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Study on Uric Acid as Biomarker for Insulin Resistance in Type 2 Diabetic Mellitus.

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ABSTRACT

Background: Serum uric acid (SUA) is an end product of purine metabolism. SUA is excreted mainly through the kidneys. Multiple mechanisms have been reported to show the association of hyperuricemia with glucose intolerance. The association between insulin and renal resistance to absorption of urates has been found out to be the most important among these mechanisms. **Methods:** This comparative study contains 50 subjects of type 2 diabetes having an age group of 40-65 years were participated in case & 50 healthy subjects as control group. This case control study conducted in the department of department of biochemistry, LPS institute of Cardiology, GSVM medical college, Kanpur. **Results:** In the case-control study were found 54% male and 46% female in case group & 42% female and 58% female. We suggested that in study group 44% cases were belongs to 61-65 age group followed by other while in control group 42% were belongs to 61-65 age group followed by other age group. **Conclusion:** This study conclude that there were significant correlation between uric acid and HOMA-IR value. Hyperuricemia is related to risk factors for insulin resistance in type 2 diabetes. The study concluded a significant progressive relationship between increased uric acid level with respect to HOMA-IR levels which is an indices of insulin resistance.

Keywords: Serum uric acid, Type 2 diabetes mellitus, HOMA-IR

INTRODUCTION

Serum uric acid (SUA) is an end product of purine metabolism. SUA is excreted mainly through the kidneys. Multiple mechanisms have been reported to show the association of hyperuricemia with glucose intolerance. The association between insulin and renal resistance to absorption of urates has been found out to be the most important among these mechanisms.[1] In various epidemiological studies, increased levels of SUA have been described to be associated with multiple chronic disorders such as hypertension,[2,3] cardiovascular diseases,[4,5] and chronic kidney diseases.[6] A positive association between high levels of SUA and diabetes has been reported in multiple studies.[7-10] On the other hand, no association as well as an inverse association has also been reported.[11,12] An important role of UA has been established in animal models in worsening insulin resistance by inhibiting the bioavailability of nitric oxide, which is essential for insulin-stimulated glucose uptake.[13] The elevated levels of UA have been emphasized in a study as a risk factor for insulin resistance and components of the metabolic syndrome.[14]

Cases of all the types of diabetes mellitus have been reported to be increasing worldwide. Approximately 382 million people have been found to be suffering from it. Type 2 diabetes mellitus (T2DM) cases have been expected to increase by 55% by the year 2035.[15] T2DM has been noted to be mostly found in persons having older age, obesity, family history of diabetes, previous history of gestational diabetes, physical inactivity, and certain ethnicities.[16] This diabetes is characterized by a combination of impaired insulin secretion from pancreatic beta cells and insulin resistance of the peripheral target tissues. For controlling its epidemic trend, it is critical to identifying individuals with high risk of T2DM at an early reversible stage.[17]

SUA is often found to be elevated in subjects with Metabolic Syndrome (MetS) as a compensatory mechanism to counteract the increased oxidative stress.[18] In various studies,[19-21] the associations between hyperuricemia and MetS components

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obesity, hypertension, hyperlipidemia, and glucose intolerance have been reported. Various researchers considered hyperuricemia a marker as well as a component of metabolic syndrome.[22,23] It has been estimated that around 10 to 30 % of the world's adult population suffer from MetS.[24] Prevalence of metabolic syndrome has recently increased in developing countries. It has been established that the prevalence of the MetS is highly age dependent and the highest prevalence among women compared to men.[24] Relationship of hypertension with hyperuricemia has been associated and it has been reported that 25 to 40 % of untreated hypertensive and 75% of malignant hypertensive patients are having hyperuricemia.[25] Hyperuricemia has been found to cause hypertension by reduction of nitric oxide synthase in the macula densa of the kidneys, stimulation of rennin-angiotensin-aldosterone system (RAAS), and reduction of renal perfusion. All these effects have been found to get ameliorated by UA lowering drugs.[26] Uric acid is a product of glucose metabolism that is filtered by glomeruli and reabsorbed by the proximal convoluted tubule. Greater serum concentrations of insulin have been reported to cause higher renal reabsorption of UA, and increasing SUA.[27]

MATERIALS AND METHODS

Study population

This comparative study contains 50 subjects of type 2 diabetes having an age group of 40-65 years were participated in case & 50 healthy subjects as control group.

Study Area

This case control study conducted in the department of ……..in ……medical college.

Study Duration

The duration of study was six month.

Data Collection

Patients with cardiovascular, thyroid function disorder and other hormonal disorders that may exaggerate the insulin resistance in type 2 diabetes were excluded from the study. 5 ml of venous blood was obtained after a 12 hour fast from type 2 diabetic patients. Blood samples were transferred into tube, allowed to stand for 15 minutes at room temperature, centrifuged at 3500 rpm for 10 minutes. Then do the determination of uric acid, fasting glucose, fasting insulin, insulin resistance.

Data Analysis

Data were analyzed by using Microsoft excel & chi-square test.

