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A Study of Biochemical Profile in Metabolic Syndrome

KEYWORDS: Metabolic Syndrome, Dyslipidemia, Insulin Resistance, Hypertension, Central Obesity

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ABSTRACT *Metabolic Syndrome refers to a conglomeration of various interrelated cardio-metabolic risk factors that predispose to the development of Atherosclerotic Cardiovascular disease (ASCVD) and Type 2 Diabetes Mellitus.*

Aims and Objectives: The aim of the present study is to identify persons with metabolic syndrome using Modified NCEP ATP-III criteria and study their biochemical and anthropometric parameters and assess Insulin Resistance by simple indices like fasting serum Insulin, TG/ HDL-C and HOMA-IR values.

Materials and Methods: The current study included a total of 100 participants divided into two groups Cases(n=50) and Controls (n=50) aged above 35 years from Departments of General Medicine, Government General Hospital, Kadapa. Each group, namely Cases and Controls, includes 25 males and 25 females. Participants with Cardiac, Hepatic and Renal impairments were excluded from the study. The biochemical and anthropometric profile of Cases were compared with those of Controls. Each subject was screened for the presence of metabolic syndrome based on the criteria set by modified NCEP ATP-III which required the presence of at least three risk factors.

Results: The mean and S.D of serum total cholesterol, triglycerides, VLDL-C, LDL-C in controls are 168.2 ± 8.55, 136.72 ± 12.87, 27.38 ± 2.62, 91.78 ± 7.34 respectively as compared to 214.94 ± 20.94, 196.26 ± 21.56, 39.22 ± 4.32, 141.22 ± 20.16 in cases. The comparative data of HDL-C (mg/dL) of controls and cases (both the sexes separately) infers the mean and S.D of male controls is 45 ± 2.45 as compared to 31.96 ± 3.79 in cases. The corresponding data in females is 53.08 ± 1.96 in controls and 37.04 ± 4.89 in cases. The p-value is <0.0001 in both groups, highly significant. The mean and S.D. of fasting serum glucose in controls is 87.48 ± 6.86 as compared to 140.37 ± 10.01 in diabetics and 92.3 ± 5.90 in non diabetics. The p-value is <0.0001(highly significant) in those with history of type 2 DM. The mean and S.D. of HOMA-IR of controls is 1.47 ± 0.33, the mean and S.D. of HOMA-IR of cases with history of type2 DM is 9.99 ± 1.41 as compared to 3.78 ± 0.51 in those without history of type2 DM. The p-value in both the groups is < 0.0001, which is considered highly significant

Conclusion: Metabolic syndrome is a constellation of lipid and non lipid risk factors of metabolic origin. The clinical relevance of metabolic syndrome is related to its role in the development of cardiovascular disease. The best reason to consider the diagnosis of metabolic syndrome is to identify obese people who are most likely to be benefited from aggressive efforts. A focus on metabolic syndrome will encourage public health efforts to give more priority to the promotion of weight control and physical activities in their societies. Simple and economical measures like Life Style Modifications (LSM) and lipid lowering therapy may reduce the burden cardiovascular morbidity and mortality.

INTRODUCTION: Metabolic Syndrome refers to a conglomeration of various interrelated cardio-metabolic risk factors that predispose to the development of Atherosclerotic Cardiovascular disease (ASCVD) and Type 2 Diabetes Mellitus. The prevalence of Metabolic Syndrome is increasing paralleling the epidemic of Obesity owing to rapid changes in the demographic, nutritional as well as socio-economic factors i.e., the transition phase. World Health Organization (W.H.O) estimates that with 19.4 million people with diabetes in India in 1995, the number is projected to 80 million by the year 2030 [50].

