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COMPARATIVE STUDY OF URIC ACID LEVELS IN DIABETES MELLITUS AND METABOLIC SYNDROME

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ABSTRACT

Diabetes mellitus (DM) is a systemic metabolic disorder characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The metabolic syndrome consists of a constellation of metabolic abnormalities.Serum Uric acid (UA) level has been suggested to be associated with factors that contribute to the metabolic syndrome. However the association between serum UA level and number of components that contribute to the metabolic syndrome and DM (diabetes mellitus) was associated most with higher serum UA level. This study compared the serum Uric Acid Levels in Diabetes Mellitus and Metabolic Syndrome. The Present study was carried out in the department of Biochemistry, Sri Lakhsmi Naryana Institute of Medical Sciences, Puducherry. The present study was conducted on 200 patients with Type II diabetes mellitus, 200 patients with metabolic syndrome, and 200 patients with controls as per IDF criteria and waist circumference. Serum uric acid levels are elevated when compare to other parameters (FBS, HbA1C, LDL-C, Urea, Creatinine, TGL, Lipoprotein (a)). This facilitates the claim that serum uric acid in association with the lipid ratios could serve as simple and economically viable biochemical marker. UA have a strong association with Diabetes and Metabolic syndrome.

KEY WORDS: **Metabolic syndrome, Uric acid, Hypertension, Lipoprotein a, Diabetes Mellitus.**

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INTRODUCTION

Diabetes affects more than 120 million people world-wide and it is estimated that it will affect 220 million by the year 2020[1] and it is almost double in 2030. [2,3] Diabetes mellitus is a syndrome of chronic hyperglycemia due to relative insulin deficiency, resistance or both.[4] Hyperuricemia is a one of the condition that is significantly associated with markers of metabolic syndrome such as dyslipidemia, glucose intolerance, high blood pressure, and central obesity, which are accepted as risk factors for developing cardiovascular disease(CVD). Hyperuricemia associated with glucose intolerance due to various mechanism, however, the most important is the association between insulin and renal resistance to absorption of urates.[5,6] Patients with diabetes mellitus are at greater risk of developing cardiovascular diseases because of lipid changes. It has been well observed that controlling diabetes and lipid levels provide great benefit to diabetic patients. Metabolic syndrome is a global public health concern.[7] Core features of metabolic syndrome include central obesity, dyslipidemia.[8] An association between diabetes and hypertention has long been recognized and a syndrome has been described of hyper insulinaemia[9], glucose intolarence[9], reduced levels of HDL cholesterol and hypertriglyceridaemia in association with hypertention. This association is a major risk factor for cardiovascular disease[5]. There are few results providing data for the relationship between physiologically interrelated risk factors and metabolic syndrome.[10] Uric acid act as a natural antioxidant. Uric acid cannot scavenge all radicals, with superoxide as an example. Uric acid is an antioxidant only in the hydrophilic environment, which is probably a major limitation of the antioxidant function of uric acid.[11]Hyperuricemia is one of the risk factors of metabolic syndrome and it clearly has a strong correlation between various components of diabetic dyslipidemia including raised LDL-C, reduced HDL, raised triglycerides, and also urea, bilirubin, creatinine levels are elevated.[11-12] Thus the role of UA in the pathogenesis and the development of the diabetic complications is controversial.[13] Several studies shown that hyperuricemia is one of the risk factors of metabolic syndrome and it clearly has a strong correlation between various components of diabetic dyslipidemia including increased LDL, TGL and reduced HDL.[14] Therefore, the present study was designed to look for any association of serum uric acid with oxidative stress(OS) in DM and metabolic syndrome

MATERIALS & METHODS

The Present study was carried out in the department of Biochemistry, Sri Lakhsmi Naryana Institute of Medical Sciences, Puducherry. In this study total number of patients divided in to 3 different groups. The distributions of subjects in the study were as follows:

I. Diabetes mellitus- 200 subjects
II. Metabolic syndrome- 200 subjects
III. Control group – 200 subjects

The study was approved by the institutional ethical committee of Sri Lakhsmi Naryana Institute of Medical Sciences, Puducherry (No.IEC/C-P/44/2014). All the data were collected in a prescribed preform. The questionnaire contained questions regarding the duration of diabetes, the family history of diabetes, smoking, the dietary history and the history of hypertension, alcohol drinking, etc. Obtained informed consent form from the subjects.The Group I Patients diagnosed as diabetes mellitus with FBS > 126mg/dl, RBS>200mg/dl and HbA1C of > 6.5%. The 200 (Group II) patients were diagnosed as having metabolic syndrome based on the history, clinical examination. The control groups were 200, they were collected from medical staff members and relatives who were free from signs and symptoms of metabolic syndrome, like lipid disorders, diabetes mellitus and hypertension. All the patients were asked to fast overnight for a period of minimum 12 hours. 5ml of the blood samples which were taken for analysis were obtained from the antecubital vein. 5 ml of venous blood samples were collected from patients and controls. Same up to criteria .The analysis of plasma glucose was done by the glucose oxidase method, while the serum, TG, UA, Urea, Bilirubin, Creatinine, HbA1C, were done by using enzymatic kits on Siemens fully automated analzyer. Lipoprotein (a)-estimated through the turbidometic method. The LDL-C was calculated by the following equation:

LDL-C = TC – HDL-C – (TG × 0.2).

Statistical Methods

The statistical analysis was done by the unpaired two tailed‘t’ test and the Pearson’s correlation coefficient by using online calculator. The data were presented as mean with SEM. P<0.005 is considered as statistically significant.

RESULTS

Increased serum UA levels were found in DM (P<0.001) comparing with metabolic syndrome and controls with respect to metabolic parameters in DM, patients in the higher UA levels quartiles exhibited higher levels of systolic blood pressure, BMI, waist circumference.Increased serum fasting blood sugar (p<0.001), HbA1C (P<0.002), TG (P<0.001), LDL (P<0.002), Bilirubin (p<0.001), creatinine levels (P<0.001) were found in DM and comparing with metabolic syndrome and controls. In contrast, the patients with higher uric acid levels displayed shorter duration of diabetes and lower levels of LP(a) were found in diabetes comparing with metabolic syndrome. Strong correlation between UA and BMI, waist circumference, TG, HbA1c, LDL-C, Bilirubin, Creatinine were found. Remarkably serum UA levels increased association gradually in DM comparing with metabolic syndrome. Pearson’s correlation coefficient for the relationship between UA and each variable were as follows: Age: 0.24/-0.10; BMI, 0.26/0.22; Systolic blood pressure, 0.24/0.12; diastolic blood pressure, 0.25/0.14; total bilirubin 0.02/0.03; TG. 0.21/0.21; Glucose, 0.10/-0.10; and HbA1c, 0.14/-0.10. A P value of P<0.001 were obtained for all these correlations except for urea.

Table 1
The Mean±SEM values of Urea, creatinine, LDL-C FBS, HbA1C, Uric acid, bilirubin, Lipoprotein (a) in diabetes mellitus and metabolic syndrome patients and control

S.No.	Parameters	DM(number of patients-200) Mean ± SEM	MetS(number of patients-200) Mean ± SEM	Controls(number of patients-200) Mean ± SEM	p Value
1	FBS	168.55± 4.92	156.55± 4.82	106.12± 1.68	p<0.001
2	HbA1C	43.2±1.7	41.1±1.2	3.86±1.0	P<0.002
3	TG	258±31.02	243±28.62	169.2±28.4	P<0.001
4	Uric acid	8.2 ± 0.06	6.5± 0.42	5.22± 0.23	p<0.001
5	LDL-C	126.2±30.1	123.8±31.4	68.3±13.2	P<0.002
6	Bilirubin	1.2 ± 0.07	1.0± 0.04	0.07 ± 0.02	p<0.001
7	Urea	19.2±1.23	18.6±1.28	12.2±1.01	p<0.001
8	Creatinine	1.3±0.08	1.1±0.06	0.08±0.02	p<0.001
9	LP(a)	27.69±12.13	35.10±13.2	13.0±6.78	p<0.003

DISCUSSION

Uric acid is the end product of purine catabolism. Uric acid is a diprotic acid produced by the enzyme xanthine oxidase from xanthine and hypoxanthine. Xanthine oxidase uses molecular oxygen as electron acceptor and generates superoxide anion and other reactive oxygen species (ROS).[15,16] Uric acid converted in to allnton. Uric acid is chain breaking antioxidant; it plays an important role in plasma. Increased serum uric acid levels are found to be associated with insulin resistance and components of the Metabolic syndrome include central obesity, dyslipidemia (elevated triglycerides and low levels of HDL-C. dysglycaemia (including pre-diabetes or diabetes) and high blood pressure,[17-21] mild kidney disease, endothelial dysfunction and chronic inflammation.[22] UA is also a physiological free radical scavenger and one of the major contributors of the plasma antioxidant capacity. Thus UA plays a dual role, both as a prooxidant and assay antioxidant. DM is associated with OS increased free radical formation.[23] While on one hand, hyperglycemia generates free radicals an the other hand it also impairs the endogenous antioxidant defense system.[11] Under the condition of increase oxidative stress, there occurs the depletion of the local antioxidants, which causes a reduction in the antioxidant status of the body.[24] Hyperuricemia associated with elevated circulating endothelial levels and are of the major sites of the production of UA in cardiovascular system. High UA levels were independently associated with increased proximal tubular sodium re absorption in men UA other hand cause to hypertension in metabolic syndrome and DM. Higher UA levels may be a risk factor for Hypertension and Cardiovascular diseases due to excess of lipids in blood stream leads to major complications like atherosclerosis and hyper lipoproteinemia.[25] Finally increased UA levels in DM and metabolic syndrome may be a response to oxidative stress in patients. This increasing UA may act in conjugation with the lipids to cause atherosclerotic complications.[26] From the present study, it appears that uric acid alone acts as an risk marker for DM and metabolic syndrome. UA may have a direct role in the atherosclerotic process because human atherosclerotic plaque contains more UA they do control arteries. Inflammatory is of the features of atherosclerotic plaque contains more UA than do control arteries. An inflammatory response is one of the features atherosclerosis and UA crystals may induce inflammatory responses that are reduced of lipoproteins, which have ability to bind UA crystals.[27] UA had a strong association with metabolic syndrome, a prospective study is warranted to determine if the prevention or treatment of hyperuricemia affects the development of metabolic syndrome.[28] The findings of our study revealed a significant increase in serum uric acid levels in cases as compared to controls (p<0.001). We also observed a positive correlation between serum uric acid levels and Triglycerides and LDL-C, HbA1C, Urea, Creatinine, Bilirubin, and Lipoprotein(a) levels.The increases in serum uric acid, plasma lipid concentrations, and other parameter levels in patients with concurrent diabetes and Metabolic Syndrome demonstrated in this study correlated with previous reports. According to study by Satoru Kodama et.al.[29] An increased risk of diabetes associated with an incremental increase in SUA was consistently found within all strata of each study characteristic According to study by Johnson and colleagues, they have reported a positive association of hyperuricemia with hypertension in T2DM with complications.[30] According to study by Narasimman Gurusamy [31] shows that an elevated serum uric acid level was a causal factor contributed to an increased risk of Metabolic syndrome. Higher levels of serum UA are associated with risk of metabolic syndrome in adult, we were not compared in men and women. But our study is the only study 200 patients were assessed in DM, Metabolic syndrome an controls. Future prospective studies in gender wise ideally include such information to strengthen an the study findings.

CONCLUSION

In present study shows that hyperglycemia, dyslipidemia are having positive association with hyperuricemia. As hyperuricemia cases leads to increased synthesis of pro oxidants and causes oxidative stress. We conclude that there is strong association between oxidative stress and Diabetic mellitus as well as metabolic syndrome. We found a positive association between oxidative stress and DM as well as metabolic syndrome with UA in adults. Our data shown that serum UA was significantly associated with the diagnosis of DM and metabolic syndrome patients. Future prospective studies to be conducted role of UA in the pathogenesis of DM and metabolic syndrome and impact on renal mechanism dysfunction leads to decreased UA levels and clinical findings.

CONFLICTS OF INTEREST

Conflicts of interest declared none.

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