ORIGINAL PAPER

UROLITHIASIS

Metabolic syndrome and the composition of urinary calculi: is there any relation?

Pedro Valente[1], Hélder Castro[1], Inês Pereira[2], Fernando Vila[1], Paulo Barros Araújo[1], Cristina Vivas[1], Ana Silva[2], Ana Oliveira[2], Joaquim Lindoro[1]

[1]*Department of Urology, Centro Hospitalar do Tâmega e Sousa, E.P.E., Penafiel, Portugal*
[2]*Unidade de Saúde Familiar Terras de Souza, Paredes, Portugal*

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Corresponding author
Pedro Valente
Department of Urology
Centro Hospitalar
do Tâmega e Sousa
Av. do Hospital Padre
Américo N210
4564-007 Penafiel
Portugal
phone: +255 714 469
pedrovalente.md@gmail.com

Introduction Epidemiologic studies demonstrate that obesity and diabetes increase the prevalence of urinary lithiasis. Most of these studies did not stratify the chemical composition of calculi and the physiological mechanisms responsible for this increased risk are not well understood. This study aims to investigate the relation between the metabolic syndrome and the composition of the urinary calculi.

Material and methods Observational and retrospective study of all urinary calculi analysis performed at the Centro Hospitalar do Tâmega e Sousa, Portugal – from January 2009 to September 2015. Calculi were analyzed by infrared spectroscopy.

Results 302 analyses of urinary calculi were identified. Metabolic syndrome was diagnosed in 20.5% of patients. A total of 7 different mineral compounds were identified: 51.6% (N = 156) contained calcium oxalate, 41% (N = 124) calcium phosphate, 37.7% (N = 114) uric acid, 22.1% (N = 67) ammonium urate, 9.6% (N = 29) ammonium magnesium phosphate, 6.3% (N = 19) sodium urate and 1.3% (N = 4) contained cystine. Patients with metabolic syndrome presented a higher proportion of uric acid calculi (66.1% vs. 0%, p <0.001) and ammonium urate calculi (38.7% vs. 17%, p = 0.001). Patients without metabolic syndrome had a higher proportion of calcium oxalate calculi (58.8% vs. 24.2%, p <0.001) and calcium phosphate (46.7% vs. 19.4%, p <0.001).

Conclusions There is a statistically significant relation between metabolic syndrome and uric acid and ammonium urate calculi. Metabolic syndrome may be considered risk factor for this calculi and the diagnosis and treatment of this syndrome must be considered for urolithiasis prevention. Further studies are needed to better the understanding of physiological mechanisms underlying this relationship to improve our strategy of prevention of urinary lithiasis.

Key Words: cardiovascular disease ‹› insulin resistance ‹› metabolic syndrome ‹› urinary calculi ‹› urolithiasis

INTRODUCTION

Urinary lithiasis is a very common pathology worldwide, whose incidence is around 5% to 10% [1]. The prevalence of urinary lithiasis, in the general population, has been increasing in recent years, which can be explained by environmental factors such as decreased fluid intake, hypersaline, hyperproteic or hypercaloric feeding associated with a genetic predisposition to the development of urinary calculi [1–9]. In addition, calculi may also be related to systemic diseases, such as metabolic syndrome (MS) [9].

MS is a chronic and multifactorial disease characterized by an association between clinical manifestations of pathologies that share a common pathophysiological mechanism: insulin resistance [6, 7, 9]. Its prevalence varies according to age, gender and ethnicity, affecting 24% to 42% of the adult population and more than 66.4% of the older population [7]. Its definition, by the International Diabetes Federation, include increased abdominal perimeter [males

greater than or equal to 94 centimeters (cm)] and females greater than or equal to 80 cm] and at least two of the following criteria: elevated triglyceride levels [values greater than 150 milligrams per deciliter (mg/dL)]; HDL (high density lipoprotein) levels (male values below 40 mg/dL and female values below 50 mg/dL); High blood pressure (BP) equal to / greater than 130 millimeters of mercury (mmHg) or diastolic BP equal to or greater than 85 mmHg]; and increased fasting blood glucose (values greater than 100 mg/dL) [2, 9]. MS is associated with an increased risk of cardiovascular disease, type 2 diabetes mellitus and also urological diseases such as erectile dysfunction, benign prostatic hyperplasia, chronic kidney disease and lithiasis. Therefore, it is associated with high morbidity and mortality [1, 3, 4].

Several epidemiological studies have associated MS with an increased risk of developing urinary lithiasis [1–9] The prevalence of urolithiasis increased progressively and in parallel with the increase of the incidence of obesity, type 2 diabetes mellitus and SM [2, 4]. Moreover, although urolithiasis is more common in men than in women, there is evidence that the sex difference is declining, which can be explained by the disproportionate increase of obese and overweight women compared to men. Women have a higher percentage of body fat than men that can influence the lithogenic potential [4].

