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Evaluating HbA1c, BMI and Urinary Biochemistry as Risk Factors for Renal Tract Stones (Urolithiasis)

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ABSTRACT

OBJECTIVE: The study aimed to evaluate the role of HbA1c, BMI and urinary parameters as predictors of renal stone formation.

METHODOLOGY: This case-control study analyzed medical records of 300 patients with renal tract stones and 300 control subjects at the Ahmed Medical Complex, Rawalpindi, from January to December 2024. Clinical data included demographics, BMI, HbA1c levels and urinary parameters (pH, citrate, Calcium). Statistical analysis was performed using t-tests, chi-square tests and logistic regression to identify significant predictors.

RESULTS: Patients with urolithiasis had a significantly higher BMI (28.1 ± 3.6 kg/m²) and HbA1c levels (7.2 ± 1.4%) compared to controls ($p<0.001$). Urinary calcium excretion was elevated while citrate levels and urinary pH were lower in patients ($p<0.001$). Logistic regression identified HbA1c ≥6.5% (OR: 2.3, $p<0.001$) and BMI >25 (OR: 1.7, $p=0.002$) as significant predictors. Patients with uric acid stones exhibited higher HbA1c levels than patients with calcium oxalate stones.

CONCLUSION: Metabolic factors, particularly HbA1c and BMI, play a critical role in urolithiasis. Integrating glycemic control and weight management into preventive strategies could reduce the disease burden.

KEYWORDS: Urolithiasis, HbA1c, BMI, Urinary parameters, Renal stones, Lithotripsy, Metabolic factors.

INTRODUCTION

Urolithiasis is highly prevalent in South Asia, attributed to dietary patterns, high temperatures, and metabolic disorders. In Pakistan, the prevalence is estimated to be between 12% and 15%, with calcium oxalate stones being the most commonly observed type.[1] Similarly, India reports a prevalence of 10–12%, where the burden is exacerbated by inadequate hydration and high dietary oxalate intake.[2] In contrast, Europe and the USA have a lower prevalence of 6–9%, likely reflecting differences in healthcare access, climate and lifestyle factors.[3] An intermediate prevalence is observed in China, at 8–10%, where dietary factors and genetic predispositions significantly contribute.[4] Despite these regional variations, metabolic abnormalities such as hyperglycemia are increasingly recognized as global contributors to renal stone formation.

Renal tract stones (urolithiasis) pose a significant morbidity and healthcare costs. Their pathogenesis is multifactorial, involving genetic, dietary and metabolic factors. Among these, metabolic syndrome, particularly insulin resistance and hyperglycemia, has garnered attention for its role in altering urinary biochemistry and promoting lithogenesis. Studies in Europe and the United States have shown that hyperglycemia reduces citrate excretion, a key inhibitor of stone formation.[3] Similarly, research in China [4] and India[2] highlights the role of altered urinary pH and increased calcium excretion in individuals with poor glycemic control. Chronic hyperglycemia alters renal tubular function, promoting crystallization by increasing urinary calcium and oxalate excretion while reducing citrate levels.[3] The rationale for this study lies in the growing recognition of metabolic factors, including hyperglycemia and obesity, as key contributors to urolithiasis. Investigating the role of these factors can enhance the understanding of stone pathogenesis and inform targeted interventions. We conducted this study to evaluate the role of HbA1c, BMI and urinary parameters as predictors of renal stone formation.

METHODOLOGY

This case-control study analyzed the medical records of patients presenting at Ahmed Medical Complex for lithotripsy from January to December 2024. The hospital committee approved the study, and patient confidentiality was maintained through the anonymization of data. Informed consent was waived as this study analyzed the medical records, but all procedures adhered to the Declaration of Helsinki.

The sample size was calculated using the formula: $N = (Z^2 * P * (1-P)) / E^2$, where N represents the required sample size, Z is the Z-score, P is the estimated prevalence of the condition, and E is the desired margin of error. Using an estimated prevalence of 40% of urolithiasis,[5] 25% in controls, a confidence level of 95%, and a margin of error of 5%, the minimum required sample size per Group was 286. To account for potential missing data, 300 participants were included in each Group.

