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Original Research Paper

Biochemistry

A CROSS SECTIONAL STUDY OF ASSOCIATION BETWEEN SERUM URIC ACID AND LIPID PROFILE

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ABSTRACT

Background: The association of Serum Uric Acid (SUA) with Lipid Profile is not well studied or little is known so far, although the link between elevated uric acid and metabolic syndrome has been reported in some studies. This study was conducted to establish the relationship between SUA and Lipid Profile among the general adults. **Methods:** 560 blood samples were collected from general adult participants (male, n = 300 & female, n = 260) were analysed for serum lipid profile (TC, TG, HDL and LDL) and SUA levels. The study subjects were divided by quartiles based on SUA levels (Q1: ≤225 μmol/L, Q2: 226–285 μmol/L, Q3: 286–340 μmol/L and Q4: > 340 μmol/L). Linear regression modelling was used to evaluate the relationship between SUA and Lipid levels. **Results:** The prevalence of hyperuricemia was 9.2% in males and 10.4% in females. The mean level of SUA was significantly higher in male (317 ± 90 μmol/L) than in the female (255 ± 65 μmol/L) subjects ($p < 0.001$). An increasing trend for elevated lipid profile was observed in both genders with increasing levels of SUA in the quartiles ($p < 0.05$). In regression analysis, a significant positive correlation was found between SUA and TG, TC and LDL ($p < 0.01$) while an inverse correlation was observed between SUA and HDL ($p < 0.01$). After adjusting for potential confounders, lipid profile was linearly associated with SUA levels ($p < 0.01$ for trend). **Conclusions:** Lipid parameters (TG, TC, and LDL levels) increases with increase in SUA, whereas HDL decreases with rise in SUA. Cardiovascular risks may be reduced by early prevention of hyperuricemia and dyslipidaemias.

KEYWORDS : Lipid Profile, Serum Uric Acid (SUA), Dyslipidaemia, Cardiovascular disease

INTRODUCTION

Serum Uric Acid (SUA) is the final oxidation product of purine catabolism.[1] Excessive uric acid production and/or decreased excretion by the kidneys are one of the major causes of hyperuricemia.[2] The prevalence of hyperuricemia is rapidly increasing.[3] The variability in SUA levels is multi-factorial and influenced by both genetic and environmental factors.[4] Epidemiological studies showed that elevated levels of uric acid in serum are increasingly related to hypertension, cardiovascular disease (CVD) and metabolic syndrome.[5] Hyperuricemia is considered to be a mediator of pro-inflammatory endocrine imbalance in the adipose tissue which may be one of the important factors for dyslipidaemia and the inflammatory process that leads to atherogenesis.[6]

The relationship of uric acid with CVD risk factors has made it very complicated to determine whether uric acid has a causal role in these conditions or simply a marker for individuals at increased risk, reflecting the association with other traditional risk factors such as blood lipids, metabolic syndrome and diabetes. The exact role of SUA in these diseases is still the debate and subject of much discussion because it is always accompanied by other risk factors such as diet, dyslipidaemia and obesity.[6] Moreover, the relationship between SUA and dyslipidaemia is complex and not fully elucidated yet. A few studies have been conducted to investigate the association between SUA and lipid profiles in the adult population of India,[7] Italy,[8] and USA[9].

In this study, we aimed to assess the independent relationship between SUA and lipid profile in an adult cohort.

MATERIAL AND METHOD

This study was a cross-sectional design, conducted between January and November of 2022 in the hospital associated with Khaja Bandanawaz University-Faculty of Medical Sciences.

This study was approved by the Institutional Ethics Committee. Informed consent was obtained from all participants' prior to inclusion in the study. The study consisted of 560 general adult participants (300 males and 260 females). All the participants were apparently healthy individuals without any severe cardiovascular diseases.

Participants with myeloproliferative disorders and in therapy with cytotoxic drugs, pregnant women, lactating mothers and the individuals who are already on the diuretic, anti-hypertensive, hypolipidemic, alcoholics, known cardiovascular disorders, renal or hepatic disorders and those on anti-gout therapy were excluded from the study.

Anthropometric indices of height, weight, waist and hip circumference and other lifestyle information were obtained using the standard procedure. The quality of anthropometric measurements was ensured in presence of investigators.

SUA and lipids measurements venous blood (5 mL) was drawn from each participant in fasting condition (early morning sample) under strict aseptic precautions. Serum was separated for analysis of biochemical parameters. Serum uric acid (SUA), and serum lipids: triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were analysed by colorimetric methods using commercially available kits.

