UDC: 616.61-003.7(497.75)
Professional paper

PREVALENCE OF NEPHROTIC CALCULI IN THE POPULATION OF THE POLOG VALLEY AND SURROUNDING AREA

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Abstract

Introduction: The kidneys are divided into two main regions: the cortex and medulla. The cortex contains renal corpuscles, convoluted and straight tubules, collecting ducts, and vasculature. Medullary rays, composed of straight tubules and collecting ducts, extend into the cortex from the medulla. Kidney stones are mineral deposits formed in the renal pelvis or on the renal papillae, composed of both crystalline and organic substances. They develop when urine becomes supersaturated with minerals. Most stones are made of calcium oxalate, often forming on calcium phosphate deposits known as Randall's plaques. Kidney stones are common, with a prevalence of up to 14.8% and a recurrence rate of 50% within five years. Risk factors include low fluid intake, obesity, diabetes, hypertension, and metabolic syndrome. Stones can also lead to chronic kidney disease and hypertension. In areas near the Sharr Mountains, water quality may contribute to nephrolithiasis (kidney stone disease), also known as nephrotic calculi. Contaminated water can increase the risk of kidney and bladder diseases, including cancers. The type and severity of toxins depend on the water source and treatment.
Aim of the Study: This study investigates the prevalence of nephrotic calculi in the Polog Valley, comparing populations from villages near the Sharr Mountains, along the Tetovo-Gostivar highway, near Mali i Thatë, and in the cities of Tetovo and Gostivar. It aims to assess the potential link between drinking water quality and kidney stone formation by comparing water sources from these regions.
Materials and Method: The study includes 80 patients: 30 from the Sharr Mountain area, 10 from Tetovo-Gostivar highway villages, 30 from Mali i Thatë, and 10 in a control group. Patients will be examined using renal ultrasonography and CT-urography to identify and analyze kidney stones. The research will be conducted at the Urology Department of Tetovo Clinical Hospital.
Results: The findings will reveal the prevalence of nephrotic calculi in Polog and their association with local water sources. The study will also assess water quality and explore possible endemic patterns, particularly between the Sharr and Mali i Thatë regions.
Conclusion: The study will provide a comprehensive overview of kidney stone prevalence in Polog, the impact of drinking water quality, and the underlying causes of nephrolithiasis. The results can inform preventive measures and support early diagnosis and intervention, benefiting nephrology, urology, and public health efforts in the region.

Keywords: kidneys, nephrotic calculi, urogenital diseases, drinking water.

1. Introduction

Kidney stones (calculi) are mineral deposits located in the renal calyces and pelvis, either freely floating or attached to the renal papillae. By contrast, diffuse renal parenchymal calcification is called nephrocalcinosis (Khan SR., 2010).
Stones that develop in the urinary tract (known as nephrolithiasis or urolithiasis) form when the urine becomes excessively supersaturated with respect to a mineral, leading to crystal formation, growth, aggregation and retention within the kidneys (Finlayson B., 1978).
Globally, approximately 80% of kidney stones are composed of calcium oxalate (CaOx) mixed with calcium phosphate (CaP). Stones made up of uric acid, struvite, and cystine are also

frequently encountered, accounting for approximately 9%, 10%, and 1% of all stones, respectively (Evan AP., 2010).

