Influence of Obesity and Diabetes Mellitus on Serum and Urinary Parameters in Patients with Urolithiasis

Badr Alharbi[1] and Abdulrahman F. Alruwaily[2]

[1]College of Medicine, Qassim University, Buraidah, Saudi Arabia
[2]Division of Urology, Department of Surgrey, College of Medicine, Al-Imam Muhammad Ibn Saud Islamic University (IMSIU), Riyadh, Saudi Arabia
badralharbi@qumed.edu.sa

Abstract: Purpose: The goal of this study was to study the effect of obesity and diabetes mellitus on serum and urinary biochemical variables in patients with urinary stone disease. **Patients and methods:** A retrospective chart review of patients' medical history, serum chemistry, 24-hours urinary metabolites and body mass index were analyzed for 181 consecutive patients diagnosed with urinary stone disease. The associations between obesity defined by BMI, diabetes mellitus, serum and urinary parameters were investigated. **Results:** A total of 181 patients were included in this study and obese women comprise the majority 123 (68%) of this cohort of patients. High serum uric acid 393.7 umol/l (±11.2) was observed in the studied population. Low urinary pH, citrate and high oxalate excretion were the main significant findings found on the 24-hour urine analysis. **Conclusion:** Obesity and diabetes mellitus are major health issues in most parts of the world. Both serum and urinary biochemical derangements were found to inversely increase the risk of urinary stone formation.
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1. Introduction

Urolithiasis is a common disease and cause of morbidity with higher stone recurrence rate. The incidence of urinary stone disease increasing globally with estimated incidence of 20% and life time prevalence of 28% in Saudi Arabia. (1) Obesity, diabetes mellitus, hypertension and metabolic syndrome have been proposed risk factors for kidney stone formation in both women and men. (2) In literature, research studies have shown a relationship between obesity and altered levels of serum and urine compositions. In obese stone former individuals, urinary levels of oxalate and uric acid excretion were higher compared to non-obese patients. Urinary levels of stone inhibitors such as pyrophosphate, magnesium and citrate found to be lower in obese patients and thus increase their risk of stone formation. (3)Low urinary pH is a crucial factor and promoter for the formation of most common types of stones, such as calcium oxalate, calcium phosphate and uric acid stones. (4) Acidic urine has been observed in individuals with obesity and diabetes mellitus. The exact mechanism is not fully understood, insulin resistant decreases elimination of renal ammonia from the body and cause a imbalance of the hydrogen ion buffering system. (5) additionally, the insulin bioactivity in the proximal renal tubules decreases with insulin resistant and alter metabolism of ammonium and eventually urinary pH changes. (6)The purpose of the current study was to examine the relationship between obesity, diabetes mellitus and urinary stone disease.

2. Material and Methods

Following institutional review board approval, a retrospective review of a database of patients who were seen in urology clinic between September 2017 to January 2019. The inclusion criteria for this study include adult obese men and women who are diabetic and have past or current history of urinary stone disease. Obesity was defined by calculation of body mass index (BMI) as weight in kilograms divided by the square of height in meters (kg/m2) measured at the time of clinic visit and patients with BMI of ≥ 30 considered obese and included. Diabetes defined by fasting blood sugar of ≥ 7.0 mmol/l (126 mg/dl) on at least two reading or glycated hemoglobin (HbA_{1C}) ≥ 48 mmol/mol (≥ 6.5 DCCT %). (7) Exclusion criteria were patients without available BMI readings, 24-hour urine collections, metabolic workup, impaired renal function (serum creatinine greater than 1.5 mg/dl), or patient who are on medication that might influence the result of metabolic workup like taking thiazide diuretics or potassium citrate for alkalinization of urine. Thus, a total of 181 consecutive obese diabetic stone formers with complete metabolic assessment were included in this study. Statistical analysis was performed using statistical software package SPSS version 17.0 (SPSS Inc, Chicago, IL). Data are expressed as mean± standard deviation (SD). Inter-group comparisons were performed using Student's t-test. A probability

value of $P<0.05$ was considered statistically significant.

