function of many of the system so, they should not delay in achieving the effective control. Yoga can be an adjuvant, but not a replacement for tested and tried medical management of diabetes mellitus Type II.

Ethical Clearance: Obtained from Institutional ethics committee

Conflict of Interest: Nil

Source of Funding: None

REFERENCES

1. American Diabetes Association (ADA). Standards of medical care in diabetes. IV. Prevention/delay of type 2 diabetes. Diabetes Care 2007;30:S7-8.
2. American Diabetes Association. How Stress Affects Diabetes. 2007. Available from: http: //www.diabetes.org/type-1-diabetes/ stress.jsp. [Last retrieved on 2007 Feb 14].
3. American Diabetes Association (ADA). Standards of medical care in diabetes. V. Diabetes Care 2007;30:S8-24.
4. Srivastava A. Yoga helps in diabetes cure. Hindustan Times, 22 June 2007.
5. Sahay BK. Role of yoga in diabetes. J Assoc Physicians India 2007;55:121-6.
6. Poole I, Ravitz L. 8-Day yoga intervention. IDEA Fit J 2006;3:20-2.
7. Mercuri NE, Olivera M, Souto A, Guidi ML. Yoga practice in people with diabetes. Int J Yoga Ther 2003;13:69-73.
8. Aljasir B, Bryson M, Al-Shehri B. Yoga practice for the management of type II diabetes mellitus in adults: A systematic review. Evid Based Complement Alternat Med 2010;7:399-408.

Call for Papers/Article Submission

International Journal of Contemporary Medicine is a double blind peer reviewed international journal

The following guidelines should be noted:

- The article must be submitted by e-mail only. Hard copy not needed. Send article as attachment in e-mail.
- The article should be accompanied by a declaration from all authors that it is an original work and has not been sent to any other journal for publication.
- As a policy matter, journal encourages articles regarding new concepts and new information.
- Article should have a Title
- Names of authors
- Your Affiliation (designations with college address)
- Abstract
- Key words
- Introduction or back ground
- Material and Methods
- Findings
- Conclusion
- Interest of conflict
- References in Vancouver style.
- Please quote references in text by superscripting
- Word limit 2500-3000 words, MSWORD Format, single file

All articles should be sent to : editor.ijocm@gmail.com

Our Contact Info:

Institute of Medico-Legal Publications

4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110001,
Tel No: +91 - 09971888542, Fax No: +91 11 3044 6500
Email: editor.ijocm@gmail.com, Website: www.ijocm.org.in

INTERNATIONAL JOURNAL OF CONTEMPORARY MEDICINE

Institute of Medico-Legal Publications
4th Floor, Statesman house building
Barakhamba Road, Connaught Place, New Delhi-110001
Tel No: +91 - 09971888542, Fax No: +91 11 3044 6500
Email: editor.ijocm@gmail.com
Website: www.ijocm.org.in

CALL FOR SUBSCRIPTIONS

ISSN 2320-9623 (Print Version) ISSN 2321-1032 (Online Version) Frequency Half yearly **International Journal of Contemporary Medicine** is a double blind peer reviewed international journal which has commenced its publication from January 2013. The journal is half yearly in frequency. The journal covers all aspects of medical practice. The journal has been assigned ISSN 2320-9623 (Print Version) and ISSN 2321-1032 (Online Version). The journal is indexed in many international data bases.

Journal Title	Pricing of Journal		
International Journal of Contemporary Medicine	**Print Only**	**Print+Online**	**Online Only**
INDIAN	INR 7000	INR 9000	INR 5500
FOREIGN	USD 450	USD 550	USD 250

NOTE FOR SUBSCRIBERS

- Advance payment required by cheque/demand draft in the name of **"Institute of Medico-Legal Publications"** payable at New Delhi.
- Cancellation not allowed except for duplicate payment.
- Claim must be made within six months from issue date.
- A free copy can be forwarded on request.

Send all payment to:

Institute of Medico-Legal Publications

4th Floor, Statesman House Building, Barakhamba Road,
Connaught Place, New Delhi-110001
Tel No: +91 - 09971888542, Fax No: +91 11 3044 6500
Email: editor.ijocm@gmail.com, Website: www.ijocm.org.in

Published, Printed and Owned : Dr. R.K. Sharma
Printed : Printpack Electrostat G-2, Eros Apartment, 56, Nehru Place, New Delhi-110019
Published at: Institute of Medico Legal Publications Pvt. Ltd. 4th Floor, Statesman House Building, Barakhamba Road, Connaught Place, New Delhi- 110 001
Editor : Dr. R.K. Sharma, Mobile: + 91 9971888542, Fax No: +91 11 3044 6500