RESULTS

In the case-control study were found 54% male and 46% female in case group & 42% female and 58% female. We suggested that in study group 44% cases were belongs to 61-65 age group followed by other while in control group 42% were belongs to 61-65 age group followed by other age group.The comparison between study group & control group of serum uric acid, fasting glucose, fasting insulin, insulin resistance showed in table 3.

Table 1: Distribution of case-control group according to gender

Gender	No. of cases	Percentage	No. of control	Percentage
Female	23	46%	21	42%
Male	27	54%	29	58%
Total	50	100%	50	100%

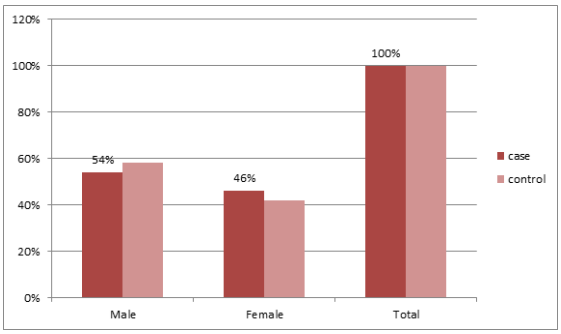

Figure 1: Distribution of case-control group according to gender

Table 2: Distribution of case-control group according to age

Age	No. of cases	Percentage	No. of control	Percentage
40-50	12	24%	10	20%
51-60	16	32%	19	38%
61-65	22	44%	21	42%
Total	50	100%	50	100%

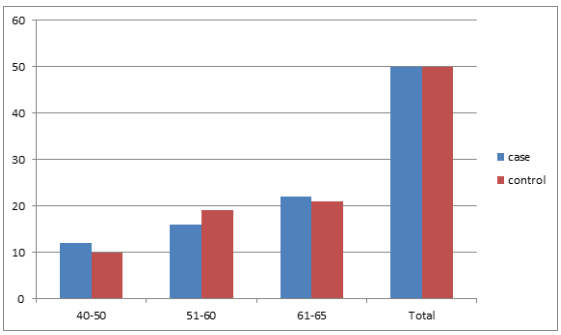

Figure 2: Distribution of case-control group according to age

Table 3: Distribution of case-control group according to laboratory findings

Parameters	Case group	Control group	P value
Serum uric acid(mg/dl)	6.27±1.39	4.39±1.24	<0.0001
Fasting Glucose (mg/dl)	176.36±16.79	86.13±11.36	<0.0001
Fasting insulin	9.11±1.89	6.23±1.43	<0.0001
HOMA-IR	3.87±0.07	1.32±0.04	<0.0001

DISCUSSION

It has been reported in the results that T2DM subjects had significantly increased SUA, fasting plasma glucose, fasting serum insulin, and HOMA-IR values in comparison to controls. The data of the present study suggested reduced clearance of UA with increase in insulin resistance and UA as a marker of diabetes period. Hyperinsulinemia has been found to decrease uric acid clearance by the kidneys. The mechanism of increased proximal tubular urate transport from the glomerular filtrate to the renal interstitium by stimulation of GLUT can be ascribed to higher levels of SUA. Results of the present study reported strong association between UA levels and HOMAIR , a combination of medical conditions that are related to insulin resistance (the body's inability to correctly process insulin) and increase a person's chances of getting heart disease and diabetes. The results of Kivity and colleagues,[28] who found that high SUA levels are associated with T2DM in females but not in males, supported our findings. The results of the present study were similar to the results of Nagahama and colleagues who reported hyperuricemia as a strong predictor of MetS both in males and females but with female preponderance.[29] Though this gender variation could not be explained but the distinct fat distribution, different levels of UA in males and females, and the effects of estrogens on renal clearance of urate may be ascribed to this variation.[30,31] It has been reported in the recent studies that there were high levels of SUA in subjects with prediabetes and early T2DM then in healthy controls.

A high level of SUA has been found to raise chances of T2DM in individuals with impaired glucose tolerance. Hyperuricemia has also been associated to the metabolic abnormalities of insulin resistance and/or hyperinsulinemia in MetS. An elevated UA levels has been reported to often precedes the development of obesity, hyperinsulinemia, and diabetes.

Though, SUA has been described in the development of MetS and hypertension; yet, high levels of SUA were not always present in persons suffering from diabetes. The elevated SUA is an established feature of hyperinsulinemia and impaired glucose tolerance. On the contrary, low levels of SUA were also reported in T2DM. Though, some of the studies have shown the role of SUA in progression of prediabetic to diabetes; but these studies are somewhat controversial and not well established. Some further studies, on this topic, were required to ascertain these claims. Therefore, in the present study the potential role of UA has been claimed as a biomarker for impaired glucose metabolism and diabetes progression by analyzing the levels of SUA in T2DM patients.

CONCLUSION

This study concludes that there were significant correlation between uric acid and HOMA-IR value. Hyperuricemia is related to risk factors for insulin resistance in type 2 diabetes. The study concluded a significant progressive relationship between increased uric acid level with respect to HOMA-IR levels which is an indices of insulin resistance.

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