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Uric Acid as a Risk Factor in Metabolic Syndrome: A Case-Control Study

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Abstract: ***Background**: Uric acid is a final end product in the degradation of purine metabolism Hyperuricemia results from increased production of uric acid, decreased excretion or a combination of both [1-3]. Hyperuricemia has been identified as having major clinical significance in the development of various co morbidities including gout, metabolic syndrome, coronary artery disease and type 2 diabetes mellitus [4-6], despite its major antioxidant property. Serum uric acid level is associated with the individual components of metabolic syndrome such as obesity, dyslipidemia and hypertension [7]. Hyperuricemia can be an accompaniment disorder with syndrome X (characterized by abdominal obesity, impaired glucose tolerance, increased LDL Cholesterol & decreased HDL Cholesterol). Its presence is an indication for screening and aggressively treating any accompanying obesity, hypercholesterolemia, diabetes or hypertension [8]. Diabetes mellitus type 2 is a common condition among middle age and older individuals. The Prevalence of diabetes mellitus type 2 is increasing globally. India have the max imum increase during the last few years. The prevalence of type 2 diabetes mellitus is 2.4% in rural population and 11.6% in urban population [9]. The metabolic syndrome is a cluster of most dangerous coronary artery disease risk factors: diabetes mellitus type 2, pre diabetes, abdominal obesity, high cholesterol and high blood pressure [10] **Methods**: This study is a cross sectional study, The sample size of this study includes 100 subjects involving 50 diabetic patients with metabolic syndrome and 50 normal controls. The parameters includes measurement of Height, Weight, Blood pressure and Waist circumference. The laboratory parameters includes Fasting plasma glucose, Post prandial plasma glucose, Serum fasting lipid profile, Serum urea, Serum creatinine, Serum uric acid levels. **Results**: Serum uric acid levels among patients with metabolic syndrome were significantly higher than normal controls with level of significance ($p < 0.05$). Fasting plasma glucose levels, Post prandial plasma glucose levels, Fasting Serum total cholesterol levels, Fasting Serum triglyceride levels, Fasting Serum LDL cholesterol levels, among patients with metabolic syndrome were significantly higher than normal controls with level of significance ($p < 0.05$). But Fasting serum HDL cholesterol levels among patients with metabolic syndrome were significantly lower than normal controls with insignificant association ($p >0.05$). Serum uric acid levels were significantly higher in patients with diabetic metabolic syndrome when compared with normal healthy controls with level of significance (t value = 10.612) $p = 0.000$, ($p < 0.05$). **Conclusions**: This study has shown that hyperuricemia is significantly present in type 2 diabetic patients with metabolic syndrome and is significantly correlated with various components of metabolic syndrome including obesity, dyslipidemia, hypertension and insulin resistance. All these components of metabolic syndrome have a bidirectional causal effect with hyperuricemia.*

Keywords: Diabetes mellitus, Uric acid, Glucose amd triglycerides.

1. Introduction

Uric acid is a final end product in the degradation of purine metabolism Hyperuricemia results from increased production of uric acid, decreased excretion or a combination of both [1-3]. Hyperuricemia has been identified as having major clinical significance in the development of various co morbidities including gout, metabolic syndrome, coronary artery disease and type 2 diabetes mellitus [4-6], despite its major antioxidant property. Serum uric acid level is associated with the individual components of metabolic syndrome such as obesity, dyslipidemia and hypertension [7]. Hyperuricemia can be an accompaniment disorder with syndrome X (characterized by abdominal obesity, impaired glucose tolerance, increased LDL Cholesterol & decreased HDL Cholesterol). Its presence is an indication for screening and aggressively treating any accompanying obesity, hypercholesterolemia, diabetes or hypertension [8]. Diabetes mellitus type 2 is a common condition among middle age and older individuals. The Prevalence of diabetes mellitus type 2 is increasing globally. India have the maximum increase during the last few years. The prevalence of type 2 diabetes mellitus is 2.4% in rural population and 11.6% in urban population [9]. The metabolic syndrome is a cluster of most dangerous coronary artery disease risk factors: diabetes mellitus type 2, pre diabetes, abdominal obesity, high cholesterol and high blood pressure [10].

