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RESEARCH ARTICLE

Study of Cardiovascular Risk Markers in Type 2 Diabetes Mellitus with Metabolic Syndrome

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Abstract: Cardiovascular diseases claim the lives of individuals worldwide and accounting for 32% of all deaths. Low-and middle-income nations accounts for about three-quarters of mortality due to heart diseases. Cardiovascular risk Markers such as HsCRP and GGT were chosen for the study because of its accuracy and cost-effective nature. This study is planned to focus on the status of inflammation to predict the risk of future cardiovascular diseases in T2DM subjects with the various components of metabolic syndrome. For this study World Health Organisation definition for metabolic syndrome were applied. This study was conducted in, Sri Lalithambigai medical college, Chennai. Total 217 subjects were selected between the age group of 40 years to 60 years. A structured questionnaire including the demographic details, surgical history, any recent infections, present and past medical history, drug history and intake of steroids was obtained. The recruited subjects were asked to visit the hospital after an overnight fast of 10 – 12 hours. The T-Test was used to analyze the demographic parameters and to establish the significance between the groups. The current study suggests that the HsCRP and GGT can be cardiovascular risk marker in T2DM subjects with metabolic syndrome. GGT can be a considerable cardiovascular risk marker in T2DM subjects with metabolic syndrome.

Keywords: Cardiovascular Disease (CVD), Mortality, Heart Attack, Stroke, India

INTRODUCTION

The term "cardiovascular disease" refers to any ailment that affects the heart or blood vessels. It is frequently linked to fatty deposits in the arteries (atherosclerosis) and an elevated risk of blood clots. It has also been linked to artery damage in organs like the brain, heart, kidneys and eyes (1). Cardiovascular Disease **(**CVD) is one of the world's major causes of mortality and disability, yet it can often be avoided by living a healthy lifestyle. CVDs claimed the lives of 17.9 million individuals worldwide in 2019, accounting for 32% of all deaths. Heart attack and stroke were responsible for 85% of these deaths. Low and middle-income nations account for about three-quarters of CVD mortality. CVDs were responsible for 38% of the 17 million premature deaths caused by non-communicable diseases in 2019 (2). At the turn of the century, Cardiovascular Diseases (CVDs) are the leading cause of deaths in India (3). This epidemiological change is mostly due to an increase in the prevalence of CVDs and CVD risk factors in India. In 2016, the estimated prevalence of CVDs in India was 54.5 million. In India, CVDs currently account for one in every four fatalities, with ischemic heart disease and stroke accounting for more than 80% of this burden (4).

Risk factors of cardiovascular disease

It is crucial to recognize cardiovascular disease as soon as possible so that treatment may begin with counseling and medication (5). Because the majority of its risk factors, such as Hypertension, Dyslipidemia, Diabetes, Obesity, Smoking, lack of physical activity, stress and unhealthy dietary practices are preventable or controllable factors. Cardiovascular Disease (CVD) is one of the most preventable causes of death in the world. The social and environmental factors of heart disease and stroke are well understood and improved population-based preventative initiatives could result in a considerable reduction in CVD morbidity and death (6).

Metabolic Syndrome (MetS)

Metabolic Syndrome (MetS) is becoming an epidemic disease as a result of population ageing and lifestyle changes, including dietary changes. The various definitions and criteria for identifying MetS involve interrelated factors such as Obesity, insulin resistance, Hyperglycemia, Hypertension and Dyslipidemia (low high-density lipoprotein and increased triglyceride). Individuals are defined to have metabolic syndrome, which is based on the presence of at least 3 of the 5 traits mentioned and are insulin resistant (7).

Metabolic Syndrome is a disorder characterized by a variety of metabolic abnormalities, as well as cardiovascular risk factors, obesity and insulin resistance. The existence of cardiovascular risk factors increases the likelihood of cardiovascular disorders such as heart attack and stroke. Atherosclerosis, Obesity and Type 2 Diabetes are all linked to cardiovascular risk factors (8). CVD is on the rise, with several studies and it was predicted that by 2020, cardiovascular diseases will be the major cause of mortality, which is the current scenario (9). This study finding reveals crucial information about the presence of several biomarkers in the various components of metabolic syndrome. The current study has gone through the presence of various

Biomarkers in Metabolic Syndrome subjects and its relations with cardiovascular complications.

