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Incidence of hyperuricemia in patients with diabetes as compared to non-diabetic patients

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Abstract

Background: Diabetes mellitus is a group of disorders characterized by chronic hyperglycemia associated with disturbance of carbohydrate, fat and protein metabolism due to absolute or relative deficiency of insulin secretion or its action. Several studies performed earlier have reported that high serum uric acid level is strongly associated with prevalent health conditions such as obesity, insulin resistance, metabolic syndrome, essential hypertension and renal disease. The aim of this study is to compare the incidence of hyperuricemia in diabetic and non-diabetic patients in southern Bihar.

Methods: A hospital based cross-sectional study was conducted at Narayan medical college and hospital, Sasaram, Bihar, India. A total of 445 patients of age more than 40 years were included in the study after obtaining an informed consent. The results were expressed as a percentage of the assessed population.

Results: Only about 42% of the total study population was normal. 57.5% were found to have elevated serum uric acid levels. Males, Elderly, obese, non-vegetarians, pre diabetic and diabetic, showed higher serum uric acid levels.

Conclusion: High prevalence of hyperuricemia was seen in diabetic patients. The uric acid levels may serve as a potential biomarker of deterioration of glucose metabolism. Further research on a larger population is required to get a wider picture about the incidence and its causes. Creating awareness, early diagnosis and treatment can help the target population.

Keywords: hyperuricemia, gout, diabetes mellitus, Hb A1c

Introduction

Diabetes mellitus, also called "Sugar Disease" by the Indians is a group of disorders characterized by chronic hyperglycemia associated with disturbance of carbohydrate, fat and protein metabolism due to absolute or relative deficiency of insulin secretion or its action. 425 million people have diabetes in the world out of which 82 million people are in the South East Asia. By 2045 this is expected to rise to 151 million. There were over 72 million cases of diabetes in India in 2017 [1]. probably, this is why India is called the diabetic capital of the world.

Diabetes causes long term dysfunction of various organs like heart, kidneys, eyes, nerves and blood vessels. Age adjusted mortality rates among diabetics is 1.5 to 2.5 times higher than general population. Much of this excessive mortality is attributable to cardiovascular disease [2].

Sir Alfred Garrod linked gout with hyperuricemia in 1948 [3]. Uric acid is the final metabolic product of purine in humans. Although purine nucleotides (adenine and guanine) are synthesized and degraded in all tissues, urate production takes place primarily in the liver and intestines due to presence of enzyme xanthine oxidase. Hyperuricemia can occur due to decreased excretion and/or increased production. Hyperuricemia manifests as gouty arthritis, urolithiasis and renal dysfunction. Urate is filtered freely by the glomerulus, secreted and reabsorbed in the proximal tubules [4].

Hyperuricemia is known to be associated with obesity and metabolic syndrome [5]. Not surprisingly, Hyperuricemia resulting from euglycemic hyperinsulinemia may precede the onset of type 2 diabetes, hypertension, coronary artery disease and gout in individuals with metabolic syndrome [5]. Recent studies have demonstrated that uric acid levels are higher in subjects with pre diabetes and early Type 2 diabetes than in healthy controls [6, 7]. Furthermore, an elevated serum uric acid level was found to increase chances for developing Type 2 diabetes in individuals with impaired glucose tolerance [8]. Hyperuricemia has been also added to the set of metabolic abnormalities associated with insulin resistance and/or hyperinsulinemia in metabolic syndrome [9, 10, 11, 12]. An elevated uric acid levels, as reported, often precedes the development of obesity [13], hyperinsulinemia [14, 15, 16], and diabetes [17, 18, 19]. In addition, uric acid has been implicated in the development of metabolic syndrome [20] and hypertension [21]. However, hyperuricemia is not always found in diabetic individuals.

