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Original article

Serum uric acid level as a determinant of the metabolic syndrome: A case control study

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ABSTRACT

Aims: To determine whether elevations of uric acid levels are associated with the cluster of disorders described in metabolic syndrome and to evaluate whether hyperuricemia may be considered a component of this syndrome.
Methods: One year case-control study was conducted in Bikaner, Rajasthan, India from January to December 2013. The study population consisted of 200 subjects, 100 with metabolic syndrome (case) and 100 without metabolic syndrome (control) aged between 18 and 80 years, attending OPD at PBM Hospital were studied. Controls were age and sex matched to the cases. Blood tests and all physical variables were examined using standard methods. Subjects were divided into 6 groups according to their possession of 0, 1, 2, 3, 4 or 5 components of the metabolic syndrome. Statistical analysis was done using ANOVA, linear regression analysis and multivariate linear regression model.
Results: Mean serum UA level was significantly associated with all components of metabolic syndrome ($p < 0.001$) and had strong positive correlation ($r = +0.66$ to $+0.77$, $p < 0.0001$) with all of them except serum HDL with which it showed strong negative correlation($r = -0.71$, $p < 0.0001$). It increased as the number of metabolic factors increased showing a highly significant trend ($p < 0.0001$). On multivariate regression analysis UA contributed to 66.84% variance of metabolic syndrome.
Conclusion: The current multivariate regression analysis clearly infers that uric acid can be considered as a marker and potential modifier of metabolic syndrome.

1. Introduction

Metabolic syndrome is evolving into a pandemic, contributing to approximately 6–7% for all causes of mortality, 12–17% for cardiovascular disease, and 30–52% for diabetes in the population [1]. The increased risk for cardiovascular diseases can partly be caused by a prothrombotic state that exists because of abdominal obesity [2].

Various combinations of the following five risk factors constitute the basis for the different definitions of the metabolic syndrome: obesity (total body obesity measured by body mass index, or central obesity measured by waist-to hip ratio or waist circumference), atherogenic dyslipidemia (increased triglycerides, decreased high-density lipoprotein cholesterol); elevated blood pressure (systolic and diastolic), abnormal glucose tolerance (fasting blood glucose, 2-h postprandial blood glucose), and insulin resistance measured by the homeostasis model assessment (HOMAIR) or fasting insulin [3]. Recent findings suggest that uric acid should be added to the list of determinants or biomarkers of metabolic syndrome [4].

Hyper-uricemia is associated with the MS and its prevalence is comparable in both genders and in subjects with and without hypertension [5]. The possible predictors of hyper uricemia include centripetal obesity, significant smoking history and elevated serum TG. Elevated serum uric acid levels (SUA) have been associated with an increased risk of cardiovascular diseases and the metabolic syndrome (MS). According to Lanaspa A. et al., it seems likely that uric acid may have a role as both a marker and potential modifier of the metabolic syndrome although these investigators recommended that more studies be carried out [4].

This study is planned to assess, in a hospital based sample, whether elevations of uric acid levels are associated with the cluster of disorders described in the metabolic syndrome and to

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evaluate whether hyperuricemia may be considered a component of this syndrome.

2. Subjects and methods

The present study was a case control study conducted in Bikaner, Rajasthan, India during the period of January to December 2013. The study population consisted of 200 subjects, 100 with metabolic syndrome (case) and 100 without metabolic syndrome (control) aged between 18 and 80 years, admitted in wards or attending OPD/executive health check-up at PBM Hospital, Geriatric hospital & diabetic research centre were studied. Controls were age and sex matched to the cases.

Considering prevalence of metabolic syndrome as being 50% (since no previously reported data are available), by using formula n = 4pq/d2 and allowable error of 10%, sample size of 100 cases and 100 controls was taken (where p = prevalence of study, q = 100-p, d = allowable error).

Ethical approval was taken from Medical College ethics committee. Subjects were briefed about nature of study and written consent was taken from them.

Blood tests and all physical variables were examined at nearly the same time. Blood pressure (BP) was measured using an automated sphygmomanometer, with the patient in the sitting position before the blood test. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m2). Waist circumference (WC) was measured with the measuring tape positioned midway between the lowest rib and the superior border of the iliac crest while the patient exhaled normally [6]. Hip circumference was measured at the outermost points of the greater trochanters. The ratio of waist-to-hip circumference was used as an index of fat distribution.

The blood sample was collected in the morning after at least 8 h of fasting. Fasting blood sugar levels were obtained for all the participants. It was estimated by glucose oxidase method.Serum lipid profile was obtained by autoanalyser and included total cholesterol (TC), highdensity lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG). Fasting insulin level was measured by microparticle enzyme immune assay (MEIA) method. Insulin resistance was calculated by HOMA IR i.e Fasting Insulin (μU/L)* Fasting plasma glucose (mg/dl)/405. Patients were considered as insulin resistant if HOMA-IR was more than 3.8 [7].

The components that contribute to metabolic syndrome were defined as high BP (≥130/85 mmHg), truncal obesity (WC >90 cm for men, >80 cm for women), hypertriglyceridemia (>150 mg/dL or 1.7 mmol/L), low HDL-C (<40 mg/dL or 1.0 mmol/L for men, <50 mg/dL or 1.3 mmol/L for women) and hyperglycemia (fasting blood glucose level ≥100 mg/dL or 5.6 mmol/L) [8]. Subjects were divided into 6 groups according to their possession of 0, 1, 2, 3, 4 or 5 components of the metabolic syndrome.

Serum uric acid concentration was measured enzymatically after hydrolyzation to glycerol. There is no universally-accepted definition for hyperuricemia based solely on serum UA levels. We defined participants as having hyperuricemia if their serum UA concentration was >7.0 mg/dL (416.4 μmol/L) in men or >6.0 mg/dL (356.9 μmol/L) in women [9]. These cutoffs were selected because they are commonly used in clinical laboratories and have been proposed in previously-published studies in relation to CVD outcomes to define hyperuricemia.

We also classified participants according to categories of UA. Uric acid concentrations were categorized into quartiles for men and women separately. The resulting four categories for men were 1) <4.8 mg/dL; 2) 4.8–5.5 mg/dL; 3)5.6–6.4 mg/dL and 4) ≥6.5 mg/dL. The corresponding categories for women were 1) <3.8 mg/dL; 2) 3.8–4.2 mg/dL; 3)4.3–5 mg/dL and 4) ≥5.1 mg/dL.

Baseline demographic data in the 6 groups were descriptively summarized. Continuous variables were expressed as mean ± standard deviation and mean ± standard error. Categorical variables were presented as percentages. Pearson correlation coefficient (r) in linear regression model was used to evaluate the relationship between serum UA and increasing number of risk factors. The intergroup comparisons were performed using a one-way ANOVA test followed by a Tukey's kramer test (q). Multivariate regression analysis with serum uric acid concentration as the dependent variable was used to identify significant predictors. Significance was defined as $p < 0.05$ for all statistical tests, which were performed using SPSS version 18 (Fig. 1).

3. Results

Baseline characteristics of the cases and controls have been presented in Table 1. All variables demonstrated significant differences between groups, with an increasing trend as the number of components increased (except for HDL-C, which showed a decreasing trend). Mean value of serum uric acid level in cases and controls was 7.15 ± 0.28 and 3.30 ± 0.05 mg/dl ($f = 13.39$, $p < 0.001$). Mean serum uric acid level significantly increased from 3.08 to 8.01 mg/dL with increasing number of components of metabolic syndrome from zero to five ($f = 85.0931$, p value for trend <0.0001) as seen in Table 2 and demonstrated a significant linear trend. Mean waist circumference, waist hip ratio, BMI, fasting blood sugar, HOMAIR, systolic and diastolic blood pressure and triglyceride, showed a rising trend while Mean HDL showed a decreasing trend across the quartiles of serum uric acid and p value for the trend was highly significant (<0.001).

Serum uric acid level showed strong positive correlation with waist circumference, waist hip ratio, BMI, fasting blood sugar, HOMAIR, systolic and diastolic blood pressure and triglyceride and inverse correlation with HDL as estimated by linear regression ($p < 0.001$) and shown in Table 3. Strongest correlation was with insulin resistance (FIL) followed by central obesity (BMI, WC) and with dyslipidemia (TG). Mean waist circumference, waist hip ratio, BMI, fasting blood sugar, HOMAIR, systolic and diastolic blood pressure and triglyceride across quartile of serum uric acid level, showed a rising trend and mean HDL showed a decreasing trend across the quartiles of serum uric acid and p value for the trend was significant ($p < 0.01$). By multivariate regression analysis (Table 4) we observed that 66.84% of variance in the uric acid can be explained by the various established components of metabolic syndrome (Adjusted $R2 = 0.6580$, $f = 64.82$, $p < 0.0001$), and uric acid makes a significant contribution to metabolic syndrome (t ratio = 3.216, $p = 0.0015$).

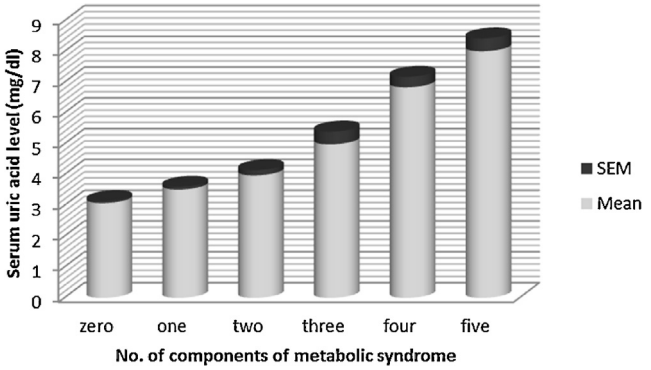

Fig. 1. Serum uric acid level of subjects according to number of metabolic syndrome components.

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