Type Two Diabetes Mellitus and the risk of uric acid stone formation

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ABSTRACT

Aim: Diabetes may be a metabolic disorder which is related to the increase risk of uric acid calculi as urine pH plays a vital role in uric acid solubility in urine; whereas many studies have shown that diabetic patients had additional uric acid excretion and stone formation, few studies investigated the variations of urine composition between both diabetic and non-diabetic non-stone formers.
Consequently, this study aims to analyze the variations between diabetic and non-diabetic patients who aren't stone formers.
Materials AND Methods: A (sample of 420 patients) who were seen and examined in Prince Hussein urology clinics between (June of 2015 and August of 2018) were recruited during this retrospective study. These patients were divided into two main groups: group-1 which comprised 210 diabetics' patients, and group-2 which comprised 210 not diabetic patients; the 24-h urine collection profiles of each team were compared.
Results: Group-1 Diabetic patients have considerably shown higher 24-h urine volumes, and urine ammonium excretion, lower urinary citrate, calcium, magnesium, and bicarbonate excretions; moreover, diabetic patients have lower 24-hour urine pH, higher net acid excretion and better uric acid excretion quantity compared to group-2 respectively.
Conclusion: Diabetic patients have presented additional daily urine volumes, higher net acid excretion, lower urine pH and more uric acid excretion. All these factors combined together would result in making the urine more acidic which is considered as a precondition for uric acid stone formation. Therefore, a thorough comprehension of epidemiology and Pathophysiology of uric acid stone formation is a crucial part of stone prevention in type-2 diabetes mellitus.
Keywords: type-2 diabetes, uric acid, renal stones, urine PH.
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Introduction

Urine PH plays an important role in the urinary tract stone formation. The diurnal urine PH variation which was discovered by Henry Bence Jones in normal individuals has been thought-about as a vital step in the study of the urinary chemistry [(1)]. Thus, relating to the urine profile acidification. Although urine PH which is below 5.5 is a means of protection against the calcium stone formation, it poses a risk of uric acid stone formation [(2)].
There are many risk factors that inflict metabolic disorders, together with low urinary PH< 5.5; different factors were expressed during a complex pathological term that was referred to as a metabolic syndrome (obesity, dyslipidemia together with high triglycerides or low levels of high-density lipoproteins (HDL), hypertension and fasting hyperglycemia).

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The presence of three of these risk factors is diagnostic of this syndrome [3]. Hence and because of that, obesity and type-2 diabetes are changing into constant epidemic issues worldwide [4]as well as the prevalence of uric acid stones raised in aparticularltype-2 diabetes over nondiabetic[5], a study of 24-hour urine collection was conducted in order to assess the chance of uric acid stones formation in these patients is changing into anessentialpart of the investigation analysis of those patients [6]. Additionally, to lower urinary PH which is a risk factor for uric acid nephrolithiasis there are other predisposing factors like: a low urinary volume and hyperuricosuria which may be inspected within the 24-hour urine collection. Additionally,Several studies prompt that insulin resistance is the main pathological feature in type-2 diabetes that inflict these urinary and metabolic disorders with uric acid stone formation [7, 8].

Additionally, vital progress has been attained within the pathologic process of uric acid and calcium stones that check with the connection between them ,and thus affected the event of treatment of this sort of stones [9]. Many studies had documented the role of hyperuricosuria within the development of the monosodium urate which would lead to calcium stones [10].

Because of the continual increase in number within the prevalence of diabetes patients [11], and their square measure several studies reported that diabetic patients eject through urinating additional uric acid , especially in patients with a history of renal stones; few studies investigated the variations of urine composition between diabetic and non-diabetic patients in non-stone-forming people;in our study,we are going to concentrate on urine composition of diabetic patients in non-stone formers.

Our original hypotheses was that there are no mean variations of uric acid excretion with relation to diabetic and non-diabetic patients in 24-hour urine composition, but in the event our results did not support this view.

MATERIALS AND METHODS

A (sample of 420 patients)were registered during this retrospective study which was created in our Prince Hussein Bin Abdullah the Urology center of the Royal Medical Services. These patients were seen and examined within the urology clinics between (June of 2015 and August of 2018). The ages of those participants were ranging between (21 and 66 years); our analysis assistant divided these patients into two groups: two main groups: group-1 which comprised 210 type II diabetics patients, and group-2 which comprised 210 not diabetics patients who were diagnosed to have illness free by the medical history, normal fasting vs. postrandial glucose levels and HBA1C when available in the medical records of those patients.