Using a purposive technique, a total of 300 patients with renal tract stones confirmed through imaging were identified as the case group. A total of 300 control subjects were selected from the same clinic during the same study period. The control group consisted of adults of any gender aged 18 years or older who presented to the clinic for reasons unrelated to urological conditions. Exclusion criteria for both groups included individuals with known metabolic disorders, recent urological surgery, pregnancy, lactation, and those on medications affecting Calcium or uric acid metabolism.

Clinical data - including patient demographics, body mass index (BMI), glycated hemoglobin (HbA1c) levels, and stone composition were retrieved and analyzed from hospital medical records. Dietary assessment was based on retrospective extraction of information from clinicians' notes documented in patient charts, where available. These qualitative records included habitual intake patterns of lithogenic dietary components such as oxalate-rich foods (e.g., spinach, tomatoes, chocolate), sodium, animal protein, and fluids (including plain water and carbonated beverages), as recorded by attending clinicians during outpatient visits. Although no validated food frequency questionnaire or 24-hour dietary recall was prospectively administered, the available documentation was used to estimate nutritional exposures relevant to stone formation. For analytical purposes, dietary intake was categorized into broad risk groups (e.g., high vs. low oxalate or sodium intake) based on clinical interpretation recorded in the notes.

For urinary biochemical analysis, documentation confirmed that midstream, clean-catch urine samples had been collected from all patients during outpatient visits using sterile containers, adhering to standard aseptic collection protocols to minimize contamination and ensure specimen integrity. To maintain consistency and obtain optimally concentrated samples, all urine specimens were collected in the early morning (between 7:00 AM and 9:00 AM). Samples were either processed within one hour of collection or stored at 4°C and analyzed within six hours to prevent degradation. Urinalysis included measurement of pH, citrate excretion, urinary Calcium, and uric acid concentrations using standardized automated analyzers and validated colorimetric assays according to hospital laboratory SOPs. Internal and external quality controls were used to ensure the reliability and accuracy of test results. For patients who had undergone lithotripsy or stone extraction, stone composition was evaluated using Fourier-transform infrared (FTIR) spectroscopy, as recorded in the pathology database.

Statistical analysis was performed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation, and categorical variables were expressed as percentages. Group comparisons were made using independent t-tests for continuous variables and chi-square tests for categorical variables. The association between HbA1c levels and stone formation was assessed using logistic regression, adjusting for potential confounders, including Age, gender, BMI, and dietary habits. A p-value <0.05 was considered statistically significant.

RESULTS

The mean Age of participants in Group I was 45.6 ±12.3 years, while the mean Age of participants in Group II was 44.8 ±11.9 years. There was no statistically significant difference in the mean Age between the two groups. In terms of gender distribution, males constituted 60% of Group I and 58% of Group II. This difference was not statistically significant (p=0.89). However, the Body Mass Index (BMI) was significantly higher in Group I compared to Group II. **(Table I)**

Table I: Demographic characteristics of participants

Variable	Group I (n=300)	Group II (n=300)	p-value
Mean Age (years)	45.6 ± 12.3	44.8 ± 11.9	0.67
BMI (kg/m²)	28.1 ± 3.6	24.9 ± 2.8	<0.001

Biochemical parameters showed significant differences between the two groups. Group I had a higher mean HbA1c level compared to Group II. Similarly, urinary calcium excretion was elevated in Group I relative to Group II. Urinary citrate levels were lower in Group I. Additionally, the urinary pH was significantly lower in Group I. **(Table II)**

Table II: Biochemical characteristics of study participants

Variable	Group I (n=300)	Group II (n=300)	p-value
HbA1c (%)	7.2 ± 1.4	5.8 ± 0.9	<0.001
Urinary Calcium (mmol/day)	8.9 ± 1.2	7.2 ± 1.0	<0.001
Urinary Citrate (mmol/day)	1.2 ± 0.4	2.3 ± 0.5	<0.001
Urinary pH	5.4 ± 0.3	6.2 ± 0.4	<0.001

Logistic regression analysis identified key predictors of stone formation. Participants with an HbA1c level of ≥6.5% had an odds ratio (OR) of 2.3 (95% CI: 1.8–2.9; p<0.001), suggesting they were more than twice as likely to develop stones compared to those with lower levels. (Figure I) Those with an HbA1c level of ≥8.0% had an even higher odds ratio of 3.1 (95% CI: 2.4–4.2; p<0.001). A BMI greater than 25 was also associated with increased risk, with an odds ratio of 1.7 (95% CI: 1.2–2.4; p=0.002). **(Figure I)**

A subgroup analysis of Group I revealed differences based on stone composition. 65% of the cases had calcium oxalate, having a mean HbA1c level of 7.0 ± 1.2% in contrast to participants with uric acid stones, with a higher mean HbA1c level of 7.8 ± 1.3%. **(Figure II)**

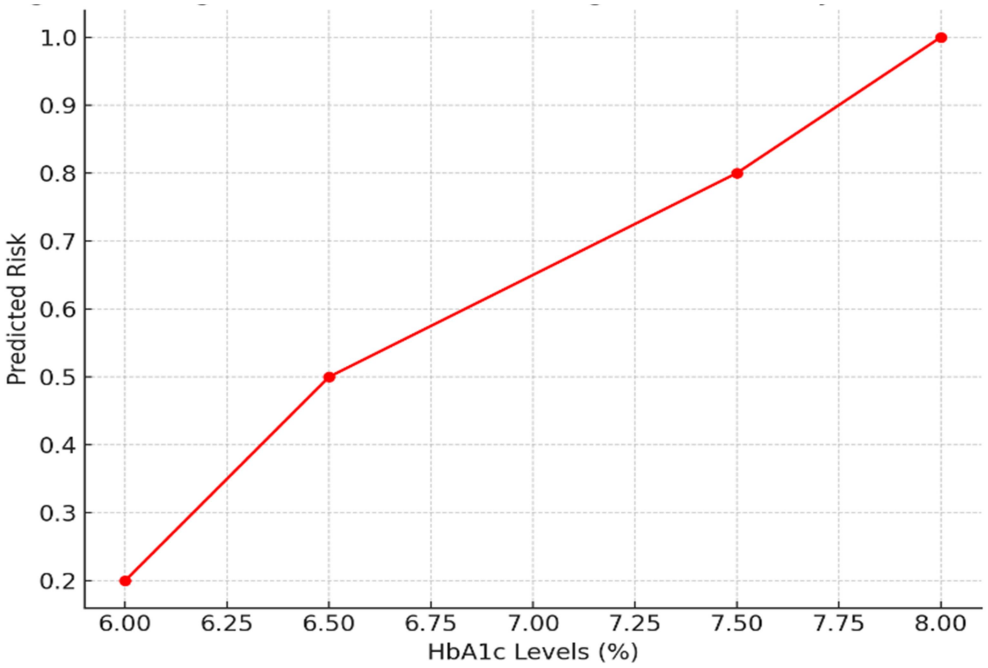

Figure I: Predicted risk of renal stone formation across HbA1c Levels

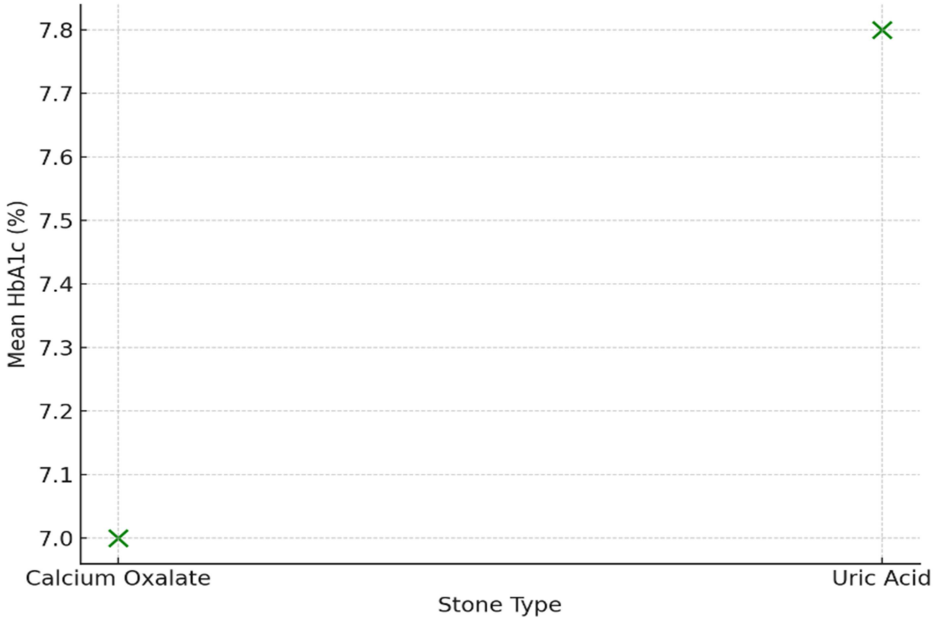

Figure II: Correlation between HbA1c and stone composition

DISCUSSION

In our study, the gender distribution of urolithiasis cases did not demonstrate a statistically significant difference, which is in contrast with global and regional trends. Many researchers have consistently shown that men exhibit a higher lifetime prevalence of urolithiasis, estimated at up to 14% compared to women and have suggested that gender-specific metabolic and hormonal differences contribute to this disparity.[6,7] Men generally have higher urinary concentrations of lithogenic agents such as Calcium, uric acid, and phosphate. In contrast, women have greater urinary citrate excretion, which offers a protective effect against stone formation.[8] Therefore, gender should be considered when evaluating the risk and development of kidney stones. Despite the absence of statistically significant gender-based differences in our study, we still observed a numerically higher prevalence of urolithiasis among males. This is consistent with findings from Pakistan [1,5] and Europe.[6] This male predominance may be explained by factors such as differential dietary patterns, hormonal influences (e.g., testosterone's role in increasing lithogenic risk) and occupational factors associated with dehydration. Furthermore, regional dietary habits—particularly the widespread intake of oxalate-rich foods common in South Asia could potentiate stone formation in predisposed individuals.[8] The difference between our findings and established literature highlights the possibility of region-specific variables, sample selection biases, or limitations in retrospective gender-stratified metabolic profiling, all of which point to a need to do further investigation in prospective, multi-centred studies.

In our study, the mean Age of individuals with urolithiasis was 45.6 years, aligning with findings from India[9] and China.[10] This suggests a consistent age distribution across different populations. However, variations may reflect differences in healthcare access and diagnostic capabilities across regions, particularly in low-resource settings.[11] The Age and gender distribution of our study mirrored reported trends. However, variations may be attributed to differences in healthcare access and dietary habits, such as the high oxalate intake prevalent in South Asia.[7]

In our study, elevated HbA1c levels correlated with altered urinary biochemistry, consistent with observations from Pakistan.[12] These findings suggest that interventions aimed at improving glycemic control may offer potential benefits in mitigating the risk of urolithiasis. Integrating metabolic screening into urolithiasis management could enable personalized interventions, focusing on weight management, dietary counseling, and glycemic control. Further research should prioritize longitudinal studies to confirm causality and explore preventive measures.

We observed significantly higher HbA1c levels in patients with urolithiasis. Elevated HbA1c levels, indicative of poor glycemic control, have been strongly associated with urolithiasis in previous studies from Pakistan [12] and India.[13] Chronic hyperglycemia may lead to altered urinary composition, increasing the risk of calcium oxalate and uric acid stones. Differences in glycemic control trends may be attributed to variations in diabetes prevalence and management practices across regions.[14]

We found that elevated BMI emerged as a significant risk factor, consistent with findings from China [11]and Europe.[6] This association is likely mediated by obesity-induced insulin resistance, leading to increased urinary calcium excretion and decreased citrate levels. We observed a significant difference in BMI between urolithiasis patients and controls. This finding is consistent with research from China [11]and Europe [6] where elevated BMI was identified as a risk factor for urolithiasis. Obesity and overweight status contribute to metabolic abnormalities, including insulin resistance, which promotes stone formation through hypercalciuria and reduced

urinary citrate. Differences in BMI associations across regions may stem from varying genetic predispositions and lifestyle factors, such as physical activity levels and dietary sodium intake.[14]
Urinary calcium levels were significantly elevated in the urolithiasis group. Hypercalciuria is a significant risk factor for calcium stone formation, with similar observations noted in European studies.[15] Regional differences in dietary Calcium and vitamin D intake might influence urinary calcium levels.[16]
Urinary citrate levels were markedly lower in the urolithiasis group. Citrate acts as an inhibitor of stone formation by chelating Calcium, and hypocitraturia has been highlighted as a key factor in studies from China[17] and Europe.[6] This difference might be linked to dietary acid loads and potassium intake, which vary significantly between Asian and Western diets.[18]
Urinary pH was significantly lower in the urolithiasis group. Low urinary pH is a recognized risk factor for uric acid stone formation, corroborating findings from studies in India[2] and Pakistan.[1] Differences in urinary pH across regions may reflect dietary acid-base balance and hydration habits.[8]
Logistic regression identified HbA1c levels ≥6.5% and ≥8.0% as significant predictors of stone formation. These results align with research from India [13], where poor glycemic control was a strong predictor of urolithiasis. BMI >25 was also associated with an increased risk, consistent with findings from Europe[3]. Regional variations may influence differences in the strength of predictors in the prevalence of metabolic syndrome and access to healthcare.[14]
Our subgroup analysis revealed differences in stone composition based on HbA1c levels. Participants with calcium oxalate stones had a higher mean HbA1c. These findings are in line with studies from Pakistan[12] and China[10], which reported metabolic differences influencing stone type. The higher HbA1c levels in uric acid stone formers emphasize the role of insulin resistance and acid-base imbalance in their pathogenesis.[19] Regional dietary patterns and genetic predispositions may explain differences in stone composition prevalence.[16]
This study stands out for its comprehensive approach to investigating risk factors for kidney stone formation. A large sample size provides robust statistical power, enabling a reliable comparison of demographic and biochemical parameters between stone-forming individuals and a control group. The analysis is further strengthened by subgroup analysis, which examines the relationship between stone composition and metabolic markers, such as HbA1c, thereby enhancing the study's clinical significance. Ultimately, the application of logistic regression analysis successfully identifies key predictors of kidney stone formation, including BMI and HbA1c levels, providing valuable insights for the prevention and management of this prevalent health issue. Nevertheless, the study has several limitations. Firstly, the cross-sectional design precludes the establishment of a causal relationship between metabolic factors and kidney stone formation. Secondly, the study did not directly assess potential confounding factors such as dietary intake, fluid consumption, physical activity, and genetic predispositions, which could significantly influence the observed associations. Thirdly, the single-centre design may limit the generalizability of the findings to other populations or regions. Fourthly, the absence of longitudinal data restricts the ability to understand the temporal relationship between metabolic changes and stone formation. Finally, while regional dietary patterns are considered, the lack of direct dietary data, such as oxalate, sodium, and calcium intake, limits a comprehensive understanding of their impact on urinary parameters and subsequent stone risk.
Despite its limitations, our study highlights the crucial role of metabolic factors in the risk of urolithiasis. Integrating BMI and HbA1c into routine assessments allows for the identification of high-risk individuals, particularly those with poor glycemic control or obesity. This knowledge

highlights the importance of lifestyle modifications, including weight management programs and dietary adjustments to reduce sodium, oxalate, and acid-forming foods, while increasing intake of citrate-rich foods. Effective diabetes management through medication, diet, and exercise is crucial for reducing the risk of stone formation in this population. Furthermore, individualized interventions are necessary, with uric acid stone formers potentially benefiting from alkalization therapy to address low urinary pH, and calcium oxalate stone formers requiring specific dietary and pharmacological approaches to manage hypercalciuria and hypocitraturia. Given the significant contribution of metabolic risk factors, public health initiatives should prioritise raising awareness about the link between obesity, diabetes, and urolithiasis, implementing screening programs, and promoting preventive measures at the community level to address the burden of this disease effectively.

CONCLUSION

There is a significant association between metabolic factors such as BMI, HbA1c levels and urinary composition with stone formation.

Ethical Permission: Ahmed Medical Complex, Rawalpindi, Pakistan, Ethical exemption letter No. DCA/Amc/25/129.
Conflict of interest: There is no conflict of interest between the authors.
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Data Sharing Statement: The corresponding author can provide the data proving the findings of this study on request. Privacy or ethical restrictions bound us from sharing the data publicly.

AUTHOR CONTRIBUTION

Awan MFA: Data collection, data analysis
Ilyas M: Interpretation of data
Malik A: Study design and concept
Farooq M: Literature search

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