Cardiovascular risk Markers such as HsCRP and GGT were chosen for the study because of its accuracy and cost effective nature. This study is planned to focus on the status of inflammation to predict the risk of future cardiovascular diseases in T2DM subjects with the various components of metabolic syndrome by following the WHO definition of metabolic syndrome. The finding from this study supports in prevention, early detection, management of metabolic syndrome and cardiovascular disease risk.

MATERIALS AND METHODS

For this study World Health Organisation definition for metabolic syndrome were applied (Table 1). This study was conducted in, Sri Lalithambigai medical college, Chennai. The Participants were selected on the basis of inclusion criteria and exclusion criteria of the study. Total 217 subjects were selected between the age group of 40 years to 60 years.

Table 1

1.Type 2 Diabetes Mellitus
Plus any two of the following
2.Antihypertensive medication and/or high blood pressure (≥140 mm Hg systolic or ≥90 mm Hg diastolic)
3.Plasma triglycerides ≥150 mg/dL (≥1.7 mmol/L)
4.HDL cholesterol <35 mg/dL (<0.9 mmol/L) in men or <39 mg/dl (1.0 mmol/L) in women
5.BMI >30 kg/m^2 and/or waist: hip ratio >0.9 in men, >0.85 in women

Inclusion Criteria

They were screened for T2DM and components of Metabolic Syndrome. The study protocol was approved by institutional ethical committee. All participants were explained about the study and given an information leaflet and written informed consent was obtained. Details of study participants were collected which includes demographic information, medical history, surgical history, recent infections and steroid usage.

Exclusion Criteria

The study excluded smokers, alcoholic, patients with chronic liver diseases, thyroid disorders, renal diseases, cardiovascular disease, respiratory diseases, other inflammatory conditions, autoimmune diseases and recent surgery. Subjects who did not meet the WHO criteria of the MetS were also excluded from the study.

METHODOLOGY

A structured questionnaire including the demographic details, surgical history, any recent infections, present and past medical history, drug history and intake of steroids was obtained. The recruited subjects were asked to visit the hospital after an overnight fast of 10 – 12 hours. 6 ml of the blood sample was collected in EDTA tube and it was used to estimate the biochemical parameters and CVD biomarkers.

Biochemical Assessment

All the study participants were informed in advance to have overnight fast and requested to report on the next day at central lab for the collection of blood sample. 6 ml of blood was withdrawn and dispensed into three vials. 1 ml in EDTA vial for HbA1c measurement. 1 ml in fluoride oxalate vial for Fasting Blood Glucose and was analyzed by Glucose Oxidase-Peroxidase method for the analysis of Blood Glucose level, 4 ml blood in a plain vial for lipid profile, Thyroid function test, Renal function test, Liver Enzymes (GGT), HsCRP. After centrifugation of whole blood at 3000 rpm for 5 mins, serum from plain vial, plasma and Red Blood Cells (RBCs) from anticoagulant vials were collected. Separated serum vials stored at -80ºC until analyzed (within 2 months). All routine parameters were assayed on same day and recorded in proforma. For unknown Thyroid disorder and Renal disorders of study participants, Thyroid function test and Renal Function test were done to follow the exclusion criteria.

Sphygmomanometer was used to measure the blood pressure. Minimum of three readings were taken and the mean of both Systolic and Diastolic Blood Pressure were noted.

Body Mass Index (BMI) was determined by measuring body height and weight. Height was measured in centimeters and body weight was estimated in kilograms (kg) with light clothes and bare feet. BMI was calculated by using the formula weight (kg)/height (meter^2). WHO classification was used to grade the BMI of the subjects

RESULTS AND DISCUSSION

Total 217 subjects were divided in to two groups on the basis of presence or absence of metabolic syndrome (Table 2). Group 1 comprises of T2DM subjects with metabolic syndrome and Group 2 subjects are without metabolic syndrome. Group 1 includes 140 subjects and Group 2 includes 77 subjects.

