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Evaluation of Serum Uric Acid and Serum Gamma Glutamyl Transferase in Patients with Metabolic Syndrome

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Abstract: *Most individuals who develop cardiovascular disease (CVD) have cluster of multiple risk factors like dyslipidaemia, hypertension and hyperglycaemia. This cluster have termed as* metabolic syndrome. *It is well known that the prevalence of obesity, diabetes and metabolic syndrome all increase with age and linking to oxidative stress markers. Very few studies have been done to show the role of oxidative stress markers in metabolic syndrome.*

Methodology: *A prospective randomized double blinded case control study was undertaken on 30 metabolic syndrome patients and 30 healthy controls in the age group of 40-70 years of either sex admitted to the respective specialty unit. The study protocol was approved by the institutional ethical committee. Aseptically 3ml of venous blood was collected with due consent from the patients and the controls for estimating : GGT and Uric acid*

Result: *The statistical significant difference were observered in the mean values of GGT and uric acid parameters between study groups. Both the parameters shows a direct correlation with the syndrome.*

Conclusion: *Hence, by periodically estimating the above said parameters with regular treatment protocols in diagnosed or in suspected metabolic syndrome patients will predict early and better outcome.*

Keywords: *oxidative markers, obesity, metabolic syndrome, dyslipidaemia, hyperglycaemia.*

I. Introduction

Most individuals who develop cardiovascular disease (CVD) have multiple risk factors. Some risk factors that commonly cluster together (like dyslipidaemia, hypertension and hyperglycaemia) have been termed the metabolic syndrome [1]. Most people with this syndrome have insulin resistance, which confers an increased risk of type 2 diabetes. When diabetes becomes clinically apparent, CVD risk rises sharply. Apart from CVD and type 2 diabetes, individuals with metabolic syndrome are susceptible to other conditions, notably polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma etc [1,2].

ATP (Adult Treatment Panel) III defined the metabolic syndrome essentially as a clustering of metabolic complications of obesity. The criteria listed include abdominal obesity, determined by increased waist circumference, raised triglycerides, reduced HDL, elevated blood pressure, and raised plasma glucose. Patients having at least three of the following five criteria were considered to have Metabolic Syndrome: (i) fasting blood glucose ≥110 mg/dl; (ii) serum triglyceride ≥150 mg/dl or being on lipid lowering therapy; (iii) serum HDL <40 mg/dl in men and <50 mg/dl in women or being on antilipidemic therapy; (iv) blood pressure ≥130 mmHg systolic and/or ≥85 mmHg diastolic or being on antihypertensive therapy; and (v)waist circumference >102 cm in men and >88 cm in women[1,2].

WHO Clinical Criteria for Metabolic Syndrome[1]:
Insulin resistance, identified by one of the following:
- Type 2 diabetes
- Impaired fasting glucose
- Impaired glucose tolerance
- or for those with normal fasting glucose levels (<6.1 mmol/L), glucose uptake below the lowest quartile for the background population under investigation under hyperinsulinemic, euglycemic conditions,

Plus any two of the following:
- Antihypertensive medication and/or high blood pressure (≥140 mm Hg systolic or ≥90 mm Hg diastolic)
- Plasma triglycerides ≥1.7 mmol/L
- HDL cholesterol <0.9 mmol/L in men or <1.0 mmol/L in women
- BMI >30 kg/m2 and/or waist: hip ratio >0.9 in men, >0.85 in women
- Urinary albumin excretion rate ≥20 µg/min or albumin: creatinine ratio ≥3.4 mg/mmol

Uric acid, a oxidative stress marker act as a defense mechanism against advanced atherosclerosis, or hyperuricemia-induces endothelial dysfunction and thus facilitates the smooth muscle cell proliferation causing atherogenesis [3].

Serum gamma-glutamyltransferase is a marker of hepatobiliary disease and alcohol consumption. Factors responsible for elevated liver enzymes, especially GGT, have been shown to include increasing age, obesity, DM, physical inactivity, insulin resistance, hypertension, and dyslipidaemia (metabolic syndrome)[4,5].

II. Aim Of Study

To evaluate oxidative stress markers like uric acid, gamma-glutamyl transferase in these patients which may help in predicting the prognostic outcome of metabolic syndrome cases.

III. Materials And Methods

The sample size will consist of around 30 metabolic syndrome patients in the age group of 40-70 years of either sex admitted to the respective specialty unit/OPD, and around 30 non-metabolic syndrome patients aged between 40-70 years of either sex admitted to the respective specialty unit/OPD.

Inclusion Criteria

Metabolic syndrome patients aged between 40-70 years of either sex. And non metabolic syndrome patients(control) aged between 40-70 years of either sex, admitted to the respective speciality units/OPD in JSS medical college and hospital.

Exclusion criteria

1) Critical ill patients.
2) Patients aged either <18 years and >60 years of either sex.
3) Female patients with menstruation/pregnancy.

Three millilitre of venous blood will be collected under all aseptic precaution and used for estimation of oxidative stress markers like gamma glutamyl transferase and serum uric acid.

The methodologies for the above parameters are mentioned below:

- Glucose is estimated by GOD-PAP method.
- Total cholesterol is estimated by CHOD-PAP method.
- HDL cholesterol is estimated by immunoinhibition method.
- Triglycerides is estimated by GPO-PAP method.
- LDL cholesterol is estimated by enzyme selective protection method.
- VLDL is estimated by calculation method
- Uric acid is estimated by using uricase method by Toshiba analyser.
- GGT is estimated by szasz methodology by Toshiba analyser.

Statistical methods to be employed:

Mean and standard deviation will be estimated to assess the level of serum uric acid and gamma glutamyl transferase in the study and control groups. Student- t test will be applied to test the significance of difference in the parameters between the study and the control groups. Data entry and statistical analysis will be carried out using Microsoft excel and EPI-INFO. Package version 3.5.1. Pearsons co-relation will be applied among various parameters under study.

All the above mentioned statistical methods will be performed through software SPSS (Statistical Package for Social Sciences) version 16 for windows.

IV. Result

The present study analyzes the correlation between oxidative stress markers in metabolic syndrome patients with healthy controls.

The study was compared between 30 metabolic syndrome patients with 30 non- metabolic syndrome patients. The cases and controls were age and sex matched.

The age group was between 40 years to 70 years. The mean age in metabolic syndrome patients was 54.7±9.2 years and in controls was 52.8 ± 8.310 years. The cases and controls were age matched with $p > 0.05$. This is also shown graphically in terms of mean ± SD as bar diagrams in figure 1.

Table no 2 shows gender distribution in the study groups. Patients with metabolic syndrome consisted of 10 males and 20 females. In the control group there were 9 males and 21 females. The cases and controls were sex matched with $p > 0.05$. This is also shown graphically as pie charts in figure 2.

The mean and standard deviation (SD) of Uric acid levels in metabolic syndrome patients and in controls respectively are represented in the table 3.

The table 3 shows that mean levels of uric acid were significantly increased in metabolic syndrome patients when compared to controls. The statistical significant difference in the mean values of the above parameters between study groups was < 0.01. This is also shown graphically in terms of mean as bar diagrams in figure 3.

The table 4 shows that mean levels of gamma glutamyl transferase were significantly increased in metabolic syndrome patients when compared to controls. The statistical significant difference in the mean values of the above parameters between study groups was < 0.01. This is also shown graphically in terms of mean as bar diagrams in figure 4.

Table 1: Mean values of age distribution between the study groups

Age groups (years)	Metabolic syndrome	Controls
40-55 years	19	20
56-70 years	11	10
Mean±SD	54.7±9.2	52.8 ± 8.310

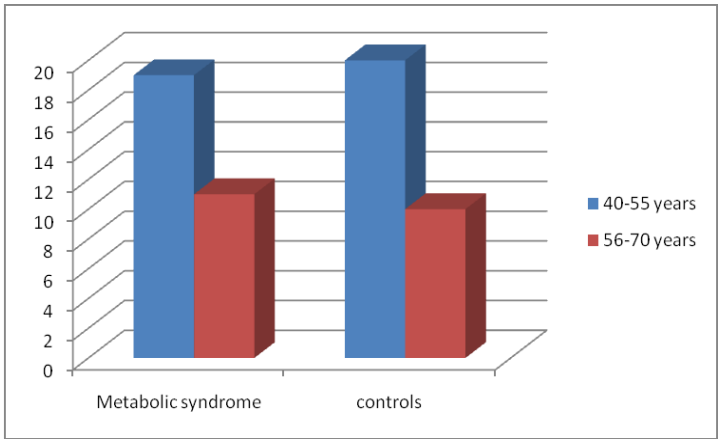

Figure 1: Mean values of age distribution between the study groups.

Table: 2

Gender	Cases		Controls	
	Number	%	Number	%
Male	10	33.3	9	30.0
Female	20	66.6	21	70.0
Total	30	100.0	30	100.0

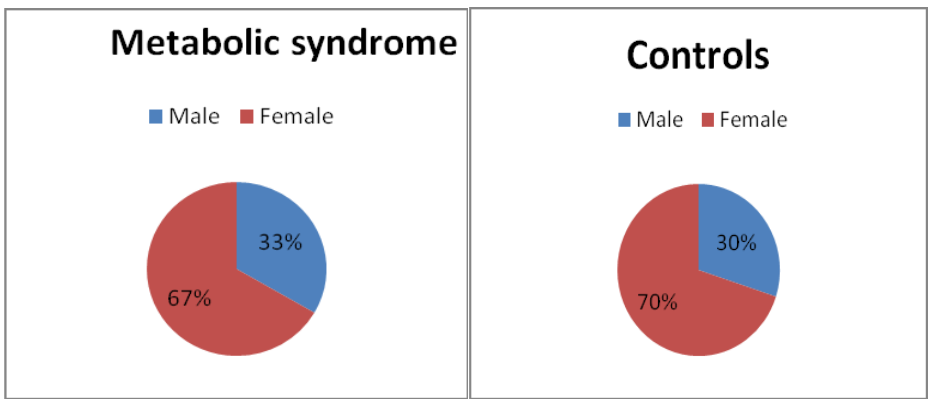

Figure 2: Gender distribution between the study group

Table 3: Mean values and SD with significance of Uric acid between the study groups.

Uric Acid	Group		P value
	Cases	Controls	
Mean	8.04	4.09	<0.01
Stand deviation	2.07	1.20	

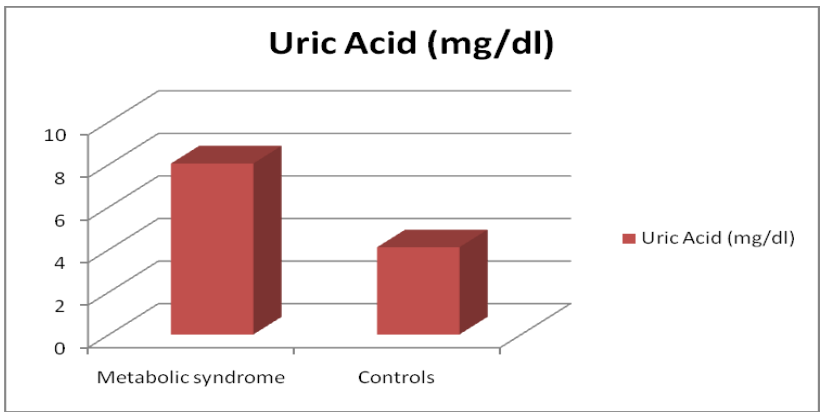

Figure 3: Mean values of Uric acid levels in the study groups

Table 4: **Mean values and SD with significance of Gamma Glutamyltransferase between the study groups.**

Gamma Glutamyltransferase	Group		P value
	Cases	Controls	
Mean	59.23	23.53	<0.01
Stand deviation	67.75	5.27	

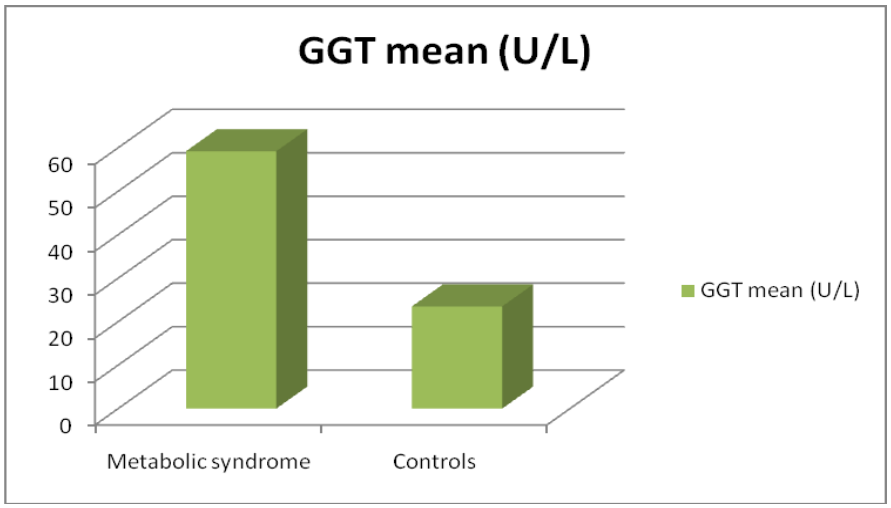

Figure 4: Mean values of Gamma glutamyltransferase levels in the study groups

V. Discussion

Metabolic syndrome is a complex condition that is characterized by a cluster of closely related clinical features linked to obesity, including insulin resistance, dyslipidemia and hypertension. Using data from NHANES IV, the age-adjusted prevalence of metabolic syndrome in Americans is 27%.[2,6] Metabolic syndrome is associated with an increased risk of cardiovascular disease, which is ultimately responsible for a considerable proportion of diabetic mortality. The most accepted and unifying hypothesis to describe the pathophysiology of the metabolic syndrome is insulin resistance[7,8].

Obesity is the most common and important risk factor for the development of type 2 diabetes mellitus (T2DM). Obesity leads to the reduction in the sensitivity to the biological actions of insulin, a pathophysiological state known as insulin resistance[9].

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both[10]. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Hypertension is a very common condition which frequently remains undiagnosed until relatively late in its course, leading to a variety of other life-threatening conditions like kidney damage and heart failure. It is a very prominent feature of the metabolic syndrome, present in up to 85% of patients. In the context of global cardiovascular risk, metabolic syndrome is indeed a high risk condition, involving obesity, dyslipidemia, hypertension and diabetes. In spite of controversy surrounding its definition and etiology, metabolic syndrome

represents a useful and simple clinical concept which allows for earlier detection of type 2 diabetes and cardiovascular disease. The establishment of hypertension as a component of the syndrome has enabled better insight into the condition and allowed for earlier detection and treatment[2,7].

In the present study it was observed that the gender distribution in metabolic syndrome patients was 10 males and 20 females respectively which suggests that metabolic syndrome is more prevalent in women when compared to men. Many previous studies state that women are more likely to develop metabolic syndrome when compared to men[8].

In the present study, we found that the serum uric acid levels in metabolic syndrome patients group were marginally elevated than compared to the control group which was consistent with study done by Hairong Nan in finland, 2008. UA is an end product of purine metabolism and is related to the purine bases of the nucleic acids in humans. The serum UA level is determined by the balance between purine intake and UA production. Approximately two thirds of total body urate is produced endogenously, the remaining one third is accounted for by dietary purines. Approximately 70% of the urate produced daily, however, is excreted by the kidneys. The rest is eliminated by the intestines. Long-term hyperuricemia is a causal factor to damage development in the joints, connective tissues, and kidney. Hyperuricemia is associated with, and may predispose to, hypertension, diabetes, renal disease, and cardiovascular disease (metabolic syndrome) {chart 2-vide supra}[11].

In the present study, we found an significantly raised gamma glutamyltransferase levels in metabolic syndrome patients group than compared to control groups, which is evident and consistent from other recent studies[12]. GGT protein catalyzes an enzymatic action, which is the transfer of a glutamyl residue to an acceptor through the glutamate's gamma carboxylic acid to an amine or other amino acid. The most abundant natural substrate is glutathione. Glutathione is extracellular and cannot pass through the cell membrane. Adequate supply of intracellular glutathione protects cells against oxidants produced by normal metabolism[13]. Glutathione can be broken down into 3 amino acids (including cysteine, which may be deficient in low-protein diets) at the cell membrane by GGT. Figure 1 shows suspected pathways relating GGT to type 2 diabetes {?metabolic syndrome}. It is likely that insulin resistance leads to increased fat deposits in the liver, which cause oxidative stress and inflammation, leading to type 2 diabetes {?metabolic syndrome}[14].

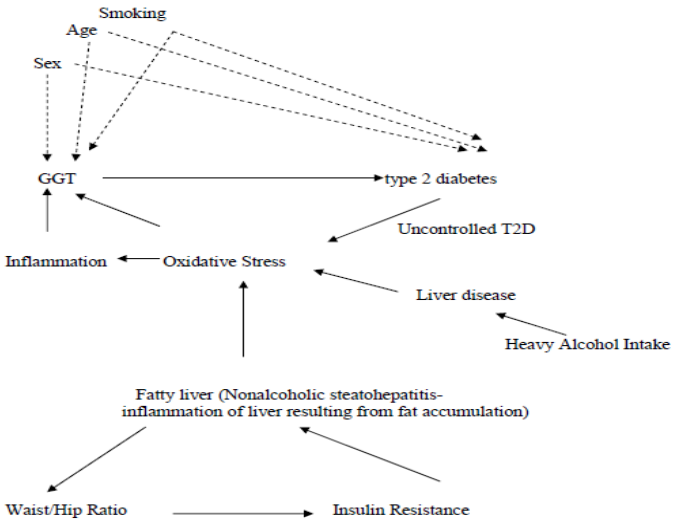

Figure 1. Diagram of known and theoretical pathways.

VI. Conclusion

ATP (Adult Treatment Panel) III defined the metabolic syndrome essentially as a clustering of metabolic complications of obesity. Based on the present study and data available from the literature, it is implicated that there is association between lipid profile parameters, oxidative stress markers with their increased risk for insulin resistance disorders, such as Type-2 diabetes, metabolic syndrome and cardiovascular disease. There is also an association between oxidative stress marker and metabolic syndrome. Given the high prevalence of the metabolic syndrome, it is essential that patients with this syndrome are to be identified as early as possible and followed regularly so as to prevent the development of various lethal complications emerging from the pathogenesis of this syndrome.

Thus estimation of the above said parameters regularly will help in the better management of the metabolic syndrome patients and proves as better prognostic markers in such patients.

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