Atherosclerotic cardiovascular disease is the principal cause of death, disability and excess health care cost in diabetes mellitus. The association of type 2 DM and cardiovascular disease led to the hypothesis that both arise from common antecedents like Insulin resistance, Dyslipidemia, Obesity or Hypertension. In 1988, Gerald Reaven noted clustering of such risk factors and named it as Syndrome X. This was later modified by W.H.O as Metabolic Syndrome and recognized cardiovascular disease as its primary outcome. National Cholesterol Education Program Adult Treatment Panel has considered Obesity as a key component of Metabolic Syndrome. Obesity is a reflection of an affluent society with increasing sedentary life style combined with intake of high caloric food. Abdominal or central obesity is strongly associated with Metabolic Syndrome.

Insulin resistance (IR) is primary mediator of Metabolic Syndrome [33] and fasting Hyperinsulinemia, a marker of Insulin resistance is associated with atherosclerosis and cardiovascular morbidity [47]. The Hyperinsulinemic euglycemic glucose clamp remains the gold standard for assessment of Insulin resistance [54]. As the procedure is laborious and challenging, simple and minimally invasive laboratory methods like fasting insulin, Homeostasis Model Assessment serve as accessible and practical tools to measure IR [57]. A simple predictor of IR in Metabolic Syndrome, Triglycerides to HDL-Cholesterol ratio, is as reliable as fasting serum insulin levels [64].

Asian Indians have an increased prevalence of Coronary Heart Disease and type 2 DM amongst all ethnic groups [42]. When the risk for the new onset diabetic was examined for the Framingham cohort, in both men and women, the presence of metabolic syndrome was highly predictive of new onset diabetes. In Framingham, the metabolic syndrome alone predicted approximately 25% of all new o

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set cardiovascular disease. Metabolic Syndrome is thus a predictor of Diabetes Mellitus (DM) and Cardiovascular disease (CVD). [54]

The prevalence of Metabolic Syndrome is increasing exponentially in India, both in urban and rural areas. Applying the criteria of Metabolic Syndrome serves as simple and inexpensive tool to identify those at high risk for diabetes and cardiovascular disease particularly those who do not fall into traditional risk categories. Since Metabolic Syndrome and Obesity track into adulthood, recognition of these clinical entities in early life-course provides an insight for effective prevention of ASCVD and T2DM.

Aims and Objectives: The aim of the present study is to identify persons with metabolic syndrome using Modified NCEP ATP-III criteria and study their biochemical and anthropometric parameters and assess Insulin Resistance by simple indices like fasting serum Insulin, TG/ HDL-C and HOMA-IR values.

Materials and Methods

A) ***Study Design:*** The current study included a total of 100 participants divided into two groups Cases(n=50) and Controls (n=50) aged above 35 years from Departments of General Medicine, Government General Hospital, Kadapa. Each group, namely Cases and Controls, includes 25 males and 25 females. Participants with Cardiac, Hepatic and Renal impairments were excluded from the study. The biochemical and anthropometric profile of Cases were compared with those of Controls. Each subject was screened for the presence of metabolic syndrome based on the criteria set by modified NCEP ATP-III which required the presence of at least three risk factors.

Each participant was interviewed and completed a standardized questionnaire format **(Table No:A)** containing information regarding demographics, anthropometric profile; individual characteristics associated with the major risk factors of CVD, past medical history, and biochemical parameters.

B) ***Anthropometric Profile:*** All anthropometric measurements are recorded on subjects without heavy outer garments. The length of the measuring tape is checked with the calibrated length rod periodically.

C) **The anthropometric measurements include:**

- **Body mass index (BMI):** BMI is calculated using Quetelet's Index. Weight was recorded for subjects without any shoes and using an electronic balance. Height was measured using a wall mounted non-extendable measuring tape to the nearest resolution of the tape with the subjects standing with their feet together.

BMI: weight (kg) / Height ^{2} (mt)

Based on the BMI values, the cases of Metabolic Syndrome were categorized into overweight and Obesity classes as per the guidelines from **Table No. B**

- **Waist circumference (WC):** Waist circumference is measured by placing the measuring tape in a horizontal plane around the abdomen at the level of uppermost lateral border of the iliac crest. The plane of the tape is held parallel to the floor and the tape is snug without compressing the skin. The measurement is made at a normal minimal respiration, at the end of gentle exhaling.