This study has enclosed and separated the patients who have (inclusion criteria): type Π diabetes > 1 year duration , diabetics with retinopathy or neuropathy, benign prostatic hypertrophy or prostate carcinoma, urinary tract infections or tumors, renal pathologies apart from stones like (tumors, cysts, pelvic ureteric obstruction and congenital abnormalities), urine bladder pathologies like (tumors, infections either acute or chronic and interstitial cystitis), testicular pathologies like (varicocele, hydrocele and tumors), normal kidney functions tests, normal coagulopathy profile and hypermetabolic syndrome risk factors (HTN, Hyperlipidemia and obesity); taking into consideration that the exclusion criteria were: Whereas the exclusion criteria were: ages less than twenty-one years, diabetics with nephropathy, patients with chronic diarrhea, liver disease, hyperparathyroidism patients, pregnancy, stone formers, patients with a history of recent hematuria, urine bladder stone patients, patients on dialysis, patients with neurogenic bladder and patients with a history of gouty diathesis.

The data of 24- hours collected urine composition analysis (2-3 samples for every patient) and different details concerning these patients were collected from our computerized system of patients' medical records that were our dependent resources of this study. Blood chemistries: HBA1C, FBS, KFT and Serum Uric Acid for all patients were checked on our data system. Diagnosis of diabetes mellitus was created by self-report within the history and current medication use, taking into consideration that the unwellness free was confirmed by fasting blood sugar samples below a hundred and ten mg\dl.
All patients were given antibiotics either oral or intravenous to avoid errors in case that there have been obvious or hidden infections before the analysis of the urine chemistry.
Most of the information was provided within the style of a tabulated comparative statistics; the numbers and also the percentages were generated from the categorical data by using SPSS software version 24; moreover, an independent t-test was used to compare mean urinary values; the point biserial correlation was used to correlate diabetic statues with the uric acid excretion value. P-value < 0.05 was considered statistically significant.
An ethical committee approval was granted by our royal medical services institution for publication of this study.

RESULTS

After the division of the concerned (420) participants within the previous mentioned two teams (type ΙΙ diabetics and non-diabetics), we have a tendency to note that the ages of group-1 were between (34 and sixty-six years);however,that the ages of group-2 were between (21 and fifty-seven years) with insignificant P-value. In group-1 the number of males was over females as well as in groups-2. Additionally, the number of males was higher than females with insignificant P-value;we have atendency to use ***(Table I)*** to match between the continual variables between both teams.

Table I: a comparison between the continuous style of each team.

Variables	Group1(n=210)	Group2(n=210)	P value
Ages (%)	34-66(50%)	21-57(50%)	0.68
Males (number\ %)	(143\68%)	(129\61.4%)	0.24
Females (number\ %)	(67\32%)	(81\38.6%)	0.43

According to the 24-hrs urine collection, analytic information, the comparison between each team was created relating to 24-hrs urine volumes, urine PH, urinary calcium and magnesium excretion, urine net acid excretion, urine ammonium excretion, urinary citrate excretion, urine bicarbonate excretion, and uric acid excretion. Significant P-values were marked between both groups in relevance to the previously mentioned variables in ***(Table II).***

Table II: a comparison between both groups regarding 24-hours urine collection chemistry.

Variables	Group1	Group2	P value
24-hrs volumes (Liter/day) (mean value ± SD®)	(2.7±1.8)	(2.3±1.5)	0.009

Urine PH (mean value ± SD)	(5.45±0.42)	(6.23±0.38)	0.029
Urine calcium + magnesium excretion (mean value ± SD) (mg\day)	(126±22 + 96±45)	(173±46 + 211±33)	0.034
Urine net acid excretion(mEq\dl) (mean value ± SD)	(57±12)	(38±9)	0.026
Urine uric acid excretion (mean value ± SD) (mg\dl)	(623±257)	(511±134)	0.012
Urine citrate excretion (mEq\day) (mean value ± SD)	(7.9±1.8)	(11±3)	0.005
Urine Ammonium excretion (mEq\day) (mean value ± SD)	(38±16)	(30±12)	0.017
Urine bicarbonate excretion (mEq/day) (mean value ± SD)	(2.3±2.5)	(4.6±3.8)	0.042

SD®: standard deviation.

