ORIGINAL ARTICLE

Serum Uric Acid in Relation with Insulin Resistance Associated Indices in Metabolic Syndrome and Healthy Subjects----An Observational Study

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ABSTRACT

Aim: To check the correlation of serum uric acid and the indices associated with insulin resistance in metabolic syndrome and healthy male subjects. Insulin resistance associated indices in the current study were; blood pressure, waist-circumference (WCF), body mass index (BMI), waist- hip proportion, triceps skinfold thickness (TSFT), mid arm circumference (MACF), serum glucose and insulin.
Methodology: It was an observational and correlational study; including 200 subjects 120 with Met S and 80 healthy controls. A questionnaire was filled which included demographic details, previous and present history, drug information, physical and anthropometric parameters. 5.0 ml blood was taken from an approachable vein of the upper limb with aseptic manner. It was secured in properly marked vacutainers for determination of the biochemical parameters.
Results: Blood-pressure, WCF, waist- hip proportion, BMI, MACF, TSFT, serum insulin, glucose, uric acid and HOMA-IR were higher considerably in the cases than the controls. On spearman test; serum uric acid correlated significantly and directly with the BMI, MACF, TSFT, WCF and diastolic blood pressure in the controls. Significant positive correlation between serum uric acid, glucose and HOMA-IR was observed in the cases.
Conclusion: In this current narration positive linear correlation of serum uric acid and study variables incriminates the role of uric acid in insulin resistance and associated conditions such as metabolic syndrome, central obesity and altered glycemic metabolism. Raised levels of uric acid can be targeted as a curable risk element in the control of cardiovascular and metabolic derangements.
Keywords: Serum uric acid, insulin resistance, metabolic syndrome

INTRODUCTION

Metabolic syndrome (Met S) is an insulin resistance based multi system derangement characterized by constellation of risk elements for cerebral, cardiac, hepatic and vascular accidents. Although there are various diagnostic criteria for the description and establishment of Met S; however major consensus is upon the 'Joint Interim Statement'[1, 2]. As per these guidelines diagnosis of Met S is established if 3 out of the following 5 features are present; 1) central obesity, 2) hypertension (BP>13/85 or on its treatment), 3) fasting serum triglycerides>150mg/dl or on treatment, 4) fasting serum HDL<40 mg/dl for males and 50 mg/dl for females or on treatment, 5) fasting serum glucose>100 mg/dl or on anti-diabetics.

Uric acid is the terminal output of purine (nucleotide) metabolism, produced predominantly by the liver and excreted through the kidneys. It has established antioxidant properties when its blood levels are within the normal range; however hyperuricemia is associated with insulin resistance (IR), metabolic and cardiovascular diseases[3]. IR eventuates when target cells become non responsive to the insulin action. This resistance is compensated by the increased beta cell insulin production. Hyperinsulinemia in IR decreases renal excretion of uric acid by the increased "Uric acid transporter" and the decreased "G-subfamily related ATP cassette protein" expression in the renal epithelial cells. Increased blood uric acid level worsens IR by oxidative stress and reduced vascular nitric oxide production that in turn results in endothelial dysfunction, hypertension and other vascular derangements[4]. There is association of the upper body and peri-omental adiposity with lipo-toxicity, dyslipidemia and IR. Anthropometric indices such as triceps skin fold thickness (TSFT) and mid arm circumference (MACF) are also reported to be the markers of adiposity and IR[5].

The present study is devised to figure out the correlation of serum uric acid and insulin resistance associated traits. These traits include: 1) blood pressure, 2) anthropometric obesity indices and 3) serum glycemic indices. Anthropometric indices included in the study are; waist circumference (WCF), body mass index (BMI), waist-hip proportion, TSFT and MACF. Serum glycemic indices comprise; serum levels of glucose and insulin (measured in fasting state) and homeostatic model for insulin resistance (HOMA-IR).

SUBJECTS AND METHODS

It was an observational-correlational study; carried in the settings of the Physiology Department of University of Health Sciences, Lahore. Approval was taken from the Ethical Review Board of the institution.

Study population: The study included 120 Met S subjects and 80 healthy controls. Met S patients were from the Endocrinology clinic of Sheikh Zayed Hospital, Lahore.