People with metabolic syndrome are twice as likely to die from, and three times as likely to have a heart attack or stroke compared with people without the syndrome. Cardiovascular disease is the leading cause of death throughout the world. It accounts for about 30% of death worldwide, including 40% in high income countries, and about 28% in low and middle income countries [11]. Both hyperuricemia and metabolic syndrome are associated with hyperinsulinemia. Hyperuricemia In diabetes mellitus type 2 though prevalent among those with metabolic syndrome, it is not within the diagnostic criteria for diabetic metabolic syndrome. Little is known about the prevalence of hyper uricemia among our population, which is prone for metabolic syndrome, particularly among middle aged and older populations in our society, where compliance and the glycemic control are poor. Serum uric acid a cost effective laboratory assessment could not only serve as an adjunctive, but could also become a criterion to be included 1n diagnosing metabolic syndrome.

This study was taken up in our population, of middle aged and older individuals, to investigate the association between serum uric acid levels and diabetic metabolic syndrome and to find the correlation between serum uric acid levels and various components of metabolic syndrome and thereby to study the role of serum uric acid as a risk factor in metabolic syndrome.

Objective: to study the role of serum uric acid as a risk factor in metabolic syndrome.

2. Methods

Type of study: The study was a hospital- based case control study.

Place of study: The study was conducted in the department of general medicine, KMC Manipal.

Duration of study: The study was conducted from January 2025 to November 2025.

Methodology: The ground work for the study was started after getting clearance from the research committee and the Institutional human ethical committee.

Inclusion criteria
Type 2 diabetes mellitus patients of both sexes (40-60 years of age) with metabolic syndrome and normal healthy controls of both sexes (40 - 60 years of age).

Exclusion criteria
Patients with chronic kidney disease and history of cancer and patients on treatment with systemic steroids. The sample size of this study includes 100 subjects involving 50 diabetic patients with metabolic syndrome and 50 normal healthy controls. The study parameters includes measurement of Height, Weight, Blood pressure and Waist circumference. The laboratory parameters includes Fasting plasma glucose, Post prandial plasma glucose, Serum fasting lipid profile, Serum urea, Serum creatinine, Serum uric acid levels, Electrocardiogram - 12 lead.

Sample collection
The study was explained to the participants and informed consent obtained from them before taking the blood sample. The blood samples were collected from subjects by venepuncture. Both fasting (8 hours overnight fasting) and post prandial samples were collected under aseptic precautions.

Data analysis
The statistical analysis was done with the help of epidemiologist / statistician and it includes the Pearsons correlation coefficient as the test of correlation and the Independent sample t test as the test of significance. The statistical software used for statistical interpretation was from SPSS data editor version 17.

3. Results

Serum uric acid levels among patients with metabolic syndrome were significantly higher than normal controls with level of significance ($p < 0.05$). Fasting plasma glucose levels among patients with metabolic syndromes were significantly higher than normal controls with level of significance ($p < 0.05$). Post prandial plasma glucose levels among patients with metabolic syndrome were significantly higher than normal controls with level of significance ($p < 0.05$). Fasting Serum total cholesterol levels among patients with metabolic syndrome (222.92+27.45(mg%) were significantly higher than normal controls (165.02+18.57(mg%)) with level of significance ($p < 0.05$).

Fasting Serum triglyceride levels among patients with metabolic syndrome (189.08+69.33(mg%) were significantly higher than normal controls (130.78+28.58(mg%) with level of significance ($p < 0.05$).

Fasting Serum LDL cholesterol levels among patients with metabolic syndrome (138.70+23.56 (mg%) were significantly higher than normal controls (94.92+ 16.60 (mg%) with level of significance ($p <0.05$) Fasting Serum VLDL cholesterol levels among patients with metabolic syndrome (37.92+13.82(mg%) were significantly higher than normal controls (26.08+5.70(mg%) with level of significance ($p<0.05$).

But Fasting serum HDL cholesterol levels among patients with metabolic syndrome (46.32+5. 77(mg%) were significantly lower than normal controls (44.22+5.97 (mg%) with insignificant association ($p >0.05$).

Serum unc acid levels were significantly higher in patients with diabetic metabolic syndrome when compared with normal healthy controls with level of significance, $p = 0.000$, ($p < 0.05$). Serum uric acid levels showed positive correlation with various components of the metabolic syndrome including fasting plasma glucose, post prandial plasma glucose, serum total cholesterol, serum LDL cholesterol, serum triglycerides (pearsons correlation significant at $p<0.05$) except for serum HDL cholesterol (Tables 1 to Table 10).

	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
FPG	50	116	255	153.14	32.664

Table 1: Comparison-Fasting plasma glucose. FPG-Fasting Plasma Glucose for cases (patients with diabetic metabolic syndrome): Group I

	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
FPG	50	68	125	93.04	13.96

Table 2: Comparison-Fasting plasma glucose. PPG-fasting Plasma Glucose for controls (healthy volunteers): Group II.