In the present study, participants were classified as hyperuricemia with SUA levels > 416.4 μmol/L in men and > 356.9 μmol/L in women. The levels of SUA were categorized into four quarterlies (Table 3) based on frequencies test.

Statistical Analysis

Statistical analysis was performed using IBM SPSS version 29.0. Independent sample *t-test* (two-tailed) was done to assess the differences between male and female cohort for anthropometric and baseline variables. Interrelationships between anthropometric, baseline variables and SUA were

assessed by Pearson's correlation coefficient test. One-way ANOVA was performed to determine differences among the groups. The linear regression modelling was applied to evaluate the association between SUA quartiles and lipid levels. Three models were used with progressive degrees of adjustment. Model 1 was adjusted for age, gender, BMI. Model 2 was further adjusted for age, gender, BMI and WC. Model 3 was adjusted for age, gender, BMI, waist and hip circumference. The values in tables were presented as mean ± standard deviation otherwise noted. A *p* value of < 0.05 was considered statistically significant.

RESULTS

The baseline characteristics of the study subjects are presented in Table 1. Among a total of 560 participants, 300 (~54%) were males and 260 (~46%) were females. The mean age was 32 ± 12 years (range 18–75 years), with a significant difference between male and female subjects (p < 0.01). The average BMI for all participants was 24±4 kg/m2 with no significant difference between the gender groups. The mean value of WC was 85±7 with a significant difference between male and female (p<0.05) subjects. A significant difference was also observed for the average levels of SUA, TG and HDL in the gender groups. Based on diagnostic criteria, overall the prevalence of hyperuricemia was 9.8% among the participants with 9.2% in male and 10.4% in female subjects. SUA quartiles and comparison of lipid profile in the quartiles. The characteristics of the study participants by SUA quartiles are summarized in Table 2. The individuals with higher SUA quartiles were more likely to be male participants. After adjustment of age and sex, the mean level of SUA, TG, TC and LDL were progressively increased and HDL level was progressively decreased across the SUA quartiles.

Table 1 Baseline characteristics and SUA level according to gender

	Overall	Male	Female	P-value
N	560	300 (~54%)	260 (~46%)	–
Age (years)	32 ± 12 (75)	35 ± 14 (75)	30 ± 10 (60)	0.007
Height (cm)	158 ± 8 (176)	166 ± 5 (176)	152 ± 5 (165)	0.000
Weight (kg)	63 ± 10 (90)	67 ± 9 (85)	59 ± 10 (90)	0.000
WC (cm)	85 ± 7 (115)	86 ± 8 (104)	82 ± 8 (115)	0.046
HC (cm)	94 ± 8 (122)	93 ± 6 (105)	94 ± 10 (122)	0.078
BMI (kg/m2)	24 ± 4 (36)	25 ± 3 (33)	25 ± 4 (36)	0.298
SUA (mol/L)	290 ± 85 (505)	317 ± 90 (505)	255 ± 65 (440)	0.000
Hyperuricemia (%)	9.8	9.2	10.4	0.288
TG (mg/dl)	152 ± 88 (373)	170 ± 90 (360)	130 ± 84 (373)	0.004
TC (mg/dl)	137 ± 48 (256)	130 ± 54 (256)	144 ± 40 (252)	0.065
HDL (mg/dl)	44 ± 12 (82)	40 ± 10 (64)	48 ± 15 (82)	0.000
LDL (mg/dl)	75 ± 39 (210)	70 ± 40 (210)	82 ± 35 (188)	0.110

Results are presented as mean ± SD with maximum values in parentheses. *P*-values are given for differences between the gender groups

Table 2 Characteristics of the study population by SUA quartiles

	Overall	Q1 (≤225)	Q2 (226–285)	Q3 (286–340)	Q4 (> 340)	P -value
N	560	138	144	144	134	-
Gender (m/f)	300/260	46/92	68/76	86/58	100/34	-
Age (years)	32 ± 13	34 ± 14	31 ± 13	33 ± 12	31 ± 12	0.302
BMI (kg/m2	25 ± 4	24 ± 4	25 ± 4	26+4	26 ± 3	0.003
WC (cm)	84 ± 8	80 ± 9	83 ± 10	87+7	88 ± 6	0.002
HC (cm)	94 ± 7	90 ± 6	94 ± 7	96+6	97 ± 7	0.004
SUA (mol/L)	296 ± 21	192 ± 25	258 ± 15	325 + 12	410 ± 30	0.000
TG (mg/dl)	156 ± 85	135 ±82	130 ± 70	175 ± 105	184 ±84	0.005
% of risk (TG)	26	20	25	30	31	-
TC (mg/dl)	139 ± 47	125 ± 45	129 ± 48	146 ± 48	156 ± 47	0.035
% of risk (TC)	18	12	15	21	22	-
HDL (mg/dl)	43 ± 12	46 ± 13	44 ± 14	43 ± 11	39 ± 10	0.040
% of risk (HDL)	41	34	40	45	46	-
LDL (mg/dl)	76 ± 38	67 ± 36	68 ± 43	82 ± 35	88 ± 42	0.045
% of risk (LDL)	30	24	30	30	35	-

