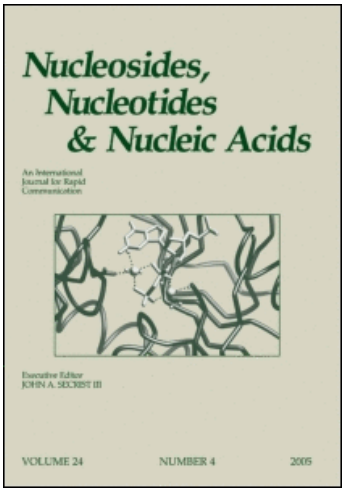

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SERUM URATE, METABOLIC SYNDROME, AND CARDIOVASCULAR RISK FACTORS. A POPULATION-BASED STUDY

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□ *We studied the associations between serum urate levels (determined in 503 subjects from a population of 1,344 subjects living in northern Madrid) and both the metabolic syndrome (MS) (defined by the Adult Treatment Panel III criteria) and C-reactive protein (CRP, determined in 382 subjects). MS was diagnosed in 25% (95%CI, 21–28%) and was associated with hyperuricemia ($p < 0.001$). There was a graded increase in serum urate levels with increasing number of MS components. Urate concentrations significantly correlated with waist circumference ($r = 0,455$, $p < 0.01$). Serum urate was not independently associated with CRP levels. This study shows that serum urate levels are associated with the presence of MS and each of its features.*

Keywords Serum urate; hyperuricemia; metabolic syndrome; CRP; cardiovascular risk factors

INTRODUCTION

Relationships between serum urate (UA) levels and several cardiovascular risk factors, such as hypertension and obesity, have been firmly established.[1] However, associations of UA levels with the metabolic syndrome (MS) and C-reactive protein (CRP) levels are less well documented,[2,3] particularly in the Mediterranean area. Accordingly, the aims of the present study were: 1) to examine associations between UA levels and MS (and each of its component features); and 2) to investigate whether an association of UA and CRP levels is an independent relationship.

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SUBJECTS AND METHODS

Subjects included in this study comprise a subsample of 503 individuals (age range: 31–70 years) from a large survey (n = 1,344 subjects) performed in the population living in the northern region of Madrid. Participants had similar demographic and cardiovascular risk features to those of subjects in the original survey. All participants gave their written informed consent. Subjects underwent clinical interview and measurement of blood pressure, body mass index, and waist circumference (WC). Fasting plasma glucose, total cholesterol, HDL-cholesterol, triglyceride, and UA levels were determined by conventional methods. CRP was measured (in 382 subjects) by nephelometry (N high-sensitivity CRP assay; Dade Behring, Marburg, Germany). Hyperuricemia was defined as a UA level $\geq$7 mg/dL. MS was defined by the modified ATP III criteria.[4] Data are presented as mean $\pm$ SD or, where appropriate, as median (interquartile interval). CRP was analyzed either by nonparametric tests or by analysis of variance as a log transformed variable. The independence of the association of SU with logPCR levels was assessed by multiple regression analysis.

RESULTS

Five hundred and three subjects (228 males; mean age 53 $\pm$ 11 years) were included. The MS prevalence was 25% (95% CI, 21–28%). Hyperuricemia (UA $\geq$7 mg/dL) was present in 56 subjects (11.3%; 95%CI, 8.3–13.9%). Mean SU levels were higher in subjects with MS than in those without MS (n = 141; 5.9 $\pm$ 1.7 mg/dL vs. n = 362; 5.0 $\pm$ 1.5 mg/dL, respectively; $p < 0.001$). Similar results were found when we compared UA levels from subjects with any MS feature (i.e., high blood pressure, dyslipidemia, etc.) to UA levels in subjects with no MS features (data not shown). UA levels significantly correlated with each MS components, but most strongly with WC ($r = 0.455$, $p < 0.001$; Figure 1). We also found a graded increase in UA levels of with increased numbers of MS components up to 3 or more (Figure 2).