	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
CHOL.	50	167	280	222.92	27.456

Table 3: Comparison: Fasting serum total cholesterol. CHOL-Fasting serum total cholesterol for cases (patients with diabetic metabolic syndrome): Group I.

	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
CHOL.	50	126	217	165.02	18.575

Table 4: Comparison: Fasting serum total cholesterol. CHOL-Fasting serum total cholesterol for controls: Group II.

HDL	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	37	58	46.32	5.773

Table 5: Comparison: Fasting serum HDL cholesterol. HDL-fasting serum HDL cholesterol for cases (patients with diabetic metabolic syndrome): Group I.

HDL	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	26	52	44.22	5.97

Table 6: Comparison: Fasting serum HDL cholesterol. HDL-Fasting serum HDL cholesterol for controls (healthy volunteers): Group II.

VLDL	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	22	69	37.92	13.82

Table 7: Comparison-Fasting serum VLDL cholesterol. VLDL-Serum fasting VLDL cholesterol for cases (patients with diabetic metabolic syndrome): Group I.

VLDL	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	16	4.3	26.08	5.7

Table 8: Comparison-Fasting serum VLDL cholesterol. VLDL-Fasting serum VLDL cholesterol for controls (healthy volunteers): Group II.

UA	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	4.8	14.31	8.0212	1.82578

Table 9: Comparison-Serum uric acid. UA-Serum uric acid for cases (patients with diabetic metabolic syndrome): Group I.

UA	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	4.8	14.31	8.0212	1.82578

Table 10: Comparison-Serum uric acid. DA-serum uric acid for controls (healthy volunteers): Group II.

UA	N	Minimum (mg%)	Maximum (mg%)	Mean (mg%)	SD
	50	1.72	8.08	4.4708	1.50439

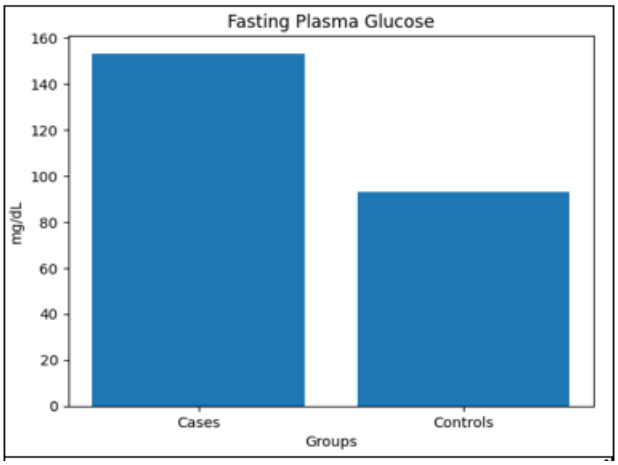

Figure 1: Bar graph illustrating mean fasting plasma glucose levels in cases and controls. Cases had significantly elevated levels (153.14 ± 32.66 mg/dL) compared to controls.

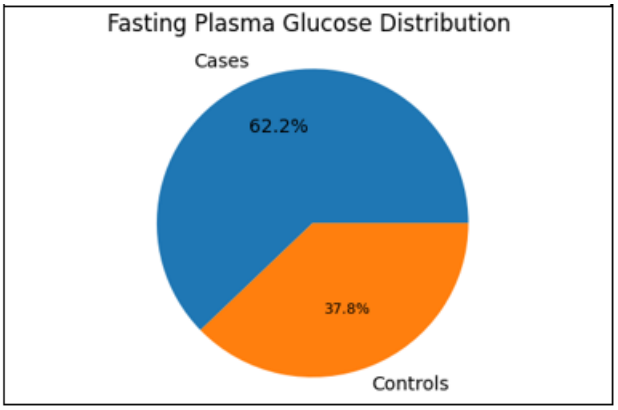

Figure 2: The pie chart shows that cases account for 62.2% of total fasting glucose distribution, whereas controls contribute 37.8%.

This reflects impaired glucose metabolism as a key component of metabolic syndrome.

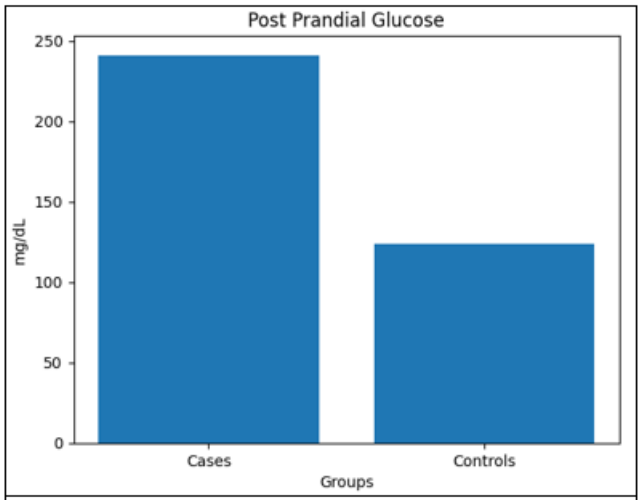

Figure 3: Bar graph comparing postprandial plasma glucose levels between cases and controls. Significantly higher levels were observed in cases (240.96 ± 54.49 mg/dL) than controls (123.90 ± 23.45 mg/dL)

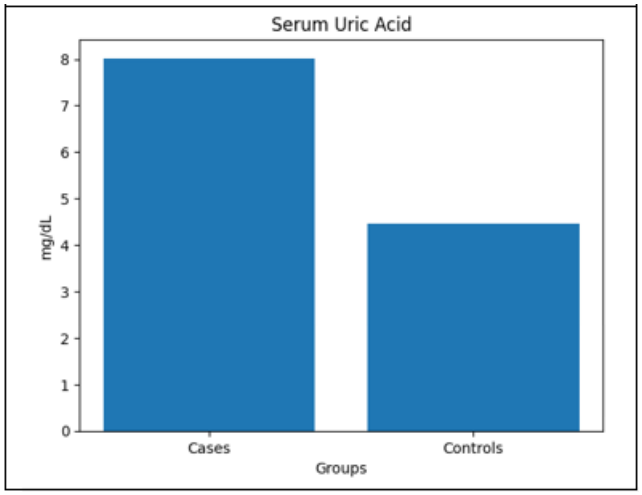

Figure 4: Bar graph showing mean serum uric acid levels in cases and controls. Patients with metabolic syndrome had

significantly higher serum uric acid levels (8.02 ± 1.82 mg/dL) compared to controls.

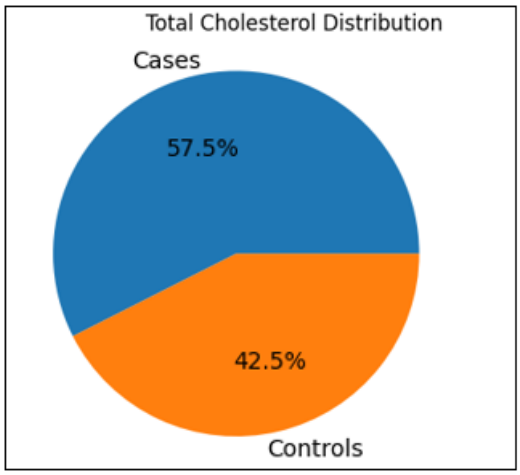

Figure 5: The pie chart indicates that cases contribute 57.5% of total cholesterol levels, whereas controls account for 42.5%. This finding supports the presence of dyslipidemia as a major component of metabolic syndrome.

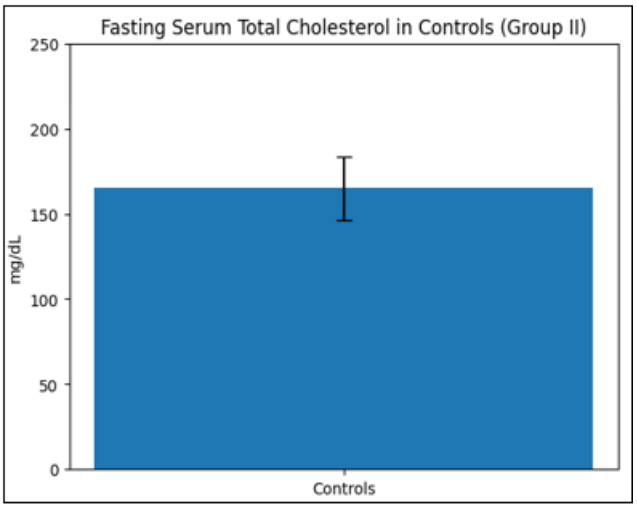

Figure 6: The bar graph represents the mean fasting serum total cholesterol levels among controls (Group II). The mean cholesterol level was 165.02 mg/dL with a standard deviation of ±18.57 mg/dL. The error bar indicates the variability of cholesterol levels within the study population.

The mean fasting serum total cholesterol level among controls falls within the near-normal to borderline range. However, the wide range (126–217 mg/dL) indicates variability among individuals, suggesting that a subset of the control population may have elevated cholesterol levels despite being classified as non-metabolic syndrome.

4. Discussion

The present study demonstrates that serum uric acid levels were significantly elevated in patients with metabolic syndrome compared to healthy controls. Furthermore, uric acid showed a significant positive correlation with fasting plasma glucose, postprandial glucose, total cholesterol, triglycerides, LDL, and VLDL cholesterol, while no significant association was observed with HDL cholesterol. c acid levels and fasting glucose as well as triglycerides in individuals with metabolic syndrome [13]. Chandalia et al. also highlighted the relationship between uric acid and insulin resistance in Asian Indians, supporting its role in metabolic dysregulation [14].

Recent Indian studies further strengthen this association. Rashmi et al. (2023) observed significantly higher serum uric acid levels in metabolic syndrome patients, with a strong positive correlation with glycemic and lipid parameters [15]. Similarly, Singh et al. (2023) reported that hyperuricemia is significantly associated with obesity, diabetes, and metabolic syndrome, indicating its contribution to insulin resistance and metabolic abnormalities [16]. A recent study by Maiti et al. (2024) from Eastern India also confirmed elevated uric acid levels in metabolic syndrome patients and demonstrated significant correlations with metabolic parameters [17]. Additionally, Mandal (2024) reported similar findings in a hospital-based study from West Bengal, reinforcing the association between uric acid, dyslipidemia, and hyperglycemia [18]. Bhorge et al. (2024) further showed a strong correlation between uric acid levels and atherogenic lipid profile components [19].

The significant positive correlation between uric acid and glycemic parameters observed in our study is supported by previous research. Elevated uric acid levels have been shown to impair insulin signaling through oxidative stress and endothelial dysfunction, leading to insulin resistance [16, 20]. This may explain the higher fasting and postprandial glucose levels observed among metabolic syndrome patients in our study.

Our study also demonstrated a significant association between uric acid and lipid parameters, including total cholesterol, triglycerides, LDL, and VLDL cholesterol. These findings are in agreement with previous studies, which suggest that uric acid contributes to dyslipidemia by promoting hepatic lipogenesis and reducing lipid clearance [17, 19]. However, no statistically significant association was observed between uric acid and HDL cholesterol in our study. Similar observations have been reported in other Indian studies, where HDL showed weaker or inconsistent correlation compared to other lipid fractions [13, 18].

Beyond Indian data, global evidence also supports the role of uric acid in metabolic syndrome. A recent meta-analysis demonstrated that individuals with hyperuricemia have significantly higher odds of developing metabolic syndrome [21]. Similarly, large population-based studies have shown that elevated uric acid levels increase the risk of metabolic syndrome by nearly 2-3 times, even after adjusting for confounding factors [22].

The pathophysiological mechanisms linking uric acid with metabolic syndrome are multifactorial. Increased activity of xanthine oxidase leads to oxidative stress and generation of reactive oxygen species. Uric acid also reduces nitric oxide bioavailability, causing endothelial dysfunction and contributing to hypertension. Additionally, it promotes inflammation, activates the renin-angiotensin system, and enhances adipogenesis, thereby facilitating the development of metabolic syndrome.

Overall, the findings of the present study are in concordance with both earlier and recent Indian studies, as well as global evidence, suggesting that serum uric acid is not merely a bystander but may play an active role in the development and progression of metabolic syndrome. Given its affordability and ease of measurement, serum uric acid can serve as a useful adjunctive biomarker for early identification of individuals at risk.

5. Conclusion

This study has shown that hyperuricemia 1s significantly present in type 2 diabetic patients with metabolic syndrome and is significantly correlated with vanous components of metabolic syndrome including obesity, dys lip id emia , hypertension and insulin res istance. All these components of metabolic syndrome have a bidirectional causal effect with hyperuricemia. The relationship between hyperuricemia and metabolic syndrome might be linked to insulin resistance and thereby with increasing body mass index. The prooxidant and pro-inflammatory effect of hyperuricemia could also explain the clustering of factors found in metabolic syndrome. Hence, Serum unc acid, a cost effective laboratory assessment could not only serve as an adjunctive, but could also become a criterion to be included in diagnosing metabolic syndrome.

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