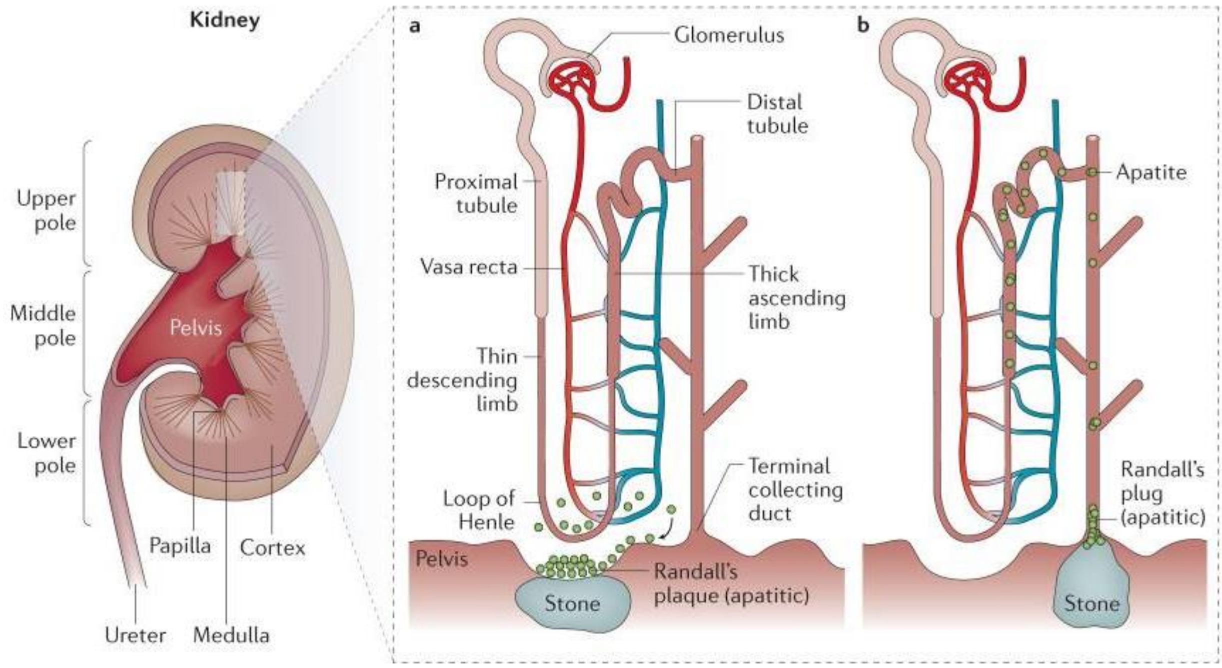


Figure 1. Macroscopic and histological morphology of human kidneys, along with the anatomical distribution of renal calculi (*Published in final edited form as:* Nat Rev Dis Primers. 2016 Feb 25;2:16008.)

Urine can also become supersaturated with certain relatively insoluble drugs or their metabolites, leading to crystallization in the renal collecting ducts (iatrogenic stones). For example, patients with HIV who are treated with protease inhibitors such as indinavir and atazanavir are at risk for developing nephrolithiasis (Tattevin P, et al. 2010).

Both indinavir and atazanavir are metabolized by the liver, but a significant portion of these drugs is excreted unchanged in the urine, which can lead to their crystallization and the development of kidney stones. (Izzedine H et al., 2014).

The propensity to form stones varies according to sex, ethnicity and geography. Although historically stones have been 2–3-times more common in men than in women, recent data indicate that this disparity is diminishing (*Scales CD, et al. 2007*).

Geographical variation in stone disease typically reflects environmental risk factors, with higher stone prevalence in hot, arid climates (*Stamatelou KK et al., 2003*).

Numerous systemic diseases and factors have been associated with an increased risk of kidney stones. Weight, weight gain, body mass index (*Taylor EN, 2005*), (Curhan GC et al., 1998), (Sorensen MD, et al., 2014) and diabetes (*Taylor EN et al., 2005*), (*Chung SD et al., 2011*) have been shown in large prospective cohort studies to correlate with the risk of incident kidney stones, with a greater effect in women than in men in some cohorts. Finally, risk of cardiovascular disease has been associated with a history of kidney stones, although a cause and effect relationship has not been definitively established.

Kidney stones are solid concretions that can vary in size from a grain of sand to the size of a pearl or larger. They may remain asymptomatic. Their color—typically yellow or brown—and surface texture, which can be smooth or irregular, depend on their chemical composition. They are composed of crystals and a ubiquitous organic matrix, which not only coats the crystals but is also present inside the crystals and the inter-crystalline spaces (Khan SR, Hackett RL., 1993), (Ryall RL et al., 2005), (McKee MD et al., 1995).