In addition to the increased risk of developing urolithiasis, clinical and experimental studies indicate that MS is associated with more severe disease expression compared to individuals who have urolithiasis without MS. Patients who have calculi and MS, at the same time, produce a greater number of calculi compared to those who do not have MS [4]. The chemical composition of the calculi appears to be dependent on urinary risk factors associated with individual characteristics of MS [6–9]. The main determinant in the development of uric acid calculi is the abnormally low urinary pH [2]. An acid urine pH promotes the formation of uric acid calculi while an alkaline urine pH promotes the formation of calcium calculi [3, 5]. However, the association between the composition of urinary calculi and the metabolic syndrome was not yet well documented [2]. Therefore, the aim of this work was to analyze the relation between MS and the composition of urinary calculi.

MATERIAL AND METHODS

Observational, retrospective study of all the composition analyses of calculi performed at the Centro Hospitalar do Tâmega e Sousa (Penafiel, Portugal) since January 2009 to September 2015. Patients were divided into two groups: patients with MS and patients without MS. Calculi were analyzed using infrared spectroscopy (Nicolet FT-IR Spectometer®) and statistical analysis was performed using SPSS software 20.0.

RESULTS

Three hundred and two analyzes of urinary calculi were identified. Of the total number of patients who participated in this study, 55.3% were female and 44.7% were male. Their mean age was 51 years [standard deviation (SD) ±14]. MS was diagnosed in 20.5% of patients. The group of patients with MS had a mean age above that of the group of patients without MS [59.1 years (SD ±12.7) versus 48.9 years (SD ±13), $p < 0.001$] and had not been identified as a statistically significant difference in what concerns the sex ratio ($p = 0.264$).

Seven different mineral compounds were identified in the calculi: 51.6% (N = 156) contained in their composition calcium oxalate, 41% (N = 124) calcium phosphate, 37.7% (N = 114) uric acid, 22.1% (N = 66.7) ammonium urate, 9.6% (N = 29) ammonium magnesium phosphate, 6.3% (N = 19) sodium urate and 1.3% (N = 4) cystine.

Patients with MS had a higher proportion of uric acid (66.1% versus 30%, $p < 0.001$) (Figure 1) and ammonium urate calculi (38.7% versus 17%, $p = 0.001$) compared to patients without MS (Figure 2).

Patients without MS had a higher proportion of calcium oxalate (58.8% vs. 24.2%, $p < 0.001$) and calcium phosphate calculi (46.7% versus 19.4%, $p < 0.001$), by comparison with patients with MS (Figure 3, Figure 4).

DISCUSSION

The association between MS and urinary lithiasis appears to be clinically relevant, as has been suggested by other research studies [7]. This research has shown that patients with MS have a higher percentage of uric acid calculi compared to patients without MS. These data are corroborated by other studies that have shown a higher prevalence of uric acid calculi formation in obese patients or with type 2 diabetes mellitus compared to patients who do not present any of these pathologies [5].

Ekeruo et al. identified hypocitraturia and hyperuricosuria as the most common metabolic abnormalities in the urine of obese urinary stone formers [10]. Taylor et al. also noted that urinary supersaturation of uric acid increased with body mass index (BMI) [11].

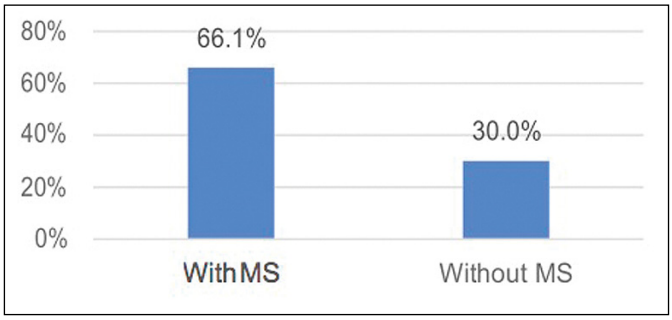

Figure 1. *Proportion of uric acid calculi in patients with and without metabolic syndrome (MS).*

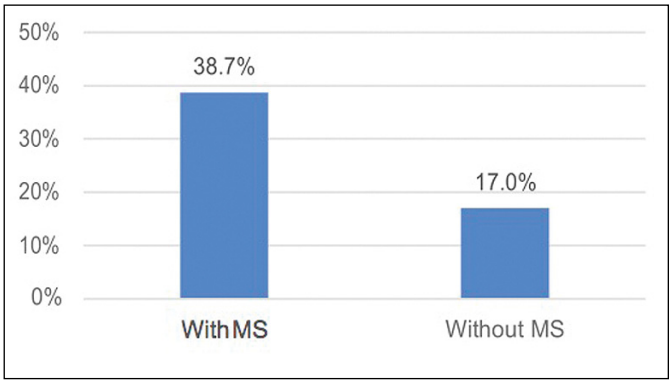

Figure 2. *Proportion of ammonium urate calculi in patients with and without metabolic syndrome (MS).*

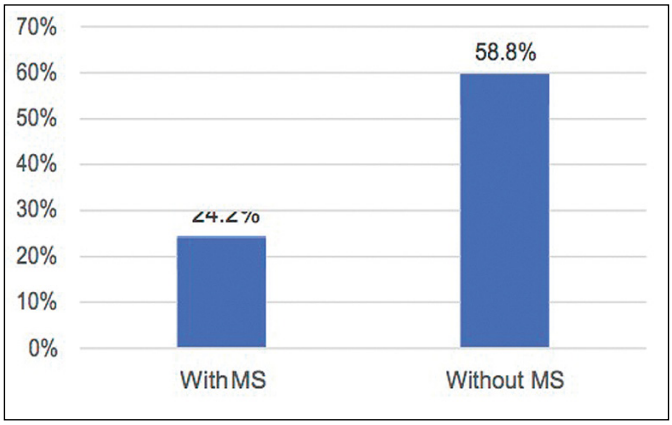

Figure 3. *Proportion of calcium oxalate calculi in patients with and without metabolic syndrome (MS).*

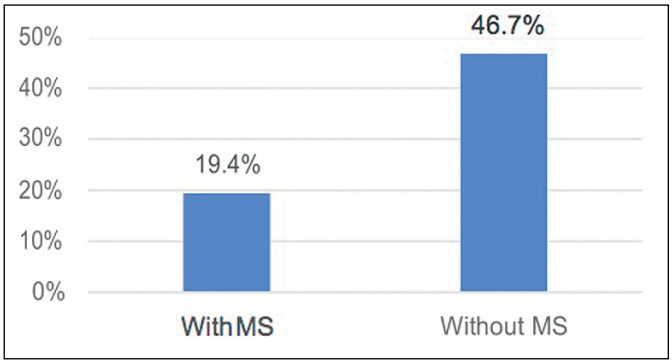

Figure 4. *Proportion of calcium phosphate calculi in patients with and without metabolic syndrome (MS).*

Within the components of the metabolic syndrome, one of the most important factors related to urolithiasis is insulin resistance [2]. Thus, it can be argued that the insulin resistance may be a pathogenic mechanism. The pathophysiological basis for this association has not been yet completely understood. Factors that promote insulin resistance, as well as the formation of calculi in the urine, environmental factors (diet, oxidative stress, inflammation and molecular changes with impact on the transport of some metabolites in the urine) may justify this association. One of the supposed physiological mechanism for this difference is the urine acidification because of insulin resistance leading to decrease of uric acid solubility [4].

If the pathophysiological mechanisms underlying MS increase the risk of calculi formation, MS should be considered as a risk factor for the development of lithiasis. The treatment of metabolic disorders should be included in the prevention of recurrence of urinary lithiasis [7]. Insulin resistance appears to be a predisposing factor and a potential target for intervention to reduce the risk of urinary calculi formation in high-risk patients or to improve clinical outcomes in patients already suffering from lithiasis [6]. The identification of MS appears as a key step that allows, through an appropriate approach, the decrease of other cardiovascular risk factors as well as the prevention of the recurrence of the lithiasis [9]. Lifestyle modification is the most potent method for preventing the formation urinary calculi in patients with MS, especially in obese patients. Notably, the impact of weight loss is very significant that it markedly improveed all aspects of MS. Increasing physical activity and lowering caloric intake will improve MS abnormalities, even in the absence of weight loss. Such changes may not only aid in the prevention of uric acid and ammonium urate stones, but also in the prevention and treatment of obesity, hypertension, coronary artery disease, as well as MS itself [3]. Thus, urolithiasis should be considered as a multifactorial systemic disease requiring a multidisciplinary approach and adequate prevention measures [4].

CONCLUSIONS

In conclusion, we can state that there is a statistically significant relation between metabolic syn-

drome and uric acid and ammonium urate calculi. Metabolic syndrome may be considered a risk factor for urinary stones and the diagnosis and treatment of this syndrome must be considered for urolithiasis prevention. Further studies are needed to gauge a better understanding of physiological mechanisms underlying this relationship to improve our strategy in the prevention of urinary lithiasis.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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