REVIEW ARTICLE

Urolithiasis and diabetes mellitus: A review of prevalence, risk factors, and clinical implications

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Abstract
Urolithiasis is a growing global health concern, particularly in regions with high rates of metabolic disorders such as diabetes mellitus. This review explores the prevalence, risk factors, and clinical implications of urolithiasis in the context of diabetes mellitus. The increasing prevalence of diabetes, projected to affect 640 million people worldwide by 2040, significantly elevates the risk of urolithiasis due to metabolic changes that alter urinary pH and increase the excretion of stone-forming substances. In Africa, the burden of both conditions is rising, with urbanization and lifestyle changes contributing to higher incidences. The review highlights the interplay between obesity, metabolic syndrome, and dietary habits as key risk factors. It also examines the clinical challenges posed by the coexistence of urolithiasis and diabetes, including recurrent stone formation, chronic kidney disease, and urinary tract infections. Effective management strategies, including lifestyle modifications, pharmacological interventions, and surgical options, are discussed. The review underscores the importance of early detection, patient education, and a multidisciplinary approach to mitigate the long-term burden of these interrelated conditions.

Keywords: Urolithiasis, Diabetes Mellitus, Kidney Stones, Metabolic Syndrome, Insulin Resistance, Chronic Kidney Disease

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1.1 Introduction:

Urolithiasis, commonly referred to as kidney stone disease, is a significant global health concern, with an increasing prevalence linked to metabolic disorders such as diabetes mellitus. The burden of urolithiasis is growing worldwide, particularly in regions with high rates of obesity, metabolic syndrome, and diabetes [1].

As of 2019, there were over 400 million cases of diabetes globally which was the fifth commonest cause of death among adults. By 2045, that figure is anticipated to increase to 548 million [2]. There may also be 640 million people with diabetes worldwide by 2060, up from the estimated 548 million by 2045 [3]. Additionally, epidemiological evidence indicates that having diabetes mellitus increases the risk of urolithiasis [4].

In Africa, the prevalence of urolithiasis varies widely across regions, with studies indicating a growing burden, especially in urbanized areas where lifestyle changes contribute to risk factors such as obesity and metabolic disorders [5]. Reports indicate that the prevalence of kidney stones in some African countries ranges from 3% to 15%, with higher incidences observed in regions with hot climates, where dehydration contributes to stone formation [6].

Diabetes mellitus, a major risk factor for urolithiasis, is also on the rise in Africa. According to the International Diabetes Federation (IDF), Africa had approximately 24 million adults living with diabetes in 2021, and this number is projected to rise significantly by 2045 [7]. Type 2 diabetes, in particular, has been linked to an increased risk of nephrolithiasis due to metabolic changes that lead to altered urinary pH, hyperuricosuria, and hypercalciuria [8]. Studies suggest that individuals with diabetes mellitus are at a higher risk of developing uric acid and calcium oxalate stones [9].

In East Africa, the prevalence of urolithiasis is not well documented, but studies indicate an upward trend, particularly in urban settings. The rise in cases is attributed to dietary transitions, increasing consumption of processed foods, and sedentary lifestyles, all of which contribute to metabolic disorders [10]. Dehydration due to high temperatures and inadequate fluid intake is another key factor contributing to stone formation in the region [11].

The prevalence of diabetes mellitus is also increasing in East Africa, with countries such as Kenya, Tanzania, and Uganda reporting higher cases over the past two decades. According to the World Health Organization (WHO), East Africa has seen a steady rise in diabetes cases, with prevalence rates ranging from 4% to 7% among adults [12]. This increase in diabetes cases further exacerbates the risk of urolithiasis, as studies have shown that individuals with diabetes are more likely to develop recurrent kidney stones [13].

In Uganda, data on urolithiasis prevalence remains scarce, but hospital-based studies suggest an increasing number of cases. The condition is often underdiagnosed, particularly in rural areas where access to diagnostic imaging is limited [14]. A study conducted at Mulago National Referral Hospital found that a significant proportion of patients presenting with renal colic had diabetes or other metabolic disorders [15].

