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

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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...
that MS is associated with more severe disease ex-
clusion, clinical and experimental studies indicate
- In addition to the increased risk of developing uro-
lithogenic potential [4].
- percentage of body fat than men that can influence the
women compared to men. Women have a higher per-
disproportionate increase of obese and overweight
difference is declining, which can be explained by the
- 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 per-
centage of body fat than men that can influence the
lithogenic potential [4].
- In addition to the increased risk of developing uro-
lithiasis, clinical and experimental studies indicate that
MS is associated with more severe disease ex-
pression compared to individuals who have uro-
lithiasis 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 com-
position 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 Spectrometer®)
and statistical analysis was performed using SPSS
software 20.0.

RESULTS

Three hundred and two analyzes of urinary calcu-
li 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 sug-
gested 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 hyper-
uricosuria as the most common metabolic abnor-
malities in the urine of obese urinary stone formers
[10]. Taylor et al. also noted that urinary supersat-
uration of uric acid increased with body mass index
(BMI) [11].
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 improved 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-
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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