CORRELATIONS BETWEEN LEVELS OF SERUM URIC ACID AND PARAMETERS OF THE METABOLIC SYNDROME

DANA STEFANA POPESCU1,2, ALIN CIOBICA3,4, LIDIA IULIANA ARHIRE1, LAURA MIHALACHE1, OTILIA NITA1, IONELA LACRAMIOARA SERBAN1, ROMEO DOBRIN1, DIDONA UNGUREANU1 and MARIANA GRAUR1

1“Grigore T. Popa” University of Medicine and Pharmacy, 16 Universitatii Street, 700115, Iasi, Romania
2Medical Center Deleni, Romania
3 “Alexandru Ioan Cuza” University, Bd. Carol I, nr. 11, Iasi, 700506, Romania
4 Center of Biomedical Research of the Romanian Academy, Iasi Branch, Romania

Abstract – The aim of this study was to investigate whether serum uric acid levels are significantly associated with the parameters that contribute to the metabolic syndrome in a rural community from Iasi County, Romania. We observed that the components associated most with the serum levels of uric acid were body mass index, triglycerides, waist circumference and hip circumference. Significant correlations were found for the levels of uric acid and total cholesterol, fasting glycemia, systolic blood pressure and diastolic blood pressure. The observed correlations point to uric acid as a potential marker of the metabolic syndrome.

Key words: uric acid; metabolic syndrome.

INTRODUCTION

Metabolic syndrome is considered a collection of cardiovascular risk factors that generally includes central obesity, hypertension, high triglyceride and low HDL cholesterol levels (Nakagawa et al., 2006). Although lately there are some discussions about the very specific parameters and their exact values that are relevant as criteria for the clinical diagnosis of metabolic syndrome (Alberti et al., 2009), there is a general consensus that the presence of metabolic syndrome is strongly associated with an increased risk of all-cause mortality (Cirillo et al., 2006).

There has been an increased prevalence of the disease in the last several years, with almost a quarter of the total population being affected in the United States (Ford et al., 2004), and prevalence has also increased in Europe (Hu et al., 2004), Africa (Longo-Mbenza et al., 2010) and China (Gu et al., 2005), and even in specific aboriginal populations around the world (O’Dea et al., 1999). This is mostly due to the so-called “westernization” of lifestyle with its high-fat and high-calorie diet and decreased physical activity. For this reason, it is important to identify the possible mechanisms and strategies to prevent and/or treat this syndrome.
Lately there has been an increased interest in the possible relevance of uric acid in mechanisms involved in the metabolic syndrome (Lin et al., 2006, Ishizaka et al., 2005, Kawada et al., 2010). The association between the metabolic syndrome and serum uric acid are not completely understood. For example, it is not known if increased uric acid concentration in the serum of patients with metabolic syndrome is a cause or consequence of the disease (Heinig et al., 2006, de Oliveira et al., 2012). While some studies suggest that uric acid may be a consequence of the presence of hyperinsulinemia and/or oxidative stress which is present in patients with metabolic syndrome (Lanaspa et al., 2011), other authors showed that elevated uric acid sometimes precedes the hypertension or obesity of metabolic syndrome (Taniguchi et al., 2001, Masuo et al., 2003). Moreover, a recent study has reported that the elevated levels of serum uric acid could predict the metabolic syndrome in adolescents (Stapleton et al., 2012).

The aim of this study was to investigate whether serum uric acid levels are significantly associated with the parameters of metabolic syndrome in a rural community from Iasi County, Romania.

MATERIALS AND METHODS

The study included 254 patients, 156 females and 98 males aged 53.98±1.01 years, with metabolic syndrome (Alberti et al., 2009) recruited from the Deleni Medical Center, Iasi, Romania. The exclusion criteria were cardiovascular diseases (defined as previous myocardial or cerebral infarction, coronary revascularization), progressive malignancy, acute infectious disease (including urinary tract infection), gout, psoriasis, diuretics or uric acid-lowering agents.

Anthropometric parameters were measured by the same trained members of the medical staff at the medical center, using standard calibrated equipment. Blood pressure was measured with the subject sitting, using a standard mercury sphygmomanometer after 5 min of rest and with the arm at heart level. Fasting blood samples were collected to determine the levels of glucose, total cholesterol, HDL and LDL-cholesterol, triglycerides and uric acid using standard methods in the hospital laboratory.

Weight was measured in the morning before breakfast with the subjects wearing light clothes. Height was measured with the subjects standing without shoes. Waist circumference was determined using a fiberglass tape at the midpoint between the bottom of the rib cage and the top of the iliac crest, at the end of a normal exhalation with the subjects standing without clothes. The hip circumference was measured by positioning the measuring tape around the largest circumference of the buttocks.

The study was conducted according to the provisions of the Helsinki Declaration and the local ethics committee’s approval was obtained before the beginning of the study. All the patients signed a consent form for their participation in this study.

Data analysis

Pearson’s correlation coefficient was used to evaluate the connection between the serum levels of uric acid and the main parameters of metabolic syndrome. Values for which p<0.05 were regarded as statistically significant.