3. Results

A total of 181 patients met the inclusion criteria included in this cohort and their data were analyzed. Among the 181 patients analyzed,58 (32%) were men and the rest were women 123 (68%). The mean age for the whole cohort of patients was 50.5 years (±10.3) and mean BMI was 49.8 kg/m2 (±9.8). The mean age of the 82 women analyzed was 49 years (±10.5) and mean BMI was 49.4 kg/m2 (±9.2). The mean age of the 39 men analyzed was 53.6 years (±9.4) and mean BMI was 50.6 kg/m2 (±11.2) (table 1). Metabolic work results revealed mean serum creatinine of 72.8 mg/d (±18.3), mean uric acid level 393.7 umol/l (±11.2), mean serum calcium of 2.33 mg/d (±0.2) and the mean serum parathyroid hormone was 6.17 ng/l (±4.4). The result of the 24-hour urine analysis for the analyzed cohort showed mean urine volume of 1901 mls (±810), urine pH of 4.9 (±0.6), uric acid 834 mg/l (±18.8), urinary sodium excretion of 193 mEq/L (±87), urinary phosphate 30.4 mg/L (±87), urinary oxalate of 431 mg/L (±280), urinary citrate 267 mg/L (±3.4) and urinary calcium 2.74 mg/d (±2.8) (table 2).

Table 1. Baseline characteristics and demographics of the analyzed subjects

	Males	Females	*P* Value
Number of Patients (Total = 181)	58 (32%)	123 (68%)	--
Age (mean in years ± SD)	53.6 years (±9.4)	49 years (±10.5)	0.62
BMI (mean ± SD)	50.6 kg/m2 (±11.2)	49.4 kg/m2 (±9.2)	0.39

Table 2. Mean serum and 24-hour urine parameters

Parameters	Mean serum parameters (± SD)	Mean 24-hour urine parameters (± SD)
Creatinine	72.8 mg/d (±18.3)	--
Uric acid	393.7 umol/l (±11.2)	834 mg/l (±18.8)
Calcium	2.33 mg/d (±0.2)	2.74 mg/d (±2.8)
Parathyroid hormone	6.17 ng/l (±4.4)	--
Citrate	--	267 mg/L (±3.4)
Oxalate	--	431 mg/L (±280)
Phosphate	--	30.4 mg/L (±87)
Sodium	--	193 mEq/L (±87)
pH	--	4.9 (±0.6)
Volume	--	1901 mls (±810)

4. Discussions

Obesity and diabetes mellitus were shown in this study to be associated with higher serum level of uric acid and increased urine excretion of stone promoters such as hyperuricosuria. Low urinary pH and hypocitraturia are among the other significant factors found in the 24-hour urine analysis of this cohort of patients. There were no statistically significant differences found in the demographic data as well as serum levels of creatinine, calcium, PTH and urinary levels of oxalate, phosphate, sodium and voided volume.

It has been estimated that more that one in five persons are overweight or obese worldwide. [8] Obesity usually accompanied by other non-communicable diseases, like hypertension, type 2 diabetes mellitus and cardiovascular diseases. Developing countries become noticeably westernized with time in many aspects such as sedentary lifestyle, eating unhealthy food and ultimately developing obesity and increased risk of type 2 diabetes mellitus. Because of its high prevalence rates, obesity has become one of the major health problem in Saudi Arabia in the present time. Several epidemiological reports found obesity is more prevalent in women than men and this finding was reinforced by this study. The incidence of diabetes mellitus in Saudi Arabia is among the highest globally. According to The World Health Organization (WHO), the incidence of diabetes mellitus in Saudi Arabia is increasing and currently has the second highest incidence in the Middle East and the seventh worldwide. [9] Both obesity and diabetes mellitus are associated with increased risks of developing chronic medical illnesses and urinary stone diseases.

Daudon et al. reported a significant association between type 2 diabetes mellitus and uric acid stones formation. Obesity was found to be an additional risk factor for hyperuricemia, hyperuricosuria and thus increasing the overall risk of uric acid stone

nephrolithiasis. [10,11] Several studies have suggested insulin resistant as one of the main influencing and predisposing factor for uric acid stone formation in diabetic and obese patients and considered an important objective to address when managing patients with nephrolithiasis. [12] Theories have postulated the importance and affect of the insulin on the metabolism of renal ammonia. [13] The net result of insulin resistance will be decrease in urinary ammonia excretion and lower urinary pH. [14]Diet rich in purines like eating animal proteins lower urinary pH and the reason behind that is the oxidation of sulfur to sulfate. [15] High animal protein diet is common traditional food in Saudi Arabia which add more risks to obesity and the high incidence of diabetes mellitus for developing uric acid nephrolithiasis.