Figure 2. Kidney stones (Laura Shammah MS, RDN, 2023)

The matrix of calcific stones contains many macromolecules, including osteopontin (which also has a role in the biomineralization of bone), inter-α-inhibitor (which is a plasma protein) and urinary prothrombin fragment 1 (UPTF1) — all of which are normally present in the urine (*Khan SR, Kok DJ., 2004*), albeit in small quantities (*Khan SR, Kok DJ., 2004*), (Atmani F, Khan SR., 1999), (Ryall RL., 2004). The matrix also includes various types of lipids, which have been shown to promote crystal nucleation (Khan SR, et al., 1996), (Khan SR, Glenton PA., 1996), (Khan SR., 2002), (Khan SR, 1988), (Khan SR,1990).The association between the crystals and the matrix seems to start early upon crystal nucleation and continues throughout the formative and growth phases of the developing stone. Although some urinary molecules, such as UPTF1, are considered crystallization inhibitors, others such as osteopontin can act as both inhibitors and promoters of crystallization (*Hunter GK., 2013*).

These molecules seem to be produced as a protective response against mineralization. However, both CaOx and CaP crystals have been shown to induce the production of macromolecules that inhibit and/or modulate crystallization (*Ryall RL.2004*), (Khan SR et al., 2002), (Khan SR et al., 2014), (Aihara K et al., 2003).

2. Material and methods

The study will involve 30 patients who gravitate to Sharr Mountain, 10 in the villages of the Tetovo - Gostivar highway and 30 patients who gravitate to Mali i Thatë and 10 patients will be the control group.

Patients will be examined with the modern advanced method Renal Echography (Kidney ultrasound), a non-invasive method to identify stones and assess their size with the CT-urography (CT-Scan) method, the most accurate method to identify nephrotic calculi and analyze their composition. The study will be conducted at the Tetovo Clinical Hospital in the Urology Department.

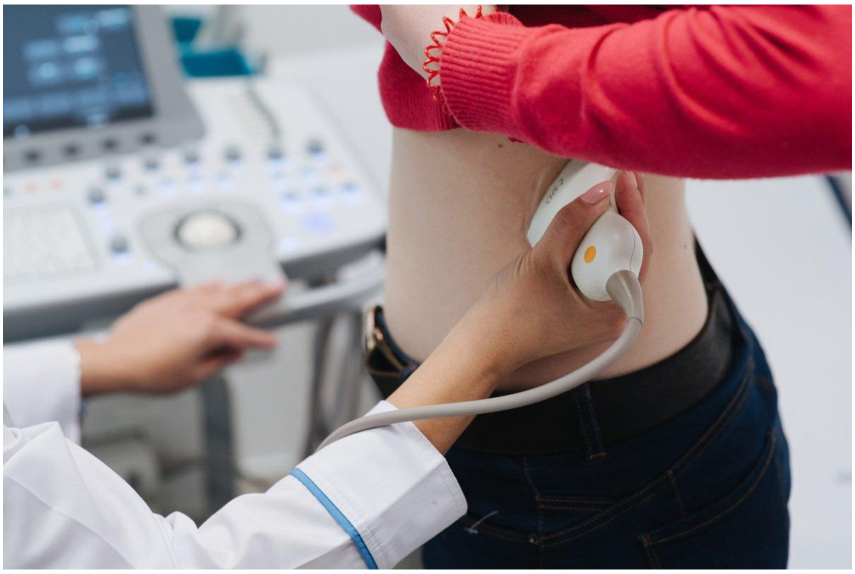
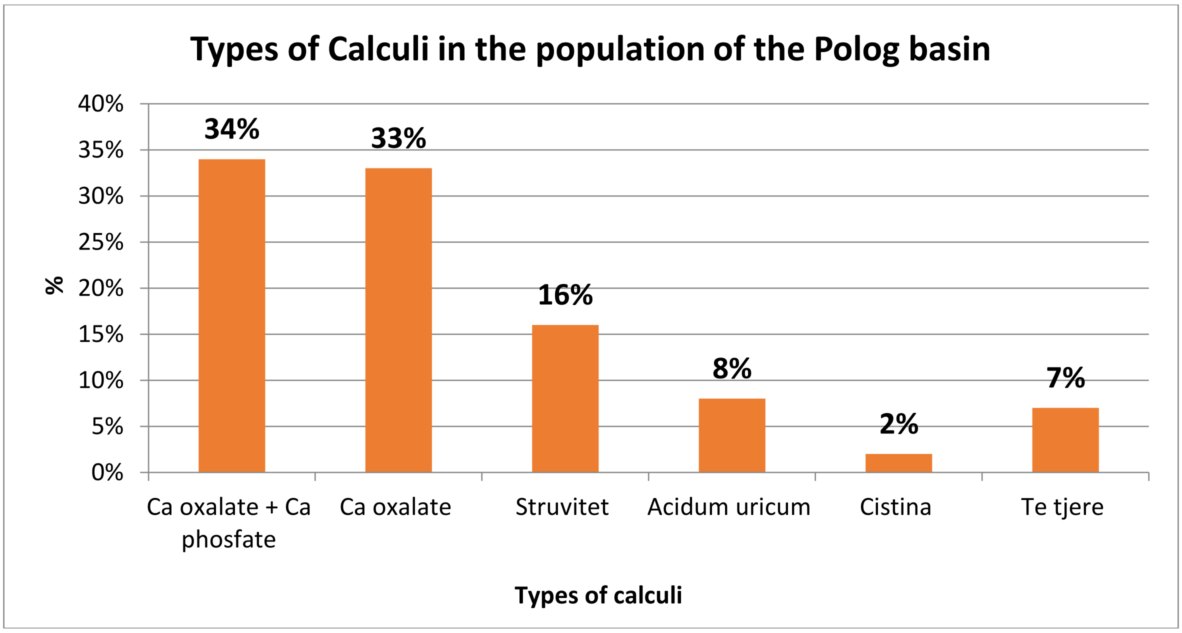


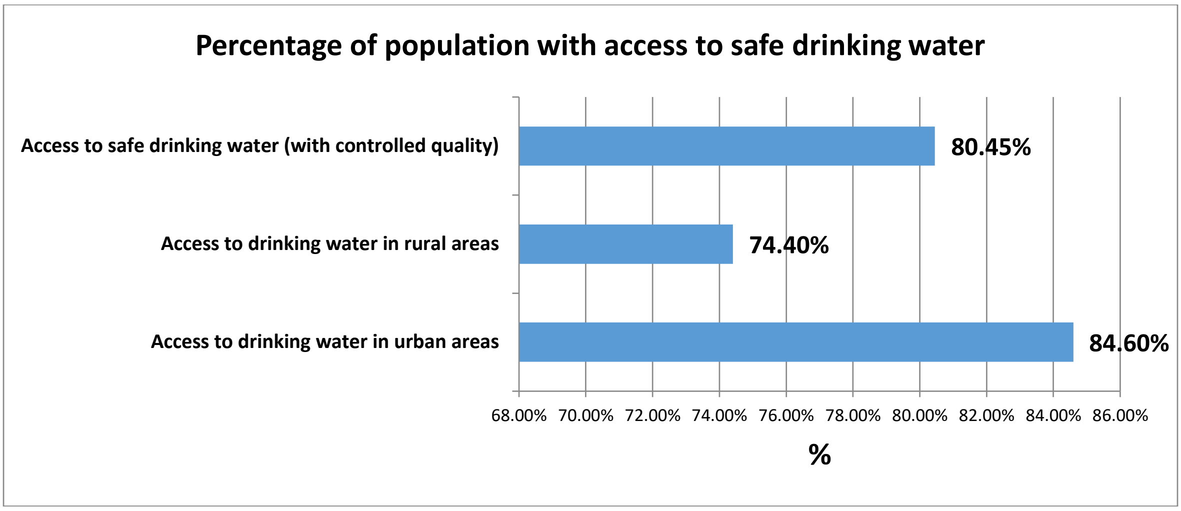
Figure 2. Renal Echography (Kidney ultrasound) (Charlie King, 2022)

3. Results

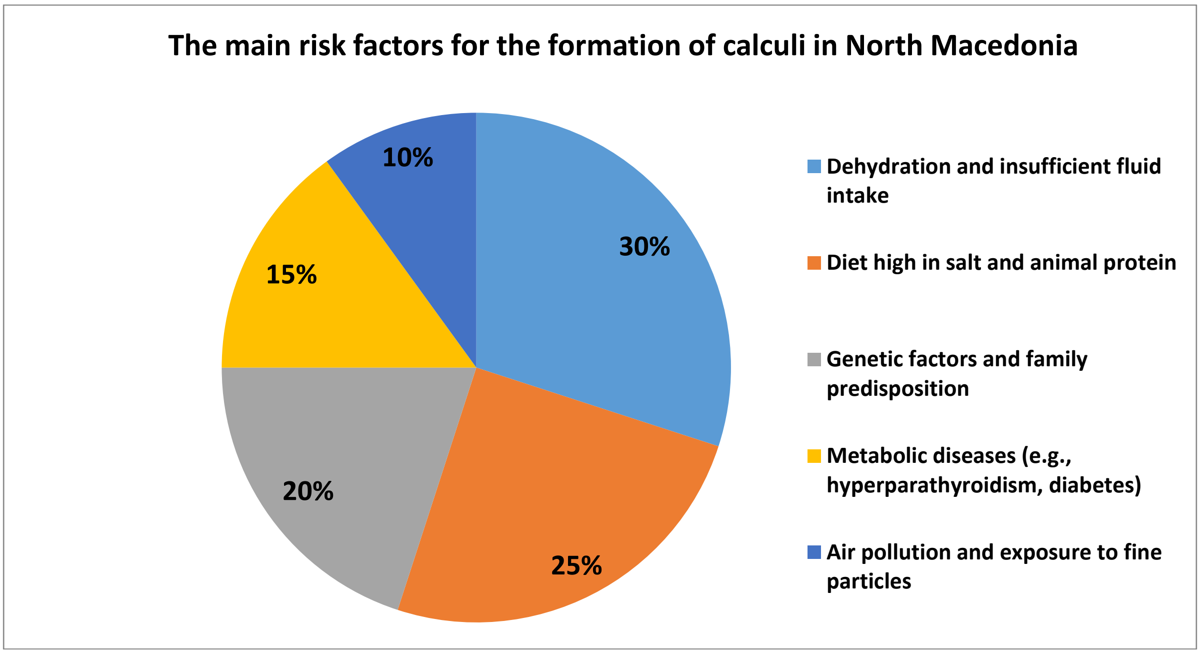
In the results section, we will present the data obtained from patients using clear and informative graphics to facilitate interpretation and highlight key findings.



Graphic 1. **Types of calculi in the population of the Polog basin:** The distribution of urinary calculi types in the Polog Basin reveals a notable predominance of calcium-based stones, with 34% of cases involving a combination of calcium oxalate and phosphate, and an additional 33% consisting of calcium oxalate alone. This indicates that two-thirds of the population are affected by calcium-containing stones, underscoring the importance of dietary and metabolic factors in stone formation. Struvite stones account for 16%, suggesting a significant contribution from infection-related etiologies. Meanwhile, uric acid stones represent 8% of cases, and rarer types like cystine (2%) and others (7%) highlight the diversity in pathophysiology. These findings can inform targeted prevention and treatment strategies specific to the region.



Graphic 2. **Percentage of population with access to safe drinking water:** The graphic illustrates the percentage of the population with access to safe drinking water, serving as a critical indicator of public health and infrastructure development. High access rates reflect strong water management systems and governmental investment in sanitation, while lower percentages point to ongoing challenges such as outdated infrastructure, geographical barriers, or economic limitations. Identifying regions with limited access is essential for prioritizing interventions, improving health outcomes, and ensuring equitable distribution of this basic human necessity.



Graphic 3. **The main risk factors for the formation of calculi in North Macedonia:** The graphic highlights the main risk factors contributing to the formation of urinary calculi in North Macedonia. Key contributors include **inadequate hydration**, which leads to concentrated urine and crystal formation, and **dietary habits high in oxalates, salt, and animal protein.** Additionally, **genetic predisposition, urinary tract infections,** and **metabolic disorders** such as hypercalciuria and hyperuricosuria play a significant role. The data underscore the importance of preventive strategies, including public health education on fluid intake, dietary modifications, and early detection of metabolic imbalances, to reduce the incidence and recurrence of stone disease in the region.

4. Discussions

The initiation of stone formation in most patients is an occasional event. Accordingly, optimal compliance can only be expected with regimens based on strictly individualized analysis of risk factors and risk periods. The information obtained from 24-hour urine collections and other long-term urine collections gives only rough average information on specific risk variables during the period. Indeed, imprecise data on urinary pH are the rule rather than the exception. Better analytical focus on periods assumed to represent particularly high risk is necessary. Such information can be obtained by combining a careful medical history with analysis of risk factors during periods when supersaturation with CaOx occurs simultaneously with low urinary pH. Such an approach might enable the design of individualized recurrence prevention (*Tiselius HG., 2015*).

Today, it is very attractive to remove kidney stones with flexible ureteroscopy (*Türk C, et al., 2015*) and, if that is not optimal, to use smaller and smaller instruments for percutaneous removal of smaller and smaller stones. However, it seems logical that for each treatment decision a balance is reached between the intention of the treatment and the efforts required to reach that goal. Active or pharmacological removal of residual fragments should be considered in view of the risk of the procedures and of the recurrence rate. There is no doubt that recurrence preventions need to be further developed, fine-tuned and used in an individually designed manner. With further increased understanding of the mechanisms behind stone formation, it is possible that some general treatment can be prescribed for many patients with idiopathic calcium stone disease.

It stands to reason, however, that further progress in the management of patients who form stones cannot be made without a genuine interest and responsibility by urologists who regularly see these patients. The need for close interaction between stone removing and recurrence preventive procedures are absolute prerequisites for success. Basic as well as clinical research must have its focus on both aspects. In this regard, the urologist, during various endoscopic procedures, has a unique possibility to visually observe and record the clinical features of the pathology involved in stone formation. It cannot be too strongly emphasized that the optimal care of patients with stone disease is not only surgical, in its widest sense, but also medical (Khan SR ET AL., 2016).

5. Conclusions

This study offers a comprehensive overview of the prevalence of urinary calculi in the population of the Polog Valley and its surrounding areas. Through a comparative analysis of individuals who consume drinking water from boreholes versus those who rely on underground wells, the research identifies a significant link between the source of drinking water and the occurrence of calculi. Studies have demonstrated that drinking water in the Polog Valley often contains elevated levels of minerals and other substances that may contribute to the formation of calculi, positioning water quality as a notable environmental risk factor in the development of this condition.

In addition to examining water quality, the study delves into the etiology of urinary calculi, analyzing a combination of endogenous (genetic, metabolic) and exogenous (dietary, environmental) causes. It identifies key risk factors such as high mineral content in water, dietary habits, and potential metabolic predispositions within the population. A notable finding from the research is that males are more frequently affected by urinary calculi than females, which aligns with global trends indicating a higher prevalence of such conditions among men, possibly due to physiological and lifestyle differences.

The data gathered from this research will play a crucial role in informing public health policies aimed at prevention. By recognizing the contributing factors—particularly the composition of drinking water—health authorities and local governments can take proactive steps to monitor and improve water quality. Educational campaigns on dietary modifications and hydration, especially for high-risk groups, may also help reduce incidence rates.

In the populations studied—specifically the 30 patients from villages near Sharr Mountain, 10 from the Tetovo-Gostivar highway area, and 30 from the region surrounding Mali i Thatë—the

formation of urinary calculi appears to be closely linked to environmental and lifestyle factors, particularly the quality of drinking water. