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RESEARCH ARTICLE

A STUDY OF VARIATION OF SERUM URIC ACID LEVELS IN PATIENTS WITH AND WITHOUT DIABETES MELLITUS WHO HAVE NORMAL KIDNEY FUNCTION

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ABSTRACT

Background: Several epidemiologic studies have reported that high serum levels of uric acid are strongly associated with prevalent health condition such as obesity, insulin resistance, metabolic syndrome essential hypertension and renal disease. This study aimed to investigate the level of uric acid in type 2 diabetes mellitus patients and in non-diabetes controls with normal kidney function. This study also included the correlation of serum uric acid with glucose, creatinine, age, gender and duration of diabetes.

Method: A single-centric, hospital based, cross-sectional study was conducted for 6 months. The study had two groups: 92 patients with diabetes and 92 patients without diabetes. All the patients were having normal kidney function. The patients were evaluated for fasting blood sugar (FBS), post prandial blood sugar (PPBS) and serum uric acid levels.

Result: No significant difference in mean uric acid levels were reported between diabetes and non-diabetes population. No significant correlation of uric acid levels with age, gender and glucose levels (FBS and PPBS) were not reported, but the significant positive correlation of uric and duration of diabetes were observed in male diabetes population.

Conclusion: Since the cross sectional study shows confounding data, the implication of uric acid levels in diabetes mellitus as well as in pre-diabetes need to be further investigated.

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INTRODUCTION

Diabetes mellitus is the most common metabolic disorder. Around 415 million across the world are living with diabetes, out of which over 69 million are Indians (International Diabetes Federation, 2015). Serum uric acid has positive association with serum glucose levels in healthy subjects (Causevic *et al.,* 2010). Recent studies have demonstrated that uric acid levels are higher in subjects with prediabetes and early type 2 diabetes mellitus (T2DM) than in health controls. Furthermore, an elevated serum uric acid level was found to increase chances for developing T2DM in individuals with impaired glucose tolerance (Iraj *et al.,* 2014). Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance and/or hyperinsulinemia in metabolic syndrome. An elevated uric acid levels, as reported, often precedes the development of obesity, hyperinsulinemia and diabetes (Hsu *et al.,* 2013). In addition, uric acid has been implicated in the development of metabolic syndrome and hypertension (Causevic *et al.,* 2010; Hsu *et al.,* 2013).

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However, hyperuricemia is not always found in diabetes individuals (Causevic *et al.,* 2010). Inconsistent data exist about association of Uric acid levels and hyperinsulinemia or impaired glucose (Pavithra *et al.,* 2016). Although, several studies have implicated the role of uric acid in progression of pre-diabetes to diabetes, studies related to uric acid levels in diabetes development are controversial and deserve further analysis. This study included the comparison of uric acid levels in diabetes and non-diabetes population with normal kidney function and the correlation of uric acid levels with glucose, creatinine, age, gender and duration of diabetes mellitus.

MATERIALS AND METHODS

A single-centric, hospital based, cross-sectional study was conducted for 6 months in Government Medical College, Trivandrum. Study included T2DM patients (35 – 65 years age group) with normal kidney function attending diabetes clinic, and non-diabetes mellitus patients (35 – 65 years age group) with normal kidney function attending medicine outpatient department. Study excluded patients having serum creatinine greater than 1 mg/dL, those who had CVD (angina, myocardial infarction, ischemic stroke, coronary vascularization, etc.), and severe chronic obstructive pulmonary diseases, malignancies, gout, using hyperuricemic drugs, pregnancy, alcoholics, etc.

Table 1. Demographic characters of participants

Group	Age in years			Gender		Duration of diabetes (years)		
	35-45	45-55	55-65	Male	Female	<5	5-10	>10
Non-Diabetes	40.2%	29.3%	30.4%	41.3%	58.7%		N/A	
Diabetes	40.2%	29.3%	30.4%	39.1%	60.9%	51.1%	42.4%	6.5%

Table 2. Pearson correlation of serum uric acid with FBS, PPBS, Age and Duration of DM in Diabetes Population

Correlation with Uric acid	Male (n = 74)		Female (n = 110)	
	Pearson Correlation	P	Pearson Correlation	P
FBS	-0.009	0.943	0.67	0.485
PPBS	-0.083	0.482	0.093	0.331
Age	-0.175	0.136	-0.04	0.676
Duration of DM	0.388	0.019	-0.159	0.242

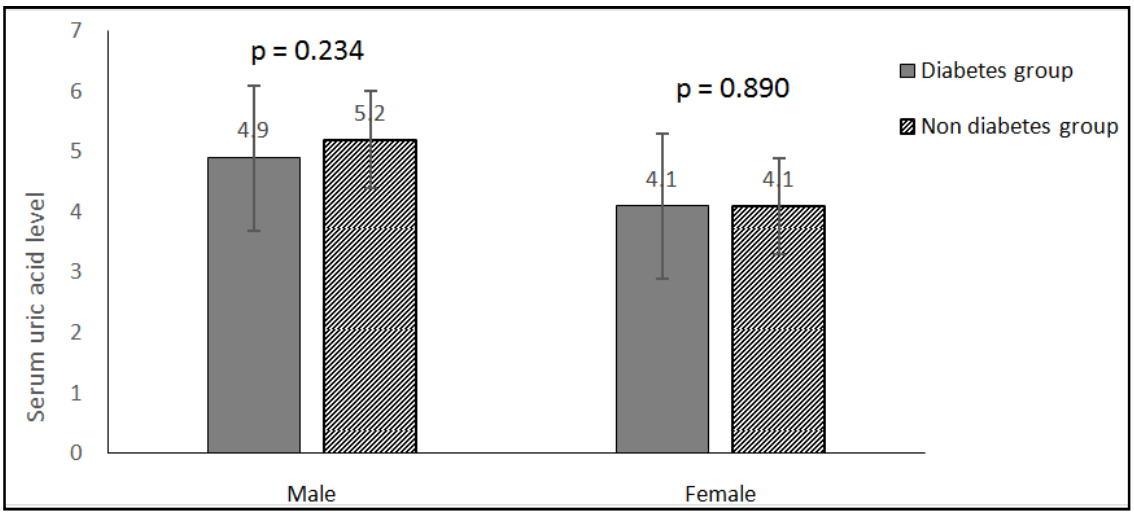

Figure 1. Comparison of serum uric acid levels

Sample size for the study was 184. Out of these patients, 92 were with diabetes mellitus and 92 patients were without diabetes mellitus. Ethical clearance for this study was obtained from Ethical Review Committee of Medical College Hospital, and informed consent of the patients was obtained before the study. Blood samples were collected for each patient to measure uric acid, creatinine, fasting blood glucose and post prandial blood glucose levels. Analysis was done using SPSS software and data was presented in mean and standard deviation. For comparison of values t-test was employed.

RESULTS

In our study, 40.2% participants were between age groups 35-45 years, 29.3% were between age groups 45-55 years and 30.4% were between age groups 55-65 years. Among diabetes patients, 39.1% were male and 60.9% were female. In non-diabetes control group, 41.3% were male and 58.7% were female. We observed that in this study 51.1%, 42.4% and 6.5% of patients were with diabetes duration less than 5 years, 5-10 years and more than 10 years respectively (Table 1). The mean value of uric acid in male diabetes was 4.9, whereas in non-diabetes was 5.2 showing no significant difference of uric acid levels in both the groups (p=0.234). Similar results were observed in female population, where the mean value of uric acid in diabetes population and non-diabetes population was 41, with p=0.890 which shows no significant difference (Figure 1). The Pearson correlation analysis revealed no significant relation between serum uric acid levels and blood glucose levels (both FBS and PPBS). Similarly the analysis revealed no significant correlation between serum uric acid and age. Conversely the analysis shown significant correlation between serum uric acid and duration of diabetes in males, but this correlation was not significant in females (Table 2).