Diabetes mellitus is a growing public health challenge in Uganda, with an estimated prevalence of 3% to 5% among adults [16]. Studies indicate that urbanization and dietary changes are major contributors to the rising burden of diabetes and its complications, including urolithiasis [17]. Individuals with diabetes in Uganda have been reported to have a higher prevalence of uric acid and calcium oxalate kidney stones, aligning with global trends [8]. Given the rising prevalence of both urolithiasis and diabetes mellitus globally and across the African continent, particularly in urbanized regions experiencing rapid lifestyle transitions, there is a critical need to better understand the intersection between these two conditions. This review aims to explore the epidemiological trends, shared risk factors, and clinical implications of urolithiasis in the context of diabetes mellitus.

1.2 Risk factors of Urolithiasis and Diabetes Mellitus.

1.2.1 Obesity and Metabolic Syndrome

Obesity is a well-established risk factor for both urolithiasis and diabetes mellitus. Excess body weight alters urinary composition, increasing the excretion of calcium, oxalate, and uric acid, which promote stone formation [18]. A higher body mass index (BMI) has been associated with lower urinary pH, predisposing individuals to uric acid stones [19]. Similarly, obesity is a key contributor to insulin resistance, which plays a central role in the pathophysiology of type 2 diabetes mellitus (T2DM) [20]. Metabolic syndrome, characterized by central obesity, hypertension, dyslipidemia, and insulin resistance, is also associated with an increased risk of nephrolithiasis due to altered renal handling of uric acid and calcium [21].

1.3 Metabolic risk factors

1.3.1 Diabetes Mellitus and Insulin Resistance

Diabetes mellitus, particularly T2DM, is strongly linked to an increased prevalence of kidney stones. Insulin resistance affects renal ammonium excretion, leading to acidic urine, which facilitates the formation of uric acid stones [22]. Additionally, hyperglycemia in diabetic individuals contributes to glycosuria, which alters calcium and oxalate reabsorption in the kidneys, further predisposing them to nephrolithiasis [23]. Studies have shown that diabetic patients are more likely to develop recurrent kidney stones compared to non-diabetic individuals [24].

1.4 Dietary and Lifestyle Risk Factors

1.4.1 High Protein and Salt Intake

Dietary habits play a crucial role in the development of both urolithiasis and diabetes. Excessive intake of animal protein increases urinary calcium and uric acid excretion while reducing urinary citrate, a known inhibitor of stone formation [25]. High salt consumption also promotes hypercalciuria, a major contributor to calcium oxalate and calcium phosphate stone formation [10]. Furthermore, high-sodium diets have been associated with hypertension and insulin resistance, exacerbating the risk of diabetes [6].

1.4.2 Low Fluid Intake and Dehydration

Inadequate fluid intake and chronic dehydration are key risk factors for kidney stone formation. Low urine volume results in supersaturation of stone-forming substances such as calcium, oxalate, and uric acid [26]. Dehydration is particularly significant in hot climates, where increased insensible water loss can lead to concentrated urine and stone formation [3]. Chronic dehydration has also been linked to impaired glucose metabolism, increasing the risk of diabetes [27]. To reduce the risk of stone formation and support metabolic health, clinical guidelines recommend a daily fluid intake sufficient to produce at least 2 to 2.5 liters of urine per day typically requiring the consumption of 2.5 to 3 liters of fluids daily, preferably water. Monitoring urine color (aiming for pale yellow) is a practical way to assess hydration status.

1.4.3 Sedentary Lifestyle

Physical inactivity is another modifiable risk factor that contributes to both urolithiasis and diabetes. A sedentary lifestyle is associated with obesity and metabolic syndrome, both of which predispose individuals to stone formation and insulin resistance [28]. Reduced physical activity also leads to increased urinary calcium excretion, promoting kidney stone formation [29, 30]. Studies show that regular physical exercise improves insulin sensitivity and reduces the risk of both diabetes and nephrolithiasis [20].

