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# Diabetes Mellitus Might Not Be Associated with Any Stone Component in a Local District

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**Keywords**

Diabetes mellitus · Urolithiasis · Stone components

**Abstract**

***Background:*** Type II diabetes mellitus (DM) is a risk factor for urinary stones, but the pathogenesis remains unclear. The aim of our study was to present the distribution of stone components between DM and no DM group from a local stone center in China and to help the prevention department in decision-making. ***Methods:*** We reviewed the records of patients with upper urinary stones attending our hospital from January 2015 to September 2018. The patients with complete information were divided into 2 groups: type II DM group (DM group) and without DM group (no DM group). The distribution of stone components was analyzed. ***Results:*** Two hundred twenty-two patients were complicated with DM, whereas 1,894 (89%) were not. Significant difference was found in the distribution of hypertension and BMI ($p = 0$, $p = 0$, respectively). Distribution of sex, age, and stone components did not differ between the 2 groups. By the binary logistic analysis, increasing age and sex seemed to be the main risk factors influencing the stone components. Only the calcium stone seemed to be free of the impact from age and sex. Occurrence of hypertension is a single risk factor for calcium stone from our analysis. Presence of diabetes and increasing BMI was not found to be significantly associated with the risk for any stone component. ***Conclusions:*** In a local district, DM might not be the main factor associated with an increased risk for uric acid stone formation or any stone component. We should also consider the local characteristics of the stone distribution.



## Introduction

Urolithiasis is a common and painful urologic problem all over the world. Unfortunately, the etiology still remains unknown for this disease. Due to this, the identification of risk factor is an important way to reduce the prevalence. The invention of stone composition analysis advanced the identification and provided an insight to the forming of the stones. Based on the composition of stone, controlling the different risk factors identified for specific stone component can reduce the occurrence of the stone or at least decrease the volume for complex stones.

Some studies reported that type II diabetes mellitus (DM) is a risk factor for urinary stones [1, 2]. The main difference for stone composition is in the distribution of uric acid stones [3]. In the meantime, Hartman et al. [4] found that DM is a risk factor for uric acid stone from the

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**Table 1.** Characteristics of stone formers both with and without diabetes. Dahllite was grouped into Dah stone. Ammonium magnesium phosphate hexahydrate was grouped into AMPH stone

| | DM | No DM | *p* value |
|---|---|---|---|
| Total number | 222 | 1,894 | |
| Hypertension | 123 | 378 | 0 |
| Sex (male/female) | 155/67 | 1,260/634 | 0.362 |
| BMI | 24.988±3.2554 | 24.076±3.2147 | 0 |
| Age, years | 49.730±12.8841 | 49.497±13.1761 | 0.738 |
| Pure UA stones | 8 | 62 | 0.795 |
| UA stones (mixed stone included) | 20 | 119 | 0.121 |
| CA stones | 211 | 1,790 | 0.716 |
| Dah stones | 128 | 1,059 | 0.616 |
| AMPH stones | 18 | 123 | 0.361 |

DM, diabetes mellitus.

**Table 2.** Logistic regression analysis: DM status, hypertension status, BMI, age, and gender was included in the regression. The significant risk factors were illustrated

| Stone components | Risk factors | *p* value | EXP *(B)* |
|---|---|---|---|
| Pure UA stone | Age | 0.002 | 0.971 |
| UA stone (mixed stone included) | Age | 0 | 0.974 |
| CA stone | Hypertension | 0.01 | 0.458 |
| Dahllite | Age | 0 | 1.025 |
| | Sex | 0 | 0.654 |
| Ammonium magnesium phosphate hexahydrate | Age | 0.007 | 1.018 |
| | Sex | 0 | 2.392 |

DM, diabetes mellitus.

analysis of 24-h urine composition. These findings hint us that the patients with DM should have a higher occurrence rate of uric acid stone than the patients without. In so, more focus may be put to the DM population in the prevention of uric acid stone. However, in our clinical practice, we found that there is no difference in the distribution of stone composition between the 2 groups of patients. Therefore, here we report the local distribution of stone composition in our stone center, in order to help the prevention department in the decision-making.

## Materials and Methods

The records of patients with upper urinary stones attending The first Affiliated Hospital of Chongqing Medical University, China, from January 2015 to September 2018 were reviewed. Patients with a complete basic characteristic, confirmed diagnosis of stone disease, and full stone composition record were divided into 2 categories: diabetes mellitus group (DM group) and without DM group (no DM group). The patients who were suspicious of or diagnosed as malignant cancer and tuberculosis were excluded from the analyses because the 2 diseases consume the body leading bias for BMI. Bladder or urethral stones were not included in this study too.

All stones were extracted from patients by spontaneous passage or surgical treatments including open surgery, percutaneous nephrolithotomy and retrograde intrarenal surgery. The extracted stone or stone fragments were analyzed to figure out the components. All the samples in this study were analyzed by LIIR-20 automatic infrared spectroscopic analysis system of Tianjin Lanmod Scientific Instrument Co., Ltd. Any component of the stone was noted and classified in our study. Calcium oxalate mono- and dehydrate were grouped into Ca stones. Anhydrous and dihydrate forms of uric acid stone were grouped into UA stones. Dahllite was grouped into Dah stone. Ammonium magnesium phosphate hexahydrate was grouped into AMPH stone. Uricite stone, brushite stone, calcite stone, ammonium urate stone, and sodium urate stone were not calculated because of the low incidence.

### Statistical Analysis

Continuous variables with normal distribution and without normal distribution were performed with Student's *t* test or Mann-Whitney *U* test, respectively. Categorical variables were performed with the $\chi^2$ test or Fisher's exact test. Potential factors associated with any stone component, including BMI (kg/m$^2$), age, sex, and presence of hypertension, were analyzed by logistic regression analysis. A $p$ value of <0.05 was considered statistically significant. All statistical analysis were done using SPSS software version 22.