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Controls were the attendants of the patients or the hospital staff.

Inclusion criteria: Met S was diagnosed on the basis of Joint Interim Statement guidelines stated as follows; as per these guidelines diagnosis of Met S is established if 3 out of the following 5 features are present; 1) central obesity, 2) hypertension (BP>13/85 or on its treatment), 3) fasting serum triglycerides>150mg/dl or on treatment, 4) fasting serum HDL<40 mg/dl for males and 50 mg/dl for females or on treatment, 5) fasting serum glucose>100 mg/dl or on anti-diabetics.

Exclusion criteria: All those were excluded having evidence of end stage renal or hepatic disease, chronic inflammation, gouty arthritis, on uric acid lowering drugs and any evidence of the proliferative disorder.

After the selection of the study participants they were educated regarding the study purpose. Documented written permission was secured. A questionnaire was filled which included demographic details, previous and present history, drug information, physical and anthropometric indices. 5.0 ml blood was taken from an approachable vein of the upper limbs with aseptic manner. It was secured in properly marked vacutainers for determination of the biochemical parameters.

Recording of the anthropometric and biochemical indices: Weight was measured in kilograms with the use of digital scale. Height was recorded with the wall fixed stadiometer. BMI was calculated as weight (in kg) divided by the height (in meter^2). Measurement of WCF was carried with non-stretchable measuring tape mid-way of the lower border of the last rib and the anterior superior iliac crest. MACF was taken mid-way of the acromion and olecranon process on the right side with the inelastic measuring tape. Hip circumference was measured. WCF was divided by the HC to get waist-hip proportion. Triceps skin fold thickness was recorded with the Harpenden caliber from the back facet of the right forearm between the acromion and the olecranon process[6]. Fasting serum glucose and uric acid were estimated with the colorimetric method. Serum insulin estimation was by the Enzyme Immunoassay kit. HOMA-IR[7] was calculated by the standard equation; HOMA-IR = "Serum glucose (fasting) x serum insulin (fasting) / 22.5"

Statistical analysis: Data was interpreted with the help of statistical software SPSS21. Distribution of the data was found to be non-normal with the Shapiro-Wilk test. Spearman principle was applied to find out the correlation between serum uric acid and other quantitative study indices. A p less than 0.05 was taken to be significant.

RESULTS

The present study consists of 200 participants. 120 were the subjects with Met S and 80 healthy controls. Blood pressure, WCF, waist-hip proportion, BMI, MACF, TSFT, serum insulin, glucose, uric acid and HOMA-IR were higher considerably in cases than the controls. The comparison of these variables between the cases and controls is published in the previous papers[5,8]. On spearman test significant ($p<0.05$) positive correlation of serum uric acid was observed with WCF, BMI, TSFT, MACF and diastolic blood pressure in the controls and significant ($p<0.05$) positive correlation of serum uric acid was observed with the serum glucose and HOMA-IR in the cases. The results are presented in Table-1 and Figures-1 to 6.

Table 1: Correlation of serum uric acid with blood pressure, anthropometric and glycemic variables in metabolic syndrome and healthy subjects

Spearman correlation of serum uric acid with the following indices	**Metabolic syndrome (n= 120)** **Rho-value** **p-value**	**Healthy group** **N=80** **Rho-value** **p-value**
Systolic BP (mm mercury)	0.012 0.858	0.192 0.089
Diastolic BP (mm mercury)	0.001 0.984	0.249 0.027*
BMI (Kg per meter square)	0.019 0.786	0.343 0.002*
Waist circumference (cm)	0.054 0.432	0.260 0.021*
Waist-hip proportion	0.013 0.845	0.097 0.393
Mid arm circumference (cm)	0.019 0.778	0.265 0.014*
Triceps skinfold thickness (mm)	0.009 0.901	0.224 0.039*
Fasting serum insulin (µIU/ml)	0.301 0.000*	0.194 0.077
Fasting serum glucose (mmol/L)	0.025 0.715	0.156 0.157
Insulin resistance (HOMA-IR)	0.302 0.000*	0.151 0.175

Spearman test is applied to determine the correlation between serum uric acid and other study indices. A p of less than 0.05 is of statistical significance