Material and Methods

This is a hospital-based cross sectional observational study which was conducted in Narayan medical college and hospital located in southern Bihar. Patients were selected from both in-patient and outpatient department of the hospital in a random manner. Detailed history and physical examination was done for each patient as per a preset proforma. The samples were analyzed for serum uric acid levels using reflectance photometry (Direct ISE) and blood sugar levels using GOD-POD technique.

Inclusion Criteria

1. Diabetic and non-diabetic patients of both sexes and aged above 40 Years.
2. Patients willing to participate in this study.

Exclusion Criteria

1. Patients below 40 years of age of both sex.
2. Patients who were unable to understand verbal command.
3. Patients with any major psychological disorder and major cognitive dysfunction.
4. Patients of known RA, Osteoarthritis, Reactive Arthritis, Infective Arthritis, etc.
5. Patients with other metabolic disorders, neurological disorders, congenital metabolic disorders, cognitive syndrome, cardiac and respiratory disorders.
6. Patients with serum creatinine > 1.5 mg/dl
7. Patients who are suffering from connective tissue disorders.

The institutional ethical committee approved this study and there was no conflict of interest.

Statistical Analysis

Statistical analysis was carried out using SPSS 17 software. A p value of < 0.05 was considered to be statistically significant.

Table 1: Socio-Demographic Profile/characteristics of the participants (n= 445)

Subject characteristics		Frequency	Valid Percent
Age	40-50	147	33.04
	51-60	189	42.47
	61 and above	109	24.49
Gender	Male	298	66.97
	Female	147	33.03
Diet	Veg	127	28.54
	Non Veg/ Mixed	318	71.46
Physical Activity / Exercise	Yes	183	41.12
	No	262	58.88
Diabetes	Present	225	50.56
	Absent	220	49.44

Table 2: Distribution of uric acid level

Characteristic		Hyperuricemia (n=256)	Normouricemia (n=189)	Chi Square	P Value
Age	40 – 50	65 (44.22%)	82 (55.78%)	16.122	0.00031
	51- 60	123 (65.08%)	66 (34.92%)		
	61 and above	68 (62.39%)	41 (37.61%)		
Gender	Male	183 (61.41%)	115 (38.59%)	5.562	0.1835
	Female	73 (49.66%)	74 (50.34%)		
Diet	Veg	64 (50.39%)	63 (49.61%)	3.702	0.0543
	Non Veg	192 (60.38%)	126 (39.62%)		
Condition	Diabetic	150 (66.67%)	75 (33.33%)	15.555	0.00008
	Non Diabetic	106 (48.18%)	114(51.82%)		

Results

Out of the total 445 patients included in the study, 298 were males and 147 were females. Patients included in the study were aged 40 years and above. Normal uric acid levels were seen in only 189 (42.47%) whereas 256 (57.52%) were hyperuricemic.

Table 1 shows that out of the 445 study subjects 220 (49.44%) were found to be non-diabetic and 225 fell into the diabetic category. According to table 2, out of these 225 subjects 150 (66.67%) were hyperuricemic and 75 (33.33%) were normouricemic. In the non-diabetic category 114 (51.82%) had normal serum uric acid levels whereas 106 (48.18%) had increased levels of serum uric acid. We found that the uric acid levels were increased in diabetec category as compared to the non-diabetics. When compared among the different age groups, the age groups with a higher percentage of serum uric acid was 51-60 years (65.08%).

Table 2 shows that according to diet, there were 127 vegetarians and 318 consumed non vegetarian food as a part of their diet. Among non-vegetarians 192 (60.38%) were hyperuricemic whereas only 126 (39.62%) were normal uric acid levels. Among vegetarians 64 (50.39%) were found to have elevated uric acid levels whereas 63 (49.61%) were normouricemic. We found an elevated level of uric acid in non-vegetarians as compared to vegetarians.

Table 2 also shows that when comparing gender, a higher percentage of males 183 (61.41%) were found to have increased uric acid levels as compared to females 73 (49.66%).