## Results

In total, 222 patients were complicated with DM (11.5%), whereas 1,894 (89.5%) were not. Table 1 compares the characteristics of patients in DM and no DM group. All the DM was type 2 DM. Distribution of sex and age did not differ between the 2 groups ($p$ = 0.362, $p$ = 0.738, respectively). Distribution of hypertension and BMI was uneven in 2 groups ($p$ = 0, $p$ = 0, respectively). There is also no significant difference in the distribution of stone components between the 2 groups.

Due to the uneven distribution of the basic characteristics, logistic regression analysis was used to determine the contribution of DM, hypertension, BMI, gender, age, and sex on the risk for different stone component formation (Table 2). By the binary logistic analysis, increasing age and sex seemed to be the main risk factors influencing the stone components. Only the Ca stone seemed to be free of the impact from age and sex. Occurrence of hypertension is a single risk factor for Ca stone from our analysis. Presence of DM and increasing BMI was not found to be significantly associated with the risk for any stone component.

## Discussion

Type II DM is a strong risk factor for urolithiasis, which has been proven by many studies and even a meta-analysis [5]. The patho-physiologic mechanism remains unclear. Most studies showing strong connection between DM and stone composition concentrated on the 24-h urine composition [4, 6]. The results of 24-h urine between DM and no DM group shows that stone patients with type II DM excrete significantly more urinary oxalate and uric acid, and their urine pH is lower than those with no DM. The patho-physiologic mechanism was deemed by some authors as the presence of insulin resistance, which has been shown to lead to decreased renal tubular generation of ammonia and increased sodium reabsorption resulting in more acidic urine [7].

These theories make us believe that normally the DM group should have more uric acid stones in a large series of study, which has been testified by some studies [3, 8]. However, these studies were mainly focusing on the relationship between DM and uric acid stones and having limitations in the classification of stone group and analysis. Nerli et al. [8] analyzed retrospectively a series of 280 calculi from 30 patients with type 2 diabetes and 250 with no diabetes. Almost all their stones were mixed stones and only the dominant stones were calculated. This introduced a big bias because uric acid stone might occur as a second dominant one, and it should be counted in the uric acid group. Dahllite and ammonium magnesium phosphate hexahydrate also account for a big part of stones [9]. However, these stones were excluded from their study. The significant difference in the basic characteristics such as BMI, age, etc. were not analyzed, either. Daudon et al. [3] analyzed the largest volume of stones with 2,464 calculi. Dahllite and ammonium magnesium phosphate hexahydrate were also excluded from their study. Only the main components of the stone sample were calculated. Since the stone composition variable is a category 1, the binary logistic regression should be more suitable than their stepwise regression. The identified risk factor, age, was ignored in their study.

Due to these reasons, our study with the same large volume of sample indicates more clinical significance. It showed there was no difference between the DM and no DM group, no matter that it was for pure uric stones or the uric stones with mixed stones accounted. Because the basic characteristics were different, we used a binary logistic regression which showed age is the only risk factor among the risk factors we assumed. In the meantime, age is also a risk factor for dahllite and ammonium magnesium phosphate hexahydrate. Woman stood for a greater chance for these 2 components. Only Ca stones were free of the influence of age and gender, but hypertension increased the risk of Ca stone. These results suggest that there may be an unknown pathogenesis for the formation of different stone types, and there is no significant connection between DM and the formation of stone components. This idea is partially supported by Bobulescu et al. [10] who found that a blunted renal ammonium excretory response to dietary acid loads may contribute to the pathogenesis of idiopathic uric acid nephrolithiasis, but not patients with DM or normal volunteers of similar body size. Some other authors also express their doubts on a key role of DM or BMI for different stone components formation using different methods [11, 12]. However, the findings of their and our studies are not robust. The frequency of pure uric acid was very low in both groups (0.4% in DM and 0.03% in no DM), which may correlate to the fact that mean BMI in both groups was close to the normal weight range (18.5–24.9); thus, incidence of metabolic syndrome in this population was probably low. This may be the real cause to the lack of correlation between DM and uric acid stone formation in our study. Unfortunately, we are unable to analysis these influences due to the lack of data. Anyway, in different a district, DM might not suggest a higher occurrence of any stone components. The general prevention measure might be more effective in reducing the stones, which is something the prevention department should take into consideration.

There are limitations in our study. We cannot provide more information from these data limited by the cross-sectional nature of our study. Insufficient patient data limit our analysis of the relationship between metabolic syndrome and stone components. Furthermore, only the stone sample was analyzed for stone composition, which is not representative for the whole information of the stones in patients. Detailed data on stone burden, medications, dietary, urinary pH, 24-h urine composition, and comorbidities except for DM and hypertension was not available in our database. These factors were important in discussing this question.

## Conclusion

Our study suggests that DM might not be significantly associated with an increased risk for UA stone formation or any stone component in a local stone center. The local stone characteristics are important.

## Statement of Ethics

Written informed consent for this study was unavailable because the data of this manuscript were from database and not related to the patient's privacy. This study was conducted in accordance with the Declaration of Helsinki, and the use of data was only for research purpose. The Institutional Ethics Committee of the First Affiliated Hospital of Chongqing Medical University approved this study. The IRB ID is 2018-003.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.


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## Author Contributions

Gang Chen was the senior arbiter and reviewed and revised the paper. Han Chen collected and analyzed the data and wrote drafts of the paper. Yang Pan collected and analyzed the data. Chaoyu Xiong, Ziyi Yang, Yunxiao Zhu, and Hualin Chen provided access to the electrical library and the analysis tool.

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