Figure-1: Correlation between serum uric acid and waist circumference

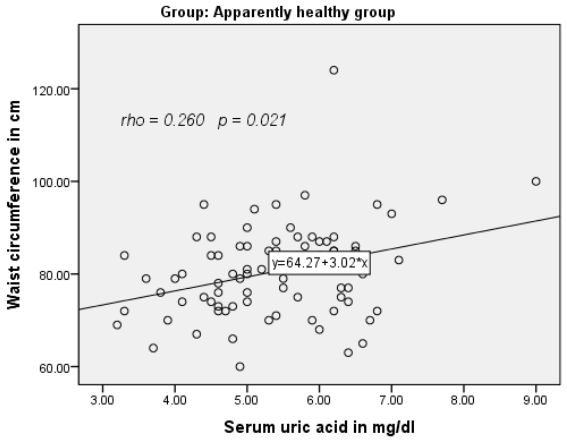


Figure-2: Correlation between serum uric acid and body mass index

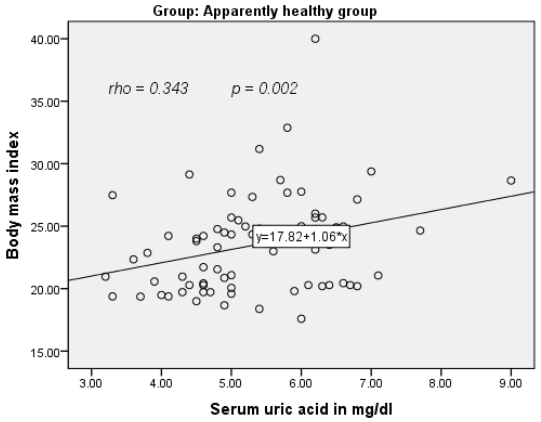


Figure-3: Correlation between serum uric acid and triceps skin fold thickness

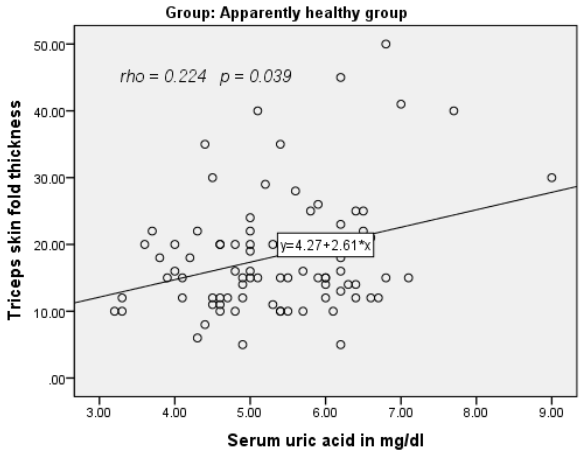


Figure-4: Correlation between serum uric acid and mid arm circumference

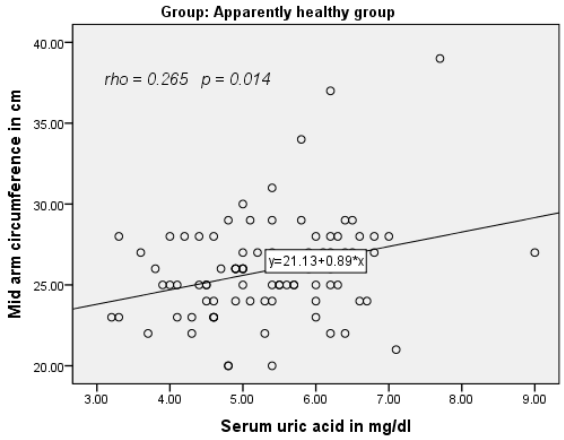


Figure-5: Correlation between serum uric acid and insulin resistance (HOMA-IR)

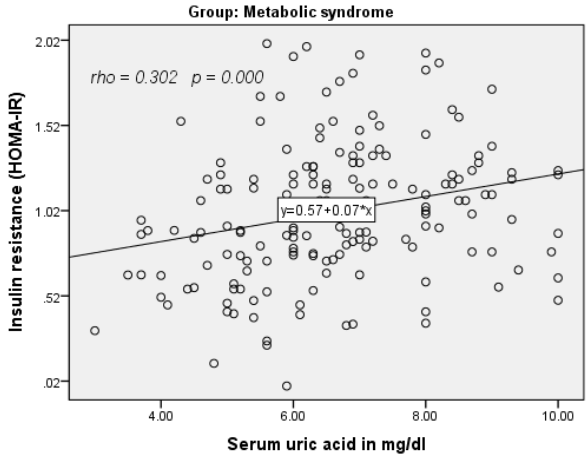
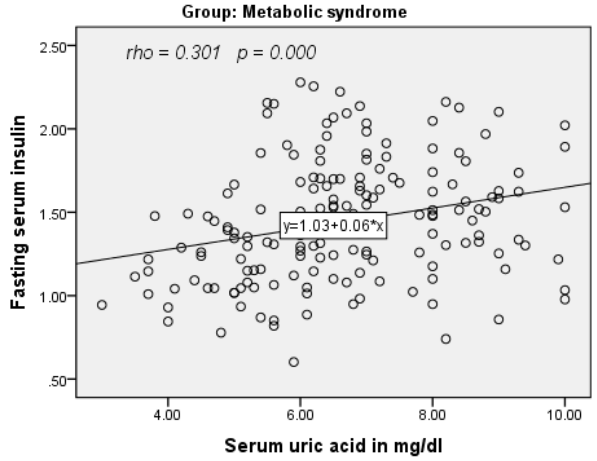


Figure-6: Correlation between serum uric acid and serum insulin



DISCUSSION

In the present study, serum uric acid was found to be in significant positive correlation with the anthropometric indices such as BMI, WCF, MACF and TSFT in the healthy subjects however no significant correlation was exhibited in the subjects with Met S. Considerable direct relation was also observed between the diastolic blood pressure and serum uric acid in the healthy subjects; no such relation was there in the Met S. These results are in agreement with the findings of an earlier study on adolescent boys and girls that documented positive correlation of uric acid with the BMI and percent body weight[9]. Another study on postmenopausal women reported significant association of the serum uric acid level with hyperglycemia, adiposity and hypertriglyceridemia[10]. A recent study on Chinese population also found substantial association of serum uric acid with acanthosis nigricans, dyslipidemia and other metabolic indices[11].

In the current study, significant correlation of diastolic blood pressure was observed with the serum uric acid; this result is also supported by a previous study on Bangladeshi cohort that reported an upward trend of blood pressure in the rising uric acid quartiles[12]. Numerous other studies also reported association between hypertension and hyperuricemia[13,14]. In this study we were unable to find the sizable relation between serum uric acid and clinico-anthropometric measurements. One possibility of the lack of association in Met S subjects might be the alteration of normal tissue homeostasis due to underlying IR; another explanation is that majority of these patients were on drugs such as antihypertensive and anti-diabetics. These also lead to altered organ and system responses[15].

In the current study significant positive correlation was displayed between the serum uric acid and insulin levels and HOMA-IR in Met S subjects only. No such relation was found in the healthy subjects. A previous study on type2 diabetics also mentioned direct correlation of serum uric acid with serum insulin in the diseased group and it was concluded that serum uric acid levels can be a predictor of glucose metabolism[16]. Various other studies also confirmed the role of uric acid as an important modulator of IR and associated traits in metabolic derangements[17,18]. The IR and serum uric acid association proceeds in bidirectional worsening manner. In insulin resistant state such as type2diabetes due to deranged glycolysis cycle; there is influx of glucose in the cycle of “Glucose-6-phosphate shunt” that results in an increased output of uric acid[19]. Another explanation of hyperuricemia in IR is hyperinsulinemia. Insulin decreases renal urate excretion by increasing uric acid transporters in the renal epithelial cells. Hyperuricemia worsens IR by oxidative stress, decreased nitric oxide production and endothelial dysfunction[4,20].

CONCLUSION

In this current narration positive direct correlation between serum uric acid and study variables incriminates the role of uric acid in insulin resistance and associated conditions such as metabolic syndrome, central obesity and altered glycemic metabolism. Raised levels of uric acid can be targeted as a curable risk element in the control of cardiovascular and metabolic derangements.

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Disclaimer: This article is from PhD work

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