Urolithiasis prevention typically involve increasing the urinary volume output and urinary citrate levels excretion. Further reduction in urinary excretion of oxalate, uric acid and calcium will help as well. Stone formation and risk of recurrence can be diminished with modification and manipulation of known dietary promoters of stones formation. [16] Weight reduction, avoidance of sedentary life styles, balanced diet and adequate water and fluid intake are simple and effective measures to decrease the risk of nephrolithiasis. For overweight and obese patients, suitable dietary modification, weight reduction and medical treatment may correct the derangements in serum and urinary metabolites thus decreasing the risk of urinary stone formation. [17]

5. Conclusion

The consequences of obesity and diabetes mellitus are important to be taken in consideration when managing patients with nephrolithiasis. Treating health care providers should consider counselling those patients with nephrolithiasis about the importance of general advices which include increased fluid volume intake, low sodium diet, low intake of animal protein and to consider weight reduction and decrease the risks of developing diabetes mellitus.

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Conflict of interest statement

Author declare no conflict of interest.

Corresponding author:
Badr Alharbi, MD
Ass. Prof. of Surgery, Consultant of Urology
MIS/Andrology and Infertility
Head, department of Surgery
College of Medicine, Qassim University
P.O. Box 6633, Buraidah 51452, Saudi Arabia
Tel: +966163800050 ext. 2481
Mobile: +966555181799
badralharbi@qumed.edu.sa

References

1. Romello A, Vitale C, Marangella M. Epidemiology of nephrolithiasis. J Nephrol 2000; 13:45- 50.
2. Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. JAMA. 2005;293:455-462.
3. Negri AL, Spivacow FR, Del Valle EE, et al. Role of overweight and obesity on the urinary excretion of promoters and inhibitors of stone formation in stone formers. Urol Res. 2008;36:303-307.
4. Alelign T, Petros B. Kidney Stone Disease: An Update on Current Concepts. Adv Urol. 2018 Feb 4;2018:3068365. doi: 10.1155/2018/3068365.
5. Weiner ID, Verlander JW. Renal ammonia metabolism and transport. Compr Physiol. 2013;3(1):201-20. doi: 10.1002/cphy.c120010.
6. Wilcox G. Insulin and insulin resistance. ClinBiochem Rev. 2005;26(2):19-39.
7. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation (PDF). *World Health Organization. 2006. p. 21.* ISBN 978-92-4-159493-6.
8. Centers for Disease Control and Prevention. Overweight and obesity. Available at: http://www.cdc.gov/obesity/.
9. Mohamed Abdulaziz Al Dawish, Asirvatham Alwin Robert, Rim Braham, Ayman Abdallah Al Hayek, Abdulghani Al Saeed, Rania Ahmed Ahmed and Fahad Sulaiman Al Sabaan, "Diabetes Mellitus in Saudi Arabia: A Review of the Recent Literature", Current Diabetes Reviews (2016) 12: 359. https://doi.org/10.2174/1573399811666150724095130
10. Wong Y, Cook P, Roderick P, Somani BK. Metabolic Syndrome and Kidney Stone Disease: A Systematic Review of Literature. J Endourol. 2016;30(3):246-53. doi: 10.1089/end.2015.0567.
11. Daudon M, Traxer O, Conort P, Lacour B, Jungers P. Type 2 diabetes increases the risk for uric acid stones. J Am SocNephrol. 2006;17(7):2026-33.
12. Abate N, Chandalia M, Cabo-Chan AV Jr, Moe OW, Sakhaee K. The metabolic syndrome and uric acid nephrolithiasis: novel features of renal manifestation of insulin resistance. Kidney Int. 2004;65(2):386-92.
13. Chobanian Mc, Hammerman Mr: Insulin

stimulates ammoniagenesis in canine renal proximal tubular segments. Am J Physiol 253:F1171–F1177, 1977.
14. Krivosikova Z, Spustova V, Dzurik R: Participation of P-dependent and P-independent glutaminases in rat kidney ammoniagenesis and their modulation by metabolic acidosis, hippurate and insulin. Physiol Res 47:177–183, 1998.
15. Sabry Zi, Shadarevian Sb, Cowan Jw, Campbell Ja: Relationship of dietary intake of sulphur amino-acids to urinary excretion of inorganic sulphate in man. Nature 206:931–933, 1965.
16. Sang-Cheol Lee, Yong-June Kim, Tae-Hwan Kim, Seok-Joong Yun, Nam Kyu Lee and Wun-Jae Kim: Impact of Obesity in Patients With Urolithiasis and its Prognostic Usefulness in Stone Recurrence. J Urol. 2008 Feb;179(2):570-4. Epub 2007 Dec 21.
17. Ekeruo WO, Tan YH, Young MD, Dahm P, Maloney ME, Mathias BJ et al: Metabolic risk factors and the impact of medical therapy on the management of nephrolithiasis in obese patients. J Urol 2004; 172: 159.

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