1.5 Genetic and Environmental Risk Factors

1.5.1 Genetic Susceptibility

Both urolithiasis and diabetes mellitus have genetic components that influence susceptibility. Family history is a well-documented risk factor for kidney stone disease, with genetic predisposition affecting urinary calcium and oxalate excretion [5]. Similarly, genetic variations in insulin receptor function and glucose metabolism contribute to the hereditary risk of diabetes [29]. Genome-wide association studies have identified common genetic markers associated with both conditions, suggesting a shared genetic predisposition [31].

1.5.2 Climate and Geographic Factors

Environmental factors, such as temperature and humidity, play a significant role in the prevalence of kidney stones. Hot and arid climates increase the risk of dehydration, leading to higher rates of stone formation [14]. Studies have reported an increased incidence of urolithiasis in regions with prolonged heat exposure [32]. Similarly, temperature extremes have been linked to higher diabetes prevalence, possibly due to stress-induced metabolic changes [33].

1.6 Comorbidities related risk factors

1.6.1 Hypertension and Chronic Kidney Disease

Hypertension is a common comorbidity in both urolithiasis and diabetes mellitus. It contributes to kidney stone formation by altering renal perfusion and promoting calcium and sodium retention [27]. Chronic kidney disease (CKD) is also a consequence of recurrent nephrolithiasis and poorly controlled diabetes [7]. Patients with diabetes and recurrent kidney stones have a significantly higher risk of developing CKD due to repeated episodes of renal inflammation and obstruction [31].

1.7 Medication-related risk factors

1.7.1 Medications and Their Effects

Certain medications increase the risk of kidney stones and diabetes. Diuretics, particularly loop and thiazide diuretics, alter urinary calcium excretion and may contribute to stone formation [14]. Long-term corticosteroid use, commonly prescribed for inflammatory conditions, has been associated with insulin resistance and increased risk of diabetes [34]. Similarly, medications such as antiretroviral therapy and certain antiepileptics have been linked to metabolic disturbances that predispose individuals to both conditions [25].

1.8 Clinical implications of Urolithiasis and Diabetes Mellitus.

1.8.1 Increased Risk of Recurrent Stone Formation

Patients with diabetes mellitus have a significantly higher risk of recurrent nephrolithiasis compared to non-diabetic individuals [34]. Insulin resistance and chronic hyperglycemia lead to alterations in urinary pH and an increased excretion of stone-forming substances such as calcium, oxalate, and uric acid [22]. Uric acid stones are particularly common among diabetic patients due to the acidification of urine caused by impaired renal ammonium excretion [24]. The presence of diabetes also affects the composition of kidney stones, leading to increased stone heterogeneity and complexity, which can complicate treatment and increase recurrence rates [18].

1.8.2 Impact on Renal Function and Chronic Kidney Disease (CKD)

Urolithiasis and diabetes mellitus are both independent risk factors for chronic kidney disease (CKD), and their coexistence significantly accelerates renal function decline [35]. Kidney stones can cause obstruction, hydronephrosis, and recurrent urinary tract infections, all of which contribute to progressive renal damage [20].

Diabetic nephropathy, a common complication of diabetes, further exacerbates this risk by promoting glomerular damage, proteinuria, and decreased renal clearance [10]. Studies indicate that diabetic patients with a history of nephrolithiasis are at a higher risk of developing end-stage renal disease (ESRD) compared to those without stones [36].

1.8.3 Urinary Tract Infections and Urosepsis Risk

Recurrent urinary tract infections (UTIs) are a major clinical concern in diabetic patients with urolithiasis. The presence of stones provides a nidus for bacterial colonization, leading to persistent infections that are often difficult to eradicate [33]. Diabetic patients are particularly susceptible to UTIs due to impaired immune function, glycosuria, and urinary stasis associated with diabetic autonomic neuropathy [19]. The combination of recurrent stones and infections increases the risk of urosepsis, a life-threatening condition that can lead to systemic inflammation and multi-organ failure [20]. The rising concern of antimicrobial resistance further complicates treatment, particularly in patients with recurrent infections and frequent antibiotic exposure. This therefore highlights the need for careful antibiotic stewardship and personalized management strategies in this population.