Table 2: Gender distribution of subjects

GENDER	Male	Female	Total
Group 1	76	64	140
Group 2	47	30	77
Total	123	94	217

Table 3: Comparison of Glycemic Markers between the groups

Variables	**Metabolic Syndrome**	**N**	**Mean**	**pvalue**
FBG	Group 1	140	186.23	0.050*
	Group 2	77	168.04	
HbA1c	Group 1	140	8.350	0.03**
	Group 2	77	7.356	

Table 4: Comparison of Metabolic syndrome components between the groups

Variables	**Groups**	**N**	**Mean**	**SD**	**p value**
BMI	Group 1	140	29.67	4.91	0.00**
	Group 2	77	26.22	4.35	
SBP	Group 1	140	140.80	10.99	0.00**
	Group 2	77	128.62	11.21	
DBP	Group 1	140	90.72	6.39	0.00**
	Group 2	77	85.48	5.51	
TGL	Group 1	140	194.9	134.86	0.00**
	Group 2	77	99.40	32.60	
HDL	Group 1	140	43.50	9.88	0.02*
	Group 2	77	46.47	8.75	

Table 5: Comparison of Cardio vascular risk markers between the groups

CVD Risk Markers	**Groups**	**N**	**Mean**	**SD**	**p value**
HsCRP	Group1	140	6.63	4.87	0.01**
	Group2	77	4.91	4.99	
GGT	Group1	140	35.63	23.73	0.00**
	Group2	77	27.43	11.17	

Statistical test used: t-test.
** p<0.01 highly significant
** p<0.05 significant
BMI-Body mass index
SBP-Systolic Blood Pressure
DBP-Diastolic Blood Pressure
FBG-Fasting Blood Glucose
$HbAI_C$–Glycated Hemoglobin
HDL-High Density Lipoprotein
TGL-Triglycerides
Group 1-Subjects with Metabolic syndrome
Group 2-Subjects without Metabolic syndrome

Clinical assessment and diagnosis of MetS

The clinical criteria for the diagnosis of MetS were not codified in a way that was effective in clinical practice, despite the fact that the notion of MetS has existed in various versions for decades. Because of this, the illness was not frequently diagnosed in patients but was long recognized by clinical research and pathophysiology. However, recent efforts have been established to maintain the standards for clinical diagnosis of the MetS. The clinical signs and symptoms that are well-documented for MetS diagnosis were specified by the WHO committee on Diabetes Mellitus.

Swarup et al. (2022) done a review study on metabolic syndrome and it was explained that the evidence for the risk of ischemic stroke seems to be higher in metabolic syndrome individuals. In addition to the incidence of cardiovascular events metabolic syndrome individual were exposed to the various risk factors such as malignancies of the gallbladder, colon, kidney, prostate gland and also it increases the risk of eclampsia and cognitive performance (10).

In the present study, the subjects were divided in to groups on the basis of presence of Metabolic Syndrome components. The study comprised 217 people with T2DM who met the WHO Clinical criteria of metabolic syndrome. Totally 217 subjects were divided in two groups (i) T2DM subject with Metabolic Syndrome Which comprises of 140 (65%) subjects and (ii) T2DM subjects without Metabolic Syndrome which includes 77 (35%) subjects. Gender distribution of overall subjects, T2DM were found to higher in the Males in our study (Table 2).Similarly Huebschmann et al. (2019) did a review study on sex differences among the T2DM individuals and the burden of cardiovascular risk and summarized that prevalence tends to be higher in males during the middle age (11). Because hyperinsulinaemic data suggest that men are more resistant to insulin when compared with female at midlife due to difference in adipocytes storage pattern and waist circumference (12). Based on the systemic review of 18 studies, it appears that individuals who have poor glycemic control for a long time (5 years) and a sedentary lifestyle were more likely to have full MetS and lower quality of life (13). In the present study, Table indicates the mean value of FBG and HbA1C were greater in individuals which was found to be 186 and 8.3 in the subjects with metabolic syndrome, than the mean value of FBG and HbA1c of 168.04 and 7.3 respectively for the subjects without metabolic syndrome. FBG and HbA1C also shows a significant difference ($p<0.050$, $p<0.03$) between the Group 1 and Group 2 (Table 3).