Discussion

This hospital based cross sectional study shows that 66.67% of diabetic patients had increased serum uric acid levels. Although the prevalence of hyperuricemia is high in type 2 DM patients, there is a controversial idea about the association between hyperuricemia and type 2 DM, possibly due to peculiarities in the excretion of glucose and uric acid in these patients. Hyperuricemia is associated with insulin resistance and may precede the onset of type 2 diabetes mellitus. Some suggest that the link between Hyperuricemia and DM is SCL 2A9 gene [22].

Hyperuricemia is an underlying risk factor for type 2 diabetes mellitus, as it causes proinflammatory endocrine imbalance in vascular smooth muscle cells and adipose tissue which lead to cell surface morphological changes and insulin resistance [23].

Hyperuricemia defined as a plasma urate concentration more than 408μmol/L (6.8 mg/dl). Most children have serum urate concentration of (3-4mg/dl). Level begins to rise in male during puberty but in female it remains low in reproductive

age. The mean uric acid level in male and pre-menopausal female is 6.8 mg/dl and 6.0 mg/dl respectively. After menopause these values in women increases approximately to those in men. In adulthood concentration varies with height, weight, BP, Renal function and alcohol intake [22].

Hyperuricemia can result from increased production or decreased excretion of uric acid or from combination of two processes. Over 90% of hyperuricemia is due to defective renal failure/uric acid handling. Defective renal handling may be due to decreased glomerular filtration, decreased tubular secretion or enhanced tubular reabsorption. Normally 2⁄3 to 3⁄4 of uric acid is excreted through the kidneys and most of the remainder is eliminated through the intestines.URAT-1 is the novel transporter expressed at the apical border of proximal nephron. Other conditions associated with hyperuricemia are hypertension, CAD, gout in patient with metabolic syndrome and pregnancy [22].

Feig *et al*. have shown that there is an association of high levels of uric acid with diabetes mellitus [24]. Obesity which is a common feature of type 2 diabetics influences the reabsorption of salts in the proximal convoluted tubule and the loop of Henle. This results in increased glomerular capillary pressure and glomerular filtration rate [25].

H.K.Choi, *et al* in their study of Haemoglobin A1c, fasting glucose, serum C-peptide and insulin resistance in relation to serum uric acid levels, observed that serum uric acid levels and the frequency of hyperuricemia increased with moderately increasing levels of HbA1c and fasting plasma glucose and then decreased with further increasing levels of HbA1c (a bell- shaped relation) [26].

According to Eckel *et al*. the presence of glucose in urine due to its elevated levels in the blood. This decreases the pH of the urine, which influences the reabsorption of uric acid in the proximal convoluted tubules into the blood [27].

Hairong Nan, *et al* in their study on serum uric acid, plasma glucose and diabetes showed that serum uric acid concentration increased with increasing fasting plasma glucose levels up to 7.0 mmol/l, but notably decreased when fasting plasma glucose was over 7.0 mmol/l [28].

Many previous cross-sectional studies have reported a strong positive association between hyperuricemia, gout and metabolic syndrome [29].

According to gender, our study shows hyperuricemia to be predominant in males (61.41%) as compared to females (49.66%). Similar results were seen in other studies. Hyperuricemia was more common in males and tended to increase with age [30, 31].

However, the comorbidity between gout and diabetes could be because of gout increasing risk of developing diabetes, or diabetes increasing risk of developing gout, or both diseases sharing common risk factors or etiological pathways. Therefore, prospective cohort studies would be useful to establish the temporal relations between the two conditions.

Conclusion

High prevalence of hyperuricemia was determined in type 2 DM and pre diabetic patients. The uric acid may serve as a potential biomarker of deterioration of glucose metabolism. Pre-diabetics probably are at a higher risk of developing uric acid related complications like gout and nephropathy. Further studies are needed on a larger scale to get a better picture of the present condition, which is important for understanding the underlying pathophysiology. This will help us in prevention and further treatment.

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