1.8.4 Metabolic Complications and Stone Composition Variability

The metabolic disturbances associated with diabetes mellitus influence the chemical composition of kidney stones, leading to variations in stone type and treatment response. While calcium oxalate stones are the most common type in the general population, uric acid stones are more prevalent among diabetic individuals due to persistently acidic urine [14]. Hyperinsulinemia and insulin resistance also promote hypercalciuria, increasing the risk of calcium-containing stones [7]. Furthermore, metabolic syndrome, which is commonly seen in diabetic patients, is associated with increased urinary sodium, phosphate, and magnesium excretion, further altering stone composition and increasing the likelihood of mixed stone formation [17].

1.8.5 Complications in Stone Management and Treatment Approaches

The management of urolithiasis in diabetic patients presents unique challenges due to the increased risk of complications and altered treatment responses. Diabetic patients often have larger and more complex stones that are less responsive to extracorporeal shock wave lithotripsy (ESWL) due to their altered stone composition and lower urinary pH [19]. As a result, more invasive procedures such as percutaneous nephrolithotomy (PCNL) or ureteroscopy with laser lithotripsy are often required [25].

Additionally, glycemic control plays a critical role in post-operative outcomes. Poorly controlled diabetes is associated with increased surgical site infections, delayed wound healing, and prolonged hospital stays following stone removal procedures [33]. The use of contrast agents during imaging studies and surgical interventions also poses a risk of contrast-induced nephropathy in diabetic patients, necessitating careful pre-procedural assessment and hydration strategies [18].

1.8.6 Cardiovascular and Systemic Implications

Both urolithiasis and diabetes mellitus are associated with an increased risk of cardiovascular disease (CVD). Chronic inflammation, oxidative stress, and endothelial dysfunction, which are common in both conditions, contribute to an elevated risk of hypertension, atherosclerosis, and myocardial infarction [33]. The presence of recurrent kidney stones has been linked to a higher incidence of hypertension and metabolic syndrome, further increasing cardiovascular morbidity [17]. Diabetic patients with urolithiasis are also at a higher risk of developing vascular calcifications, which can worsen renal and cardiovascular outcomes [31].

1.9 Prevention Strategies for Urolithiasis and Diabetes Mellitus

1.9.1 Lifestyle Modifications

Lifestyle changes play a critical role in preventing both urolithiasis and diabetes mellitus (DM). Adequate hydration is one of the most effective preventive measures for kidney stone formation, as it helps dilute urinary solutes and reduce stone formation risk [37]. A daily fluid intake of at least 2.5–3 liters is recommended, with a preference for water over sugary or carbonated beverages, which can increase stone risk [20]. Similarly, regular physical activity and weight management are essential for preventing type 2 diabetes and reducing insulin resistance, which is a risk factor for both DM and stone formation [14].

1.9.2 Dietary Modifications

A balanced diet is crucial in preventing both conditions. For urolithiasis, a diet low in sodium, animal proteins, and oxalate-rich foods (e.g., spinach, nuts, chocolate) is recommended, while maintaining adequate calcium intake to prevent oxalate stone formation [7]. Reducing excessive carbohydrate intake, particularly refined sugars, helps prevent insulin resistance and type 2 diabetes [6]. Additionally, a Mediterranean-style diet rich in fruits, vegetables, whole grains, and healthy fats has been associated with a lower risk of both conditions [28].

1.9.3 Medical Management and Pharmacological Approaches

For individuals at high risk of kidney stones, medications such as thiazide diuretics (to reduce urinary calcium excretion), citrate supplements (to alkalinize urine and prevent uric acid stones), and allopurinol (for hyperuricemia) may be prescribed [35]. In diabetes prevention, metformin is commonly used in high-risk individuals to improve insulin sensitivity and reduce the risk of progression to type 2 diabetes [17].

1.9.4 Regular Monitoring and Early Intervention

Routine medical check-ups are essential for early detection and prevention of complications. Screening for metabolic abnormalities, kidney function, and blood glucose levels allows for early interventions that can prevent disease progression [22]. Diabetic patients should undergo regular urine analysis and imaging to detect early signs of stone formation [36].

1.9.5 Patient Education and Behavioural Interventions

Educating individuals about risk factors and preventive strategies is key to reducing the burden of both diseases. Counselling on dietary habits, physical activity, and medication adherence can help patients adopt healthier lifestyles and prevent complications [4]. Behavioural interventions such as weight loss programs and diabetes prevention programs have been shown to significantly reduce the incidence of both conditions [29].

1.9.6 Clinical Management of Urolithiasis and Diabetes Mellitus

1. Urolithiasis Management

The clinical management of urolithiasis depends on several factors, including stone size, composition, location, symptoms, and patient health status. The primary goal of management is to relieve symptoms, prevent complications, and reduce the risk of recurrence.

a. Conservative Management

For small stones (less than 5mm in diameter) that are causing minimal symptoms, conservative management is often sufficient. This includes hydration therapy, pain management with nonsteroidal anti-inflammatory drugs (NSAIDs), and the use of alpha-blockers (e.g., tamsulosin) to facilitate stone passage by relaxing the smooth muscles of the urinary tract [35]. Hydration is critical to help flush out the stone, and pain relief can be achieved using NSAIDs or opioids in severe cases [11].

b. Medical Expulsive Therapy

Medical expulsive therapy (MET) with alpha-blockers is commonly used to facilitate the passage of stones in the ureter. Studies have shown that alpha-blockers improve the rate of stone expulsion and reduce the time to stone passage without increasing the risk of complications [14]. However, MET is not recommended for larger stones, or those causing significant obstruction or infection.

c. Surgical and Interventional Management

For kidney stones larger than 5 mm, or in cases involving severe pain, urinary obstruction, or recurrent infections, surgical intervention is often necessary. Several procedures are available, each suited to specific stone characteristics and locations. Among them is Extracorporeal Shock Wave Lithotripsy (ESWL); a non-invasive technique that employs shock waves to fragment kidney or upper ureteral stones into smaller pieces, making them easier to pass naturally through the urinary tract. This method is preferred for its minimal invasiveness and outpatient applicability [35]. Also, Ureteroscopy (URS) involves the insertion of a flexible endoscope through the urinary tract to directly visualize and remove or break down stones located in the mid to lower ureter. URS does not require external incisions and is highly effective for managing stones in more distal locations within the ureter [24]. Thirdly, Percutaneous Nephrolithotomy (PCNL) is a more invasive option reserved for very large stones, typically those exceeding 2 cm. This procedure requires a small incision in the patient's back to access and remove the stone directly from the kidney. PCNL offers a high success rate for complex or bulky stones but usually requires hospitalization and a longer recovery period [15].

The choice of procedure depends on the size, location, and composition of the stone, as well as the patient's overall health status and treatment goals.

d. Preventive Management
After stone removal, patients are often advised to make lifestyle modifications to prevent recurrence. This includes increased fluid intake, dietary changes (low sodium, low animal protein), and possibly medications such as thiazide diuretics, potassium citrate, or allopurinol depending on stone composition [31].

2. Diabetes Mellitus Management

The management of diabetes mellitus (DM) involves a multifaceted approach aimed at maintaining optimal blood glucose levels, preventing complications, and improving the overall quality of life for patients. The primary types of diabetes are type 1 and type 2, with type 2 being the most prevalent.

a. Lifestyle Modifications

For both type 1 and type 2 diabetes, lifestyle interventions are the cornerstone of management. These interventions include dietary modifications, increased physical activity, and weight management. A balanced diet rich in whole grains, lean proteins, vegetables, and low in refined carbohydrates is recommended to manage blood sugar levels and prevent complications (American Diabetes Association, 2020). Physical activity plays a critical role in improving insulin sensitivity, aiding in weight control, and improving overall cardiovascular health, which is essential given the higher risk of cardiovascular disease in diabetic patients [32].

b. Pharmacological Management

In type 1 diabetes, insulin therapy is required for blood sugar control as the body no longer produces insulin. Insulin can be administered through multiple daily injections or via an insulin pump [25].

In type 2 diabetes, the primary approach involves oral medications aimed at improving insulin sensitivity or enhancing insulin secretion. Metformin is the first-line treatment for most patients with type 2 diabetes, as it reduces hepatic glucose production and improves peripheral insulin sensitivity (American Diabetes Association, 2020). Other options include sulfonylureas, GLP-1 receptor agonists, and SGLT2 inhibitors, each targeting different aspects of glucose metabolism.

For patients who do not achieve adequate control with oral agents, insulin or GLP-1 agonists may be added. The choice of medication depends on the patient's specific health conditions, comorbidities (e.g., cardiovascular disease), and preferences [22].

c. Monitoring and Screening

Regular monitoring of blood glucose levels is vital in managing diabetes. HbA1c, a marker of long-term blood glucose control, is measured at least every three to six months. Continuous glucose monitoring systems (CGMS) are increasingly being used to provide real-time data on glucose levels and help adjust insulin therapy more effectively [13].

Additionally, regular screening for diabetic complications, such as diabetic nephropathy, retinopathy, and neuropathy, is recommended. Screening for microalbuminuria and kidney function tests are crucial in preventing the progression of diabetic kidney disease [32].

d. Managing Comorbidities

Patients with diabetes often have comorbid conditions like hypertension, hyperlipidemia, and cardiovascular disease. Management of these conditions is essential in reducing the risk of long-term complications. Blood pressure control is particularly important, with a target of less than 140/90 mmHg, and statin therapy is often used to manage cholesterol levels [14].

e. Prevention of Complications

The management of diabetes also involves preventing acute complications, such as diabetic ketoacidosis (DKA) and hypoglycemia. In type 2 diabetes, aggressive blood glucose control may reduce the risk of complications, including cardiovascular diseases and diabetic nephropathy. Educating patients on recognizing early signs of complications and adjusting their treatment regimens accordingly is an essential component of diabetes management [26].

1.10 Conclusion and recommendations

In conclusion, the clinical management of both urolithiasis and diabetes mellitus requires a comprehensive, individualized approach that addresses the multifaceted nature of each condition. For urolithiasis, early intervention with conservative methods such as hydration and pain management, along with medical expulsive therapy, can be effective for small stones. However, surgical options like ESWL, URS, and PCNL remain crucial for larger stones or those causing significant complications. Diabetes mellitus management relies heavily on lifestyle modifications, pharmacological treatment, and vigilant monitoring to prevent complications, including cardiovascular diseases and diabetic nephropathy. Both conditions benefit from early detection and the prevention of recurrent episodes. It is recommended that healthcare providers emphasize the importance of lifestyle changes, including diet and exercise, in preventing both urolithiasis and diabetes, while regularly screening at-risk populations for early intervention. Additionally, a multidisciplinary approach involving nephrologists, endocrinologists, and dietitians should be adopted to optimize patient outcomes and reduce the long-term burden of both diseases.

Conflicts of interest: The authors declare no conflicts of interest.

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TABLES AND FIGURES

Table 1: Summary of Common Kidney Stone Types in Diabetic vs. Non-Diabetic Patients

Stone Type	Typical Composition	Prevalence in Diabetics	Prevalence in Non-Diabetics	Key Associated Factors
Uric Acid Stones	Uric acid	High	Lower	Acidic urine, insulin resistance, hyperuricemia
Calcium Oxalate Stones	Calcium oxalate monohydrate/dihydrate	Common	Very common	Hyperoxaluria, low urine volume, dietary oxalate, glycosuria
Calcium Phosphate Stones	Hydroxyapatite or brushite	Moderate	Moderate	Alkaline urine, renal tubular acidosis
Struvite Stones	Magnesium ammonium phosphate	Less common	More common in recurrent UTIs	Infection-related, especially with urease-producing bacteria
Mixed Stones	Combinations (e.g., uric acid + oxalate)	Increasingly observed in diabetics	Variable	Metabolic syndrome, altered urinary chemistry

Figure 1: Risk factors of Urolithiasis and Diabetes Mellitus

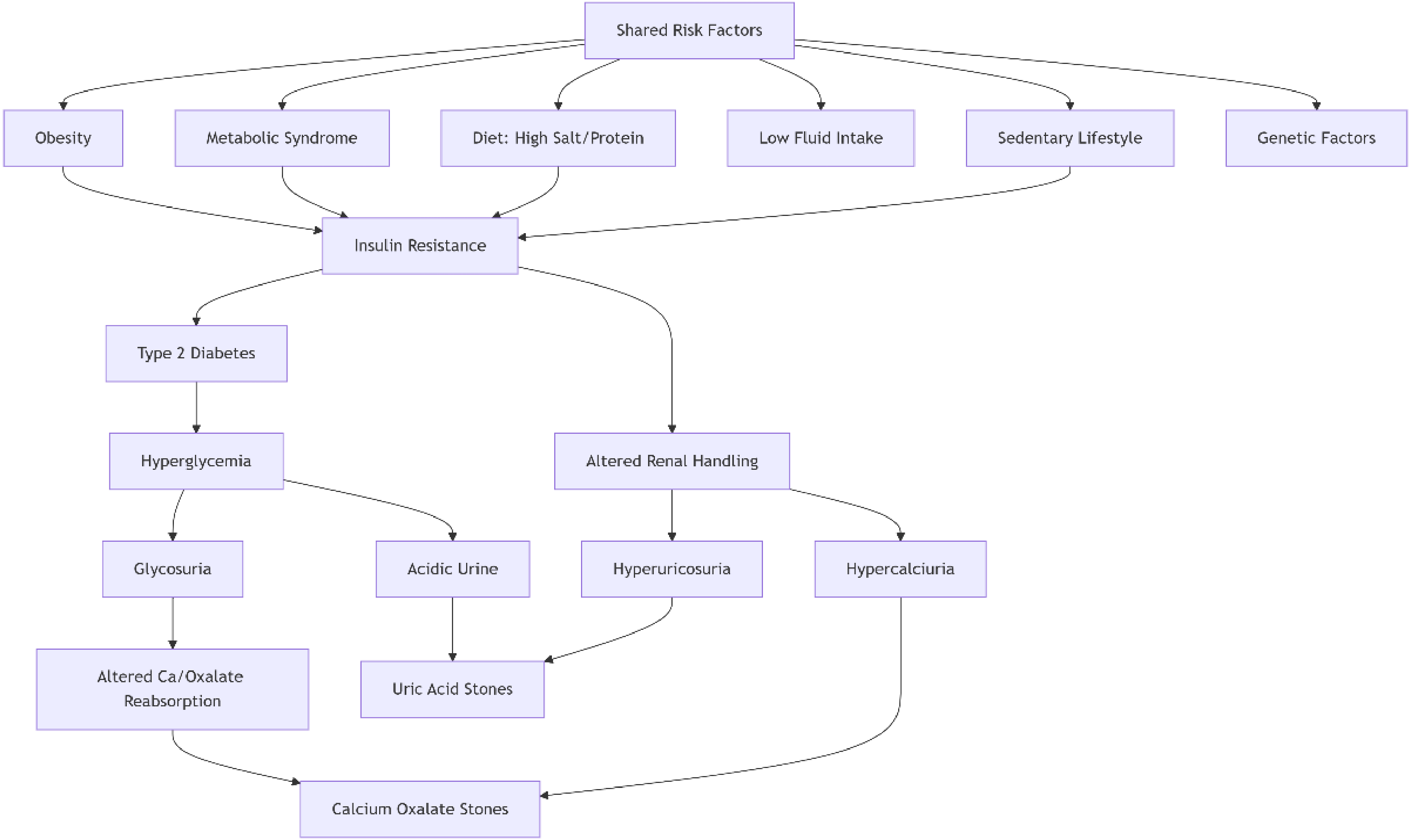

Figure 2: Clinical Management Interplay