Patients with hyperuricemia showed significantly higher CRP levels than normouricemic subjects (2.89 mg/L [1.1–4.1] vs. 2.10 mg/L [1.0–3.4], respectively; $p = 0.04$). A multiple regression analysis with logCRP as dependent variable showed that UA levels were independently associated with CRP levels, after controlling for age, gender, and smoking. However, when either systolic blood pressure or WC was added to the model, as an independent variable, the association between UA and CRP did not remain significant (data not shown).

DISCUSSION

This study identifies a significant association between the UA levels and MS in an urban Spanish population. Of interest, we found a graded increase

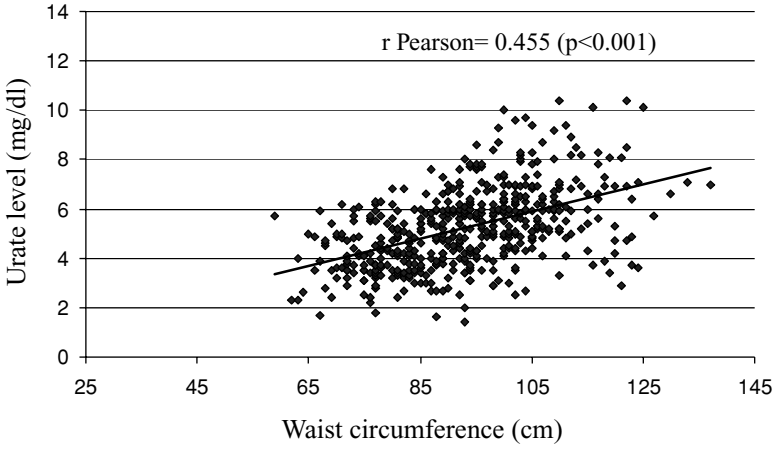

FIGURE 1 Correlation between serum urate levels and waist circumference.

in uricemia levels with increasing number of MS components (up to 3), and, in fact, uricemia correlated with all MS components, particularly with WC. In a population-based study performed in Turkey,[2] abdominal obesity was an important determinant of UA, even after adjustment for WC. In a recent study using data from the Third National Health and Nutrition Examination Survey,[3] the prevalence of the MS increased substantially with increasing uricemia levels.

We investigated the association between UA and CRP in order to better understand the role of UA as a marker of cardiovascular risk. Although we found an association between these variables that remained statistically significant after controlling for several confounders, such as age, gender, and smoking, SU and CRP were no longer independently associated after adjustment for WC or systolic blood pressure. This suggests that uricemia is a marker for abdominal obesity. Countinho et al.[5] recently investigated

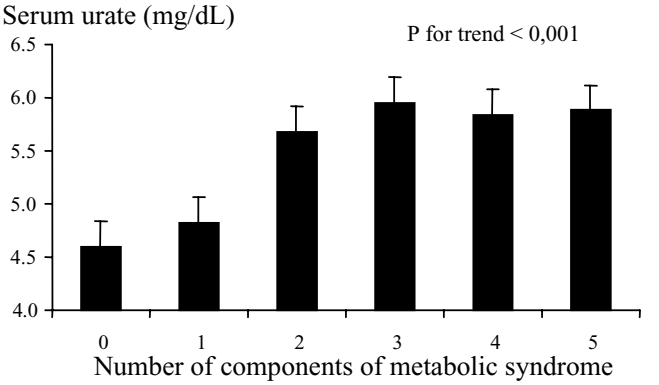

FIGURE 2 Serum urate according to the number of MS components.

the associations of UA with MS, CRP, and the presence and quantity of coronary artery calcium (CAC). UA was significantly correlated with CAC, but not after adjustment for systolic blood pressure, diabetes, total and HDL-cholesterol, smoking, and body mass index. Thus, UA appears to be a marker of for MS and subclinical atherosclerosis, but is not independently associated with the latter. We conclude that uricemia is a marker of the MS and is not independently associated with CRP. Physicians should look for MS criteria in patients with hyperuricemia in order to achieve early detection and, where appropriate, treatment of the clinically significant features of the syndrome.

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