A high BMI indicates a high risk of CVD, stroke, Hypertension, Hyperlipidemia, NIDDM, Osteoarthritis and some malignancies In our study, the Mean and SD of BMI were 29.67± 4.91 and 26.22 ± 4.35 in between the groups and the mean value is higher in Group 1 subjects with MS when compared with Group 2 subjects without MS (Fig. 4.7). BMI also shows highly significant ($p<0.00$) in between the groups (Table 4)

It was found Hypertension is a well-established risk factor for Coronary heart diseases and stroke. In those with age between 50 and 59 years, all blood pressure parameters were predictors of CHD risk. Isolated systolic hypertension is a major risk factor at all ages, both in men and women for Cardiovascular diseases (14). The mean and SD of Systolic blood pressure and diastolic pressure

for the diabetic population with metabolic syndrome was 140.80 ±10.99 and 90.72 ± 6.39 (Table 4) which was deviated towards the higher side. The pvalue (p<0.000) was found to be significant in between the Group 1 and Group 2.

Martín-Timon et al. (2014) explained that Dyslipidemia affects 95% of people with Type 2 Diabetes mellitus. Elevated Triglycerides, Low density lipoproteins and reduced High Density Lipoprotein plasma concentrations are linked to an increased risk of atherosclerosis and hypertension. The existence of low HDL cholesterol in MetS is caused in part by excessive triglyceride levels (15).

The mean and SD of TGL were 194.9 ±134.86 and 99.40 ± 32.60 in between the groups and the mean value is higher in Group 1 when compared with Group 2. Statistically TGL shows highly significant (p<0.000) in between the groups. In present study the mean and SD of HDL were 43.5 ± 9.88 and 46.47± 8.758 in between the groups and the mean value is higher in Group 2 when compared with Group 1. It was found to be significant (p<0.029) in between the Group 1 and Group 2 (Table 4).

The mean and SD of HsCRP Group 1 and Group 2 were 6.63 ± 4.87 and 4.91 ± 4.99 respectively (Table 5). HsCRP were found to be in higher side for Group 1 individuals with metabolic syndrome when compared with T2DM subjects without metabolic syndrome (Group 2) and also it was statistically significant (p<0.015). Ridker (2016) observed that HsCRP was firmly related to the incidence of cardiovascular events and also HsCRP performed better than LDL-c, indicating that HsCRP may add substantial prognostic information to that conveyed by the Framingham risk score (16). In hypertensive individual CRP may induce atherogenesis by activating the inflammatory cascade and interacting with endothelial and smooth muscle cells, resulting in foam cell formation, endothelial dysfunction and plaque destabilization that may lead to stroke (17).

In our study, the mean and SD of GGT were 35.63 ± 23.73 and 27.43 ± 11.17 in between the groups (Table 5). It was noticed that the mean was higher in T2DM subjects with Mets when compared with T2DM subjects without MetS and also it shows significance between the groups (p<0.00). Similarly a study conducted by Du Song and Zhang et al. (2013) shows increased GGT levels has been indicated to be associated with Cardiovascular Disease (CVD) risk factors including Diabetes Mellitus, Dyslipidemia, Hypertension and Metabolic Syndrome. It has also proved the link with incident CVD and higher levels of GGT have been found in individuals with atherosclerotic plaques (18).

CONCLUSION

MetS is interconnected with, clinical, biochemical, physiological and metabolic factors which directly accelerates the risk of endothelial dysfunction, atherosclerotic cardiovascular disease, chronic stress and hypercoagulable state. Pharamocological approach may be necessary to manage these conditions and reduces risk associated complications. Lifestyle interventions, such as weight loss, physical activity, and smoking cessation, are also important in the management of DM and CVD. The current study suggests that the HsCRP and GGT can be cardiovascular risk marker in T2DM subjects with metabolic syndrome. GGT can be a considerable cardiovascular risk marker in T2DM subjects with metabolic syndrome Identification of individuals at risk for developing cardiovascular diseases will allow for early implementation of healthy food habits, physical activity and therapeutics to reduce the risk in the vulnerable individuals.

Conflict of Interest

The authors declare that there are not conflicts of interest

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