D) ***Biochemical Analysis:*** Blood samples (5ml) were collected by venipuncture after a 12 hour overnight fast under aseptic conditions, dispensed into clean plain for Insulin, Lipid Profile and Uric Acid measurements. Fluoride tubes were used to collect the sample for blood glucose estimation. Measures are taken to procure serum/plasma free of hemolysis. All investigations were performed on the same day on a semi-automated analyzer (Transasia-Erba Chem 5 X) except for Insulin assay which was carried on fully automated analyzer (Roche-ELECSYS 1010/2010). Total cholesterol, Triglycerides and HDL-C, Glucose and Uric Acid concentrations were measured by International Federation of Clinical Chemistry (IFCC) approved enzymatic methods. Erba controls (Erbanorm and Erbapath) and calibrators are used for analyses. Our laboratory is enrolled in the External Quality Assessment Scheme (EQAS), Christian Medical College (CMC) Vellore, as part of External Quality control. Insulin is assayed by Electrochemiluminiscence Immunoassay (ECLIA). Based on the ATP-III guidelines **(Table No.C),** lipid profile risk stratification is done in cases with Metabolic Syndrome.

E) ***Criteria applied to screen for presence of Metabolic Syndrome:*** Each subject was screened for the presence of metabolic syndrome based on the criteria set by modified NCEP ATP-III which required the presence of at least three of the following

- Waist circumference :> 90 cm (male), > 80 cm (female).
- Systolic Blood Pressure (SBP) ≥ 130 mmHg and / or Diastolic Blood Pressure (DBP) ≥ 85 mmHg or medical treatment for previously diagnosed hypertension.
- Triglycerides (TG) ≥ 150 mg/dL.
- HDL-C < 40 mg/dL (male), < 50 mg/dL (female)
- Fasting plasma glucose ≥ 100 mg/dL.

F) ***Blood Pressure:*** Blood pressure was recorded to the nearest 2 mmHg using mercury sphygmomanometer with patient in comfortable sitting position.

G) ***Microalbuminuria:*** Type 2 diabetic patients who were tested to be dip stick negative for proteinuria were enrolled for the study of microalbuminuria. 24 hours Urine is collected in a clean container with added Thymol crystals as preservative and participants were given necessary instructions regarding the collection of 24 hours urine. Microalbumin is estimated using Pyrogallol Red Method, an end-point Colorimetric assay. Microalbuminuria is diagnosed on at least two of three, 24 hours urine collection.

H) ***Homeostasis model Assessment (HOMA):***

OMA yields the following formula for insulin resistance

$$\text{HOMA-IR} = \frac{\text{Insulin } (\mu\text{IU/ml}) \times \text{glucose (mmol/L)}}{22.5}$$

(Or)

$$\text{Insulin } (\mu\text{IU/ml}) \times \text{glucose (mg/dL)}$$

Low values indicate high insulin sensitivity where as high values indicate low insulin sensitivity. Values >2.5 were taken as insulin resistant.

Statistical Analysis: The mean and standard deviation of all variables were calculated. Statistical significance was assessed using Student's t-test. P-values < 0.05 are considered statistically significant and <0.0001 considered highly significant. The correlation between fasting serum Insulin and HOMA-IR values was assessed by applying correlation coefficient.

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RESULTS

A total of 100 subjects were enrolled in the present study divided into two groups, Cases and Controls, with 50 subjects in each group.