The Independent T-test during this study has provided us with significant results concerning the comparison between diabetic and nondiabetic patients regarding the 24- hours of urine collection chemistry. We have noted that diabetic patients had significantly higher 24-h urine volumes, and ammonium excretions and lower urinary (citrate, calcium, magnesium and bicarbonate) excretions than non-diabetic patients (all $P < 0.05$). Patients with type-2 diabetes have incontestably shown a considerably lower 24-hour urine pH (5.45 vs. 6.23, $P < 0.05$) and better net acid excretion (57 vs.38 (mEq/d)) ($P < 0.05$) compared to non-diabetic group, respectively.

Patients with type- 2 diabetes has exhibited a significantly higher uric acid excretion compared to non-diabetic cluster (623 mg\dl vs. 511 mg\dl. P=0.012), respectively.

The point biserial correlation coefficient has disclosed that there was a moderate correlation between diabetic status and the value of uric acid excretion. ($P< 0.05$).

DISCUSSION

The cause of uric acid stones are well documented. Biochemical studies on affected type2 diabetics have shown that they have several of the abnormalities. Our study has shown that even type2 diabetics who have never formed uric acid stones have some of the same abnormalities in the urine.

Naim Maalouf et al. reported that in type-2 diabetics, the elevation of net acid excretion (NAE) and the decrease the ammonium buffers in the urine will cause low urinary PH [(12)]. These findings support our results that incline to urolithiasis primarily uric acid stones. In contrast of our study in relation to ammonia, Bernhard Hess detectedina review article that insulin resistance causes low ammonium excretion , consequently a low urinary PH which leads to uric acid stone formation [(13)].

In 2007,there was an article concerning uric acid nephrolithiasis which confirmed that insulin resistance in type-2 diabetes mellitus is one of the contributing factors that aids to uric acid stones due to the following causative factors: hyperuricosuria, low urinary volume and low urinary PH [(14)].

Regarding the mean,daily urine volumes and urine PH, N. Meydan et al. reported that the DMT2 is a risk factor for urinary stone disease [(15)]. These findings were in the same side of our study.

The relationship between the acidic urine and the insulin resistance is inversely significant. This conclusion was documented by Naim Maalouf in 2007 by an original article which was published in the USA, Texas [16].

Despite a normouricoseuria state, the risk of uric acid precipitation could be increased in type-2 diabetes mellitus patients because of the low urinary ammonium and PH. Nicola Abate et al. reported that in 2004 [17].

Marry-Ann Cameron et al. found that the rise of urine ammonium in normal individuals and type- 2 diabetic patient groups was similar;nevertheless, in stone formers group,no changes were noted in the urine ammonium excretion. Moreover, the main risk factor for uric acid stone formation in type-2 diabetics is low urinary PH despite other abnormalities in urine excretion like calcium, citrate, ammonium and magnesium excretions [18].

After the evaluation of predisposing factors of uric acid stone formation, it was found that treatment relies on the alkalinisation of urine PH to > 6.5 by potassium citrate to boost the solubility of uric acid and perhaps there's a good thing about the use of " allopurinol" which inhibits uric acid formationand is used to manage the hyperuricosuria side by side the medical and surgical treatment of the stones. Therefore, in-depth comprehension of the epidemiology as well as the Pathophysiology of uric acid stones is essential for the treatment of these stones [19].

CONCLUSION

Type-2 diabetes mellitus has significant influences on urine parameters which may be considered as a precondition to nephrolithiasis mainly uric acid stones. These influences represent high urinary volumes, low urinary PH, low citrate excrection, high net acid and uric acid excretion in the urine. Therefore,the urine acidity will increase,and thus the solubility of uric acid will be affected which causes stone formation. Therefore, the management of uric acid stones contingent thorough comprehension of Pathophysiology of those stones is crucial. So, the patients who are at risk of uric acid stones formation should be followed up to see if they do form stones.

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