DISCUSSION

Studies published till date on association of diabetes mellitus and uric acid were not consistent. Moreover these data are restricted to racial/ethnic groups and gender of other countries. Few studies reported direct relation of uric acid and diabetes whereas few studies have reported inverse association (Kramer *et al.,* 2009; Nakanishi *et al.,* 2003; Kodama *et al.,* 2009). The reason for the relation between uric acid and diabetes mellitus is not well understood. Moreover the studies done in recent past are of limited sample size and included either men or women. Mechanism of inverse association of serum uric acid and diabetes mellitus are reported due to the inhibition of uric acid re-absorption in proximal tubule when glucose levels are high (Tuomilehto *et al.,* 1988; Herman *et al.,* 1976). According to Kutzing and Firestein, hyperuricemia occurs due to excess dietary or ethanol intake or decreased renal excretion of uric acid. Moreover Hyperuricemia will be asymptomatic in majority of individuals (Kutzing *et al.,* 2008). But persistent hyperuricemia may lead to accumulation of urate crystals as uric acid precipitate in tissues and other body fluids. This result in acute painful conditions characterized by gout, gouty arthritis, or urolithiasis (Riegersperger *et al.,* 2011). During past few centuries, the dietary fructose intake has been increased dramatically and corresponding serum uric acid levels have also increased which states the association of

hyperuricemia and metabolic syndrome (Feig *et al.,* 2008). Hyperuricemia is also known to be the risk factor for chronic kidney disease (CKD). Retrospective data conducted by Haririan *et al.,* recommends an influence of graft loss after kidney transplantation (Haririan *et al.,* 2010). A multicenter study of 2145 consecutive patients with essential hypertension demonstrated by Lin *et al*. reported the prevalence of hyperuricemia in 35% males and 43% females. The study also reported association between hyperuricemia and elevated creatinine levels (Lin *et al.,* 2011). A study by Chen *et al*., reported 5.4% incidence of CKD, and serum uric acid correlated with serum creatinine levels (Chen *et al.,* 2009). In this study, we selected 92 diabetes mellitus subjects with normal kidney function and 92 non-diabetes mellitus subjects with normal kidney function, attending Medicine Out Patient Department, Medical College, Thiruvananthapuram during the study period of six months. Out of these subjects with diabetes mellitus 64% were on oral anti-hyperglycemic drugs, 7% were on insulin, 23% were on both oral anti-hyperglycemic drugs and insulin, and 6% were on no medication. Blood pressure and cholesterol levels were kept in control by taking antihypertensive drugs and lipid lowering drugs. Our study reported no significant difference of uric acid levels in males and females of both diabetes mellitus group and non-diabetes mellitus group (Figure 1). The Pearson correlation analysis reported no significant correlation of serum uric acid with FBS and PPBS in both the genders (Table 2). In an earlier hospital based cross sectional study, uric acid level increased from controls to pre-diabetic subjects. The serum uric acid level increased from controls to pre-diabetes subjects. The serum uric acid level further decreased in diabetes subjects. The same results were replicable even when groups were sub divided based on age and sex. In another study uric acid – 2 hr. PPBS showed stronger association in men than in women while the uric acid – FBS association stronger in women than in men. The Pearson correlation analysis also revealed significantly correlation between serum uric acid and age in both male and female population. While most of the earlier studies showed a significant elevation of uric acid with aging, a few studies did not show any consistent relationship with age. Our study reported significant correlation of serum uric acid and duration of diabetes in male population but did not report significant correlation in female population. A population based cross sectional study in Shanghai showed negative association of uric acid levels with duration of diabetes.

Conclusion

This study presents the pattern of relationship between serum uric acid, serum glucose and Diabetes mellitus of individuals with normal kidney function in a hospital based study. The study concluded

- No significant difference between the mean levels of uric acid in diabetes and non-diabetes subjects
- No significant correlation in the levels of uric acid with glucose levels (FBS and PPBS), both in male and female diabetes subjects
- No significant correlation with age and uric acid levels in male and female diabetes population
- No significant correlation with age and uric acid levels.
- Significant positive correlation with levels of uric acid and duration of diabetes among male diabetes population but no significant correlation with levels of uric acid and duration of diabetes among female diabetes population

Since the cross sectional study show confounding data, the implication of uric acid levels in diabetes and moreover in pre-diabetes need to be investigated to a further extend.

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