SUA levels (μmol/L)

Values are presented as mean ± SD. P-values are obtained from one way ANOVA

*Risk values of serum lipids: total cholesterol > 200 mg/dl, triglycerides >200 mg/dl, HDL cholesterol <40 mg/dl, LDL cholesterol >100 mg/dl.

Association of SUA with lipid profile

A statistically significant positive association (p < 0.01) was observed for serum uric acid levels with serum TG, TC and LDL levels; where as a significant negative association was found between serum uric acid and serum HDL level. After adjusting for age and gender (model 1), serum TG, TC and LDL levels in individuals in the highest quartile of serum uric acid levels were higher than in the lowest quartile (p for trend < 0.01). Serum HDL cholesterol in the highest quartile of SUA levels was lower than in the lowest quartile (p for trend < 0.01). The correlation remained unchanged after additionally adjusting for other covariates in model 2 and 3 (Table 3).

Table 3: Association of SUA quartiles with TG, TC, HDL, LDL and TG to HDL ratio

	Q1 (≤225)	Q2 (226–285)	Q3 (286–340)	Q4 (> 340)	P for trend
TG					
Model 1	0.00 (Ref.)	0.19 (0.16, 0.24)	0.29 (0.25, 0.34)	0.46 (0.42, 0.51)	< 0.01
Model 2	0.00 (Ref.)	0.13 (0.08, 0.18)	0.14 (0.06, 0.20)	0.26 (0.21, 0.34)	< 0.01
Model 3	0.00 (Ref.)	0.13 (0.08, 0.18)	0.14 (0.04, 0.18)	0.27 (0.22, 0.35)	< 0.01
TC					
Model 1	0.00 (Ref.)	0.23 (0.18, 0.28)	0.34 (0.28, 0.38)	0.45 (0.38, 0.50)	< 0.001
Model 2	0.00 (Ref.)	0.19 (0.12, 0.26)	0.21 (0.12, 0.30)	0.26 (0.15, 0.35)	< 0.001
Model 3	0.00 (Ref.)	0.17 (0.08, 0.24)	0.19 (0.11, 0.28)	0.24 (0.16, 0.34)	< 0.001
HDL					
Model 1	0.00 (Ref.)	−0.05 (−0.05, −0.03)	−0.09 (−0.08, −0.06)	− 0.13 (− 0.14, − 0.10)	< 0.01
Model 2	0.00 (Ref.)	− 0.04 (− 0.04, − 0.01)	− 0.06 (− 0.07, − 0.04)	−0.08 (− 0.12, − 0.06)	< 0.01

Model 3	0.00 (Ref.)	– 0.04 (– 0.03, – 0.01)	–0.06 (– 0.06, – 0.03)	–0.05 (– 0.10, – 0.04)	< 0.05
LDL					
Model 1	0.00 (Ref.)	0.12 (0.05, 0.18)	0.22 (0.14, 0.30)	0.30 (0.24, 0.38)	< 0.01
Model 2	0.00 (Ref.)	0.10 (0.04, 0.20)	0.15 (0.05, 0.28)	0.24 (0.10, 0.36)	< 0.01
Model 3	0.00 (Ref.)	0.10 (0.02, 0.20)	0.15 (0.04, 0.26)	0.22 (0.08, 0.34)	< 0.01
TG to HDL ratio					
Model 1	0.00 (Ref.)	0.18 (0.13, 0.24)	0.28 (0.22, 0.34)	0.54 (0.44, 0.56)	< 0.01
Model 2	0.00 (Ref.)	0.10 (0.04, 0.18)	0.12 (0.06, 0.20)	0.30 (0.20, 0.38)	< 0.01
Model 3	0.00 (Ref.)	0.10 (0.01, 0.16)	0.10 (0.01, 0.18)	0.32 (0.22, 0.40)	< 0.01

SUA levels (μmol/L)

Adjusted covariates:
model 1 = age, gender, and BMI; model 2 = age, gender, BMI and WC, model 3 = age, gender, BMI, WC and HC

DISCUSSION

This study was conducted to know whether hyperuricemia without a known cardiovascular disease (CVD) is associated with increased lipid levels so that identifying and treating such individual can prevent the development of CVD. This study reports a strong association between SUA and lipid profile in an adult cohort. Two important implications can be drawn from the present study. First, SUA levels were positively associated with serum TG, TC, LDL cholesterol and the ratio of TG to HDL cholesterol. Second, there was an inverse association between SUA and HDL cholesterol level regardless of adjustment for gender and several potential confounders, indicating a crucial role of uric acid in the regulation of dyslipidaemias. These findings are in line with previous studies that showed a pathogenesis overlap among hyperuricemia and dyslipidemia.[8,9] A number of risk factors are associated with CVD, which can be grouped into modifiable and non-modifiable. Atherogenic dyslipidaemias, including high TG, and LDL cholesterol levels with low HDL cholesterol levels is a modifiable risk factor in humans.[10]

The association of atherogenic dyslipidaemia to cardiovascular risk has been reported in previous epidemiological studies.[11,12] The link of between hyperuricemia and CVD has been established in several studies.[13,14] Hyperuricemia predisposes to the development of hypertension and may increase the oxidative stress and generate of free radicals, which eventually can be the source of future cardiovascular disease.[15] Although it still needs to be investigated whether the observed relationship between increased SUA and CVD is a causative or simply epidemiological; several lines of evidence report that determination of uric acid in serum or plasma might be helpful in early predict the risk of CVD.[16] In present study, LDL cholesterol showed a linear correlation with SUA even after adjusting co-variants. A similar finding has been observed in a recent study.[9] Previous Studies, also, demonstrate that hyperuricemia can affect adipocytes by increasing monocyte chemoattractant protein and reducing the production of adiponectin, thereby contributing to insulin resistance and inflammation.[17] These finding indicated a complex interaction between SUA and lipids which remains unclear. Taking into account present study results, we are agreed with a previous study remarks that uric acid may intensify several pathophysiological mechanisms that are associated with the CVD risk and may have synergistic interaction with other lipid profile causing CVD. Serum HDL cholesterol is a known protective factor for CVD risk. In our study, serum HDL cholesterol was inversely correlated with SUA which is in line with the findings of previous studies.[9] The elevated levels of SUA have been considered a significant predictor of smaller and denser of LDL and HDL particles, which offers a greater atherogenic ability.[16] The lower levels of HDL cholesterol favours the formation of atherosclerosis and eventually predisposed to CVD, although the direct evidence of the positive role of HDL in reducing CVD has not clearly understood yet.[9] A linear correlation was found between TG and SUA in some previous studies which are also in line with the results of present study. It is assumed that the synthesis of TG requires NADPH, which resulted in increased SUA production.[9]

The concurrence of dyslipidaemias and hyperuricemia has been reported in a few studies. For example, significant association was found between SUA and lipid profile in the adult population of India[7], Italy[8] and USA[9]. In recent years, the prevalence of hyperuricemia has been predisposed by the increasing frequency of several risk factors, such as obesity, hypertension and metabolic syndrome.[18] These observed associations influenced each other by diverse mechanism and precipitated by a number of factors. Therefore, it is important to develop proper treatment guidelines counting diet, lifestyle modification, and pharmacologic measures to reduce hyperuricemia and its adverse health effects. Moreover, reduction of SUA needs to be considered since this strategy may act synergistically with lipid-lowering therapies to reduce the cardiovascular risk.[16]

The limitations of present study are:

- The cross-sectional nature of the data may preclude the cause-effect relationships between SUA levels and lipid profile being assumed.
- Relatively a small sample size which may not represent the observed findings for the entire population.
- We did not have individual food habits information which may affect lipid levels.

However, present study findings are worthy as a reference; A prospective longitudinal study considering the association between prior dyslipidaemias and incident hyperuricemia would be valuable to confirm the observed association.

CONCLUSION

The present study shows a strong association between SUA and lipid profile among the adults. Early prevention of hyperuricemia and dyslipidaemias can reduce the incidence of associated cardiovascular disease among adults. Further, investigations are needed taking into account of hypertension, diabetes, and lifestyle for a better understanding of the observed association.

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