Table No 1 : General characteristics of the study population

Age	Males	Females	Total
35 to 58 years	25	25	50
Body Mass Index (BMI)			
Overweight	9	5	14
Grade I Obesity	13	17	30
Grade II Obesity	3	3	6
Type 2 Diabetes Mellitus	**17**	**13**	**30**
Hypertension	**9**	**11**	**20**
Classification of Obesity based on BMI:			

BMI	Classification
< 18.5	underweight
18.5–24.9	normal weight
25.0–29.9	overweight
30.0–34.9	class I obesity
35.0–39.9	class II obesity
≥ 40.0	class III obesity

Table No: 1 shows the general characteristics of the study group. Metabolic syndrome was identified based on the modified NCEP ATP-III consensus guidelines among Cases. The present based on modified NCEP ATP-III criteria identified 13 cases (26%)fulfilling 3 criteria; 24 subjects (48%) fulfilling 4 criteria; and the rest i.e., 13 subjects (26%) fulfilling all the 5 criteria.

Table No 2: Relative number of modified NCEP ATP III criteria obeyed by the cases

Sl.No.	Number of Criteria	Number of cases (Percentage)
1	3	13 (26%)
2	4	24 (48%)
3	5	13 (26%)

(I)Anthropometric Profile.

Table No: 3 illustrate the comparative statistical analysis of the anthropometric parameters.

Body Mass Index (BMI): The mean and S.D. of BMI of controls is 24.09 ± 0.77 as compared to 31.63 ± 2.74 in cases. The calculated p-value is < 0.0001, considered highly significant.

Based on the BMI, it is inferred from the study that 14 (28%) of the cases are found to be pre-obese overweight, 30 (60%) fall under Obesity class I category and the rest 6 (12%) come under Obesity class II category.

Waist Circumference: The mean and S.D in male controls is 86.92 ± 1.50 as compared to 109.48 ± 7.24 in cases. The mean and S.D in female controls is 77.6 ± 0.96 as compared to 104.64 ± 6.32 in cases. The p-value is < 0.0001, highly significant.

Table No 3: *Comparative statistical analysis of anthropometric profile of study group*

Parameter	Statistical Parameter	Controls	Cases
Body Mass Index	Mean	24.09	31.63
	S.D	0.77	2.74
	t-test		18.7329
	p-value		<0.0001
Waist Circumference: Males (cm)	Mean	86.92	109.48
	S.D	1.50	7.24
	t-test	21.5753	
	p-value	<0.0001	
Waist Circumference: Females (cm)	Mean	77.6	104.64
	S.D	0.96	6.32
	t- test		29.9103
	p-value		<0.0001

(II)Clinical Analysis: In the present study, 20 cases had a history of Hypertension. Table -4 shows the statistical comparison of systolic and diastolic blood pressure (mm of Hg) of controls and cases with and without history of hypertension. The mean and S.D of systolic blood pressure in controls is 119.4 ± 5.82 as compared to 139.4 ± 6.06 in hypertensive subjects and 121.27 ± 6.64 in those without history of hypertension. The mean and S.D. of diastolic blood pressure (mm of Hg) in controls is 76.36 ± 5.49 as compared to 87.9 ± 3.21 in hypertensives and 75.93 ± 4.68 in normotensives. The p-value is highly significant (< 0.0001) in hypertensives.

In the present study, 30 cases had a history of T2 DM and the mean duration of diabetes in type 2 DM patients is 5.03 years.

Table No: 4 Comparative statistical analysis of Blood Pressure of study group (with and without H/O HTN)

Parameter	Statistical Parameter	Controls	Cases	
			H/O HTN	no H/O HTN
Systolic Blood Pressure (mm Hg)	Mean	119.4	139.4	121.27
	S.D	5.82	6.06	6.64
	t- test		16.8316	1.4976
	p-value		<0.0001	<0.1375
Diastolic Blood Pressure (mm Hg)	Mean	76.36	87.9	75.93
	S.D	5.49	3.21	4.68
	t-test		12.8311	0.4215
	p-value		<0.0001	<0.6743

(III)Biochemical Analysis

Lipid Profile

Table-5 illustrates the comparative statistical analysis of li-

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pid profile parameters of controls and subjects having metabolic syndrome.

The mean and S.D of serum total cholesterol, triglycerides, VLDL-C, LDL-C in controls are 168.2 ± 8.55, 136.72 ± 12.87, 27.38 ± 2.62, 91.78 ± 7.34 respectively as compared to 214.94 ± 20.94, 196.26 ± 21.56, 39.22 ± 4.32, 141.22 ± 20.16 in cases. The comparative data of HDL-C (mg/dL) of controls and cases (both the sexes separately) infers the mean and S.D of male controls is 45 ± 2.45 as compared to 31.96 ± 3.79 in cases. The corresponding data in females is 53.08 ± 1.96 in controls and 37.04 ± 4.89 in cases. The p-value is <0.0001 in both groups, highly significant.

Table No: 5 comparative statistical analysis of lipid profile of controls and cases

Parameter	Statistical Parameter	Controls	Cases
Total Cholesterol (mg/dL)	Mean	168.2	214.94
	S.D	8.55	20.94
	t-test		14.6122
	p-value		<0.0001
Triglycerides (mg/dL)	Mean	136.72	196.26
	S.D	12.87	21.56
	t-test		16.7561
	p-value		<0.0001
VLDL-C (mg/dL)	Mean	27.38	39.22
	S.D	2.62	4.32
	t-test		16.5706
	p-value		<0.0001
LDL-C (mg/dL)	Mean	91.78	141.22
	S.D	7.34	20.16
	t-test		16.2946
	p-value		<0.0001
HDL-C : Males **(mg/dL)**	Mean	**45**	**31.96**
	S.D	2.45	3.79
	t-test		20.4318
	p-value		<0.0001
HDL-C:Females (mg/dL)	Mean	**53.08**	**37.04**
	S.D	1.96	4.89
	t-test		21.529
	p-value		<0.0001

Fasting Plasma Glucose :

Table No.6 shows the comparative data of fasting plasma glucose (mg/dL) in controls and cases with and without history of type2 DM. The mean and S.D. of fasting serum glucose in controls is 87.48 ± 6.86 as compared to 140.37 ± 10.01 in diabetics and 92.3 ± 5.90 in non diabetics. The p-value is <0.0001(highly significant) in those with history of type 2 DM.

Table No 6: Comparative statistical analysis of fasting plasma Glucose of Controls and cases (with and without H/O T2DM)

Parameter	Statistical Parameter	Controls	Cases	
			H/O T2DM	no H/O T2DM
Fasting Plasma Glucose (mg/dL)	Mean	87.48	140.37	92.3
	S.D	6.86	10.01	5.90
	t- test		30.8188	3.7668
	p-value		<0.0001	<0.0002

Markers of Insulin Resistance: In the current study, Insulin Resistance is assessed by simple laboratory indices like Fasting Serum Insulin levels, Derived parameters like HOMA-IR and TG / HDL-C ratio.

Fasting Serum Insulin Levels:

Table-7 shows the serum fasting insulin hormone levels (µIU/mL) in both controls and cases. The mean and S.D. of insulin in controls is 6.8 ± 1.34 as compared to 28.77 ± 2.95 in diabetics and 16.61 ± 1.95 in non diabetics. The p-value is <0.0001(highly significant) in both diabetics and non diabetics.

Table No 7: Comparative statistical analysis of Fasting Serum Insulin of controls and cases (with and without H/O T2DM)

Parameter	Statistical Parameter	Controls	Cases	
			H/O T2DM	no H/O T2DM
Fasting Serum Insulin (µ IU/mL)	Mean	6.8	28.77	16.61
	S.D	1.34	2.95	1.95
	t-test		47.9468	29.3180
	p-value		<0.0001	<0.0001

HOMA-IR Values

Table-8 shows the comparative analysis of homeostasis model assessment-IR of cases and controls. The mean and S.D. of HOMA-IR of controls is 1.47 ± 0.33, the mean and S.D. of HOMA-IR of cases with history of type2 DM is 9.99 ± 1.41 as compared to 3.78 ± 0.51 in those without history of type2 DM. The p-value in both the groups is < 0.0001, which is considered highly significant.

Table No 8 : Comparative statistical analysis of HOMA-IR of controls and cases (with and without H/O T2DM)

Parameter	Statistical Parameter	Controls	Cases	
			H/O T2DM	no H/O T2DM
HOMA-IR	Mean	1.47	9.99	3.78
	S.D	0.33	1.41	0.51
	t-test		41.6031	26.8896
	p-value		<0.0001	<0.0001

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The correlation between HOMA-IR and fasting serum, insulin values in type2 DM patients was measured by correlation coefficient. The correlation coefficient (r value) is found to be 0.89. In non diabetics the corresponding value is 0.88 .(Table No.9)

Table No 9: Correlation between HOMA-IR and Serum Fasting Insulin Value

	H/O of T2 DM	No H/O of T2DM
r-value between HOMA-IR and serum fasting Insulin	0.89	0.88

TG / HDL-C Ratio : Table-10 shows the comparative analysis of TG / HDL-C ratio of cases and controls. The Mean and S.D of TG / HDL-C ratio in cases is 5.80 ± 0.97 when compared to the Mean and S.D of TG / HDL-C ratio in controls is 2.81 ± 0.34.

Table No 10: Comparative statistical analysis of TG/ HDL-C of controls and cases

Parameter	Statistical Parameter	Controls	Cases
TG/ HDL-C	Mean	2.81	5.80
	S.D	0.34	0.97
	t-test	20.5694	
	p-value	<0.0001	

Urine Microalbumin Levels:The Mean and S.D values of urine microalbumin levels (mg/24hrs) in patients with history of diabetes are found to be 215.79 ± 44.74.

Serum Uric Acid Table No. 11 gives the comparative statistical analysis of serum Uric Acid levels in the study group for both sexes separately. The mean and S.D of male controls is 5.45 ± 0.89 as compared to 6.76 ± 1.25 in cases. The corresponding data in females is 4.37 ± 0.92 in controls and 5.77 ± 1.64 in cases. The p-value is <0.0001 in both groups, significant.

Table No: 11 statistical comparisons of serum uric acid levels in males and females

		Controls	Cases
Serum Uric Acid Males (mg/dL)	Mean	5.45	6.76
	S.D	0.89	1.25
	t-test		6.0367
	p-value		<0.0001
Serum Uric Acid Females (mg/dL)	Mean	**4.37**	**5.77**
	S.D	**0.92**	**1.64**
	t-test		5.2645
	p-value		<0.0001

Discussion

Metabolic syndrome represents a clustering of cardiovascular risk factors that are amalgamated into a single multiplex risk factor for atherosclerotic cardiovascular disease (ASCVD). It is well established that Metabolic Syndrome is a predictor of future onset of Diabetes Mellitus and Atherosclerotic Cardiovascular Disease (ASCVD). In Framingham, the metabolic syndrome alone predicted approximately 25% of all new onset cardiovascular disease [54]. The syndrome develops as a result of the interaction of exogenous and endogenous factors. The major exogenous factor is obesity. Endogenous factors include dysfunctional adipose tissue, genetic forms of insulin resistance, various endocrine disorders and genetic susceptibility.

The present study, based on the modified NCEP ATP- III criteria, identified 13 subjects (26%) fulfilling 3 criteria; 24 subjects (48%) fulfilling 4 criteria; and the rest i.e., 13 subjects (26%) fulfilling all the 5 criteria. Dyslipidemia and central obesity as indicated by increased waist circumference alone were common components observed in all cases.

Prevalence of metabolic syndrome rises in parallel with increasing obesity as also the physical inactivity. For the same BMI Indian type2 DM patients have more central obesity as compared to Europeans [50]. In the present study, obesity was assessed by BMI, WC. WC was significantly elevated in both sexes (p-value < 0.001). WC may provide a more practical correlate of abdominal fat distribution. It is also a simple and convenient measurement which is unrelated to height, correlates closely with BMI. As an epilog to the IDF criteria, there are suggestions that high WC alone is sensitive to the presence of IR [31]. It is inferred from the study that 14 (28%) of the cases are found to be pre-obese overweight, 30 (60%) fall under Obesity class I category and the rest 6 (12%) come under Obesity class II category. An abdominally obese patient with metabolic syndrome carries a high risk of ASCVD even before type 2DM develops. The Diabetes Prevention Program (DPP) and other studies showed that even moderate weight reduction will delay the conversion of impaired glucose tolerance (IGT)/ impaired fasting glucose (IFG) into type2DM. In patients with IGT/ IFG it will reduce the severity of metabolic syndrome [21].

Atherogenic dyslipidemia, as recognized by an increase in serum triglycerides and a reduction in HDL-C is a constant finding in the present study. Hypertriglyceridemia is an excellent marker of the insulin resistant condition [20]. As per the NCEP risk stratification for triglycerides, 26 cases (52%) are found to have levels at borderline high and the rest 24 cases (48%) are in the high risk category. Elevated triglycerides are usually a sign of an increase in apo-B containing lipoproteins, a causative agent for atherosclerosis.

The serum total cholesterol was significantly elevated with a major fraction contributed by LDL-C. In the study group, 13 cases (26%) had a desirable value of < 200 mg/dL; 29 cases (58%) are in the borderline and 8 cases (16%) in the high risk category.

The primary pathogenic and independent risk factor for ASCVD, the LDL-C was significantly elevated (p-value < 0.001). Majority of the cases, 26 (52%) fall in the borderline risk category. The near/above optimum, borderline high risk, high risk and very high risk categories constituted 16 cases (32%); 26 cases (52%); 6 cases (12%) and 2 cases (4%) respectively. Elevated LDL-C is a primary target of lipid lowering therapy in persons at risk for ASCVD [21]

A better correlate of apo-B containing lipoprotein, the

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non-HDL-C is considered a secondary target for clinical management of metabolic syndrome. Compared with the control group, the non-HDL-C was significantly elevated in the cases (p-value < 0.001) any patient who has metabolic syndrome with type 2DM deserves to have the LDL- C reduced to < 100mg / dL (non–HDL-C<130mg /dL) [21].

INSULIN RESISTANCE (IR)

IR is the basic pathology underlying metabolic syndrome. In this study an effort is made to assess IR by using simple minimally invasive laboratory tools like measurements like fasting insulin levels, HOMA-IR and TG/HDL-C ratio. From the study, the mean insulin levels in cases with history of type 2 diabetes mellitus is 28.77µIU/mL, considerably higher than those without history of type2DM (mean : 16.61 µIU/ml). The mean insulin level in the control group is 6.8 µIU/ml. The fasting insulin as a measure of insulin resistance can be taken in persons with normal glucose levels. Once diabetes is diagnosed, altered glucose metabolism and abnormal insulin levels probably due to treatment masks the true picture of insulin resistance.

The mean HOMA-IR values in metabolic syndrome cases with history of type2DM are 9.72 ± 2.04 as compared to 3.64 ± 0.85 in those without history of type2DM. The mean HOMA-IR value in controls is 1.45 ± 0.36. Fasting serum insulin levels in type2 diabetic cases significantly correlated with fasting insulin resistance index HOMA-IR (r = 0.89). The corresponding r-value in non diabetics is 0.88.

In the study by Asher Fawwad et.al. the mean fasting serum insulin (µIU/ml) in type2 DM subjects is 9.65 ± 7.08 in females and 11.47 ± 8.24 in males [1]. In another study conducted by Yokoyama et.al., the mean fasting insulin (pmol/L) is 49.8 ± 25.2 in moderately obese type2 DM subjects and 31.2 ± 26.4 in healthy subjects [62].

Hyperinsulinaemia is contributory to the excess CVD risk in presence of insulin resistance [31]. The normal response to insulin resistance is compensatory hyperinsulinaemia. The development of frank diabetes mellitus appears to require an additional defect in insulin secretion. In the absence of a defect in β-cell function, individuals can compensate indefinitely for insulin resistance with appropriate hyperinsulinemia [22].

A serum TG/HDL-C is assessed as part of lipid profile in patients with metabolic syndrome. The ratio is significantly higher in cases with a mean of 5.80 as compared to 2.81 in controls. TG/HDL-C can be considered as surrogate marker for insulin resistance.

The present study included 30 type 2 diabetics and 20 subjects without prior history of type 2 DM. The fasting serum glucose levels are considerably higher in diabetics as compared to non–diabetics (P<0.001).The mean duration of diabetes in type 2 DM patients is 5.03 years. The non-diabetic subjects may develop overt DM if genetic predisposition superimposes on impaired pancreatic β–cell secretory activity.

Microalbuminuria

The dramatic increase in the number of patients with diabetic nephropathy reflects the epidemic increase in obesity, metabolic syndrome and type-2 diabetic mellitus. Patients with history of type 2 DM and negative for dip stick for urinary protein are screened for microalbuminuria. The mean value for microalbumin in diabetic patients is found to be 215.79 mg/24hrs. Microalbuminuria is a potent risk factor for cardiovascular events and death in patients with type2 diabetes. Many patients with type 2 DM and microalbuminuria succumb to cardiovascular events before they progress to proteinuria or renal failure.

Hypertension

Only 40% of those with metabolic syndrome are found to be hypertensive in the present study. The Blood pressure in hypertensive cases is considerably higher than in the control group and statistically significant (P<0.001). There is good evidence of hypertension in the progression of microalbuminuria and overt nephropathy. Early and effective control of hypertension especially in diabetes is important because hypertension worsens both macro vascular and micro vascular complications. In the United Kingdom (UK) prospective diabetes study (UKPDS), tight blood pressure control resulted in a 29% reduction in the risk of microalbuminuria [16]. The effect of blood pressure on the risk of fatal coronary heart disease is 2-5 times greater in diabetic than in non–diabetic people [16].

Uric Acid

Hyperinsulinemia reduces the renal excretion of uric acid and sodium. Hyperuricemia resulting from euglycemia and hyperinsulinemia may precede the onset of type2DM, hypertension, coronary artery disease and gout in individuals with metabolic syndrome. Because hyperuricemia is a minor component of syndrome X, its presence is an indication to screen for and aggressively treat any accompanying obesity, dyslipidemia, type2DM or hypertension [19].

CONCLUSION

Metabolic syndrome is a constellation of lipid and non lipid risk factors of metabolic origin. The clinical relevance of metabolic syndrome is related to its role in the development of cardiovascular disease. The best reason to consider the diagnosis of metabolic syndrome is to identify obese people who are most likely to be benefited from aggressive efforts.

Atherogenic dyslipidemia and central obesity are constant observations in the present study and efforts are to be made to lower the low density lipoprotein, the primary injurious agent in atherogenesis. Because obesity is the major driving force behind metabolic syndrome, it is a reasonable primary target of therapy in both population based and individual approaches.

The application of Surrogate markers is a practical and useful tool to gauze Insulin Resistance in Metabolic Syndrome thus minimizing the costs and time. The study results provide evidence that among metabolic syndrome cases with normal glucose homeostasis, the fasting plasma insulin levels help in assessing insulin resistance. In addition a simple TG/HDL-C ratio is a good marker of insulin resistance. On the other hand, derived parameter like HOMA-IR is a validated surrogate marker to assess Insulin Resistance. These parameters of insulin resistance can be easily applied and interpreted by physicians.

A focus on metabolic syndrome will encourage public health efforts to give more priority to the promotion of weight control and physical activities in their societies. Simple and economical measures like Life Style Modifications (LSM) and lipid lowering therapy may reduce the burden cardiovascular morbidity and mortality.

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