RESULTS

Our results showed significant correlations between the serum levels of uric acid and BMI (n=254, r=0.280, p<0.0001) (Fig. 1A), uric acid and triglycerides (n=254, r=0.305, p<0.0001) (Fig. 1B), uric acid and waist circumference (n=254, r=0.335, p<0.0001) (Fig. 1C) and uric acid and hip circumference (n=254, r=0.212, p<0.001) (Fig. 1D).

We found moderate correlations between the levels of uric acid and total cholesterol (n=254, r=0.13, p=0.039) (Fig. 2A), uric acid and fasting glycemia (n=254, r=0.11, p=0.042) (Fig. 2B), uric acid and systolic blood pressure (n=254, r=0.122, p=0.04) (Fig. 2C) and uric acid and diastolic blood pressure (n=254, r=0.118, p=0.041) (Fig. 2D).
No significant correlations were found between uric acid and HDL ($n=254$, $r=-0.106$, $p=0.093$) (Fig. 3A) or uric acid and LDL ($n=254$, $r=0.039$, $p=0.54$) (Fig. 3B).

**DISCUSSION**

In the present paper, we confirmed the important correlations that exist between serum levels of uric acid and the main parameters associated with metabolic syndrome in a rural community from Iasi County, Romania. The components that were associated most with the serum levels of uric acid were BMI, triglycerides, waist circumference and hip circumference. Additionally, significant correlations were found between the levels of uric acid and total cholesterol, fasting glycemia, systolic blood pressure and diastolic blood pressure.

Our results suggest that hyperuricemia is an associated abnormality that could be considered as a possible marker in those with metabolic syndrome.
There are previous reports about the correlations between elevated levels of uric acid and factors such as hyperlipidemia, obesity, hyperinsulinemia, diabetes mellitus or glucose intolerance, as well as accelerated progression of hypertension or the development of oxidative stress and LDL oxidation (Onat et al., 2006, Mazzali et al., 2002).

Numata et al. (2008) reported that uric acid is significantly higher in subjects with the metabolic syndrome when compared to subjects without the syndrome in both sexes in the Japanese population. This was also confirmed by others (Al-Omer et al., 2007, Kawamoto et al., 2006). However, as outlined by Heinig and Johnson (2006), hyperuricemia is still not considered an important risk factor in this context.

There are different opinions whether uric acid is just a consequence of oxidative stress or hyperinsulinemia that appear in the metabolic syndrome (Lanaspa et al., 2011), or, as later studies have suggested, it has an important causative role. It was demonstrated in pair-feeding studies that fructose and not dextrose, induces some features of the metabolic syndrome, such as hyperinsulinemia, hypertriglyceridemia and hyperuricemia. As described by Nagawa et al. (2006), in rats receiving a high-fructose diet, decreased levels of uric acid with allopurinol (a xanthine oxidase inhibitor) or benzbromarone

Fig. 2. Correlations between the concentrations of serum uric acid and total cholesterol (A), fasting glycemia (B), systolic blood pressure (C) and diastolic blood pressure (D).
(a uricosuric agent) prevented the manifestation of the metabolic syndrome. The lowering of uric acid in human subjects ingesting high doses of fructose was associated with improvements in blood pressure values, but not in other specific parameters of metabolic syndrome (Lanaspa et al., 2011).

Uric acid is known as a marker of oxidative stress and may have a potential therapeutic role as an antioxidant. On the other hand, like other strong reducing substances such as ascorbate, uric acid can also act as a prooxidant, particularly at elevated levels (Al-Omer et al., 2007). There are also reports showing that uric acid is proinflammatory in rat vascular smooth muscle cells and stimulates human mononuclear cells to produce cytokines (Onat et al., 2006). Thus, it is still unclear whether elevated levels of uric acid in diseases associated with oxidative stress, such as stroke and atherosclerosis, are a protective response or a primary cause (Leyva et al., 1997).

Maalouf et al. (2011) have described the role of uric acid in mechanisms implicated in the association between the metabolic syndrome and nephrolithiasis. In addition, the correlation between metabolic syndrome and the genesis of uric acid stones was recently described (Kim et al., 2013).

There seems to be an association between metabolic syndrome and carotid atherosclerosis in patients with type 2 diabetes (Li et al., 2011). Additionally, an association between serum uric acid, metabolic syndrome, and carotid atherosclerosis was very recently shown in a cross-sectional study including 814 Japanese individuals (Ishizaka et al., 2005).

The relevance of salivary uric acid as a noninvasive biomarker of the metabolic syndrome has also discussed (Soukup et al., 2012).

CONCLUSIONS

In the present study, we confirmed a significant correlation between the serum levels of uric acid and most of the specific parameters of the metabolic syndrome. The observed correlations point to uric acid as a potential marker of metabolic syndrome. Additional studies are necessary to understand the role of uric acid in the metabolic syndrome and to determine whether the prevention of or treatment of hyperuricemia has any beneficial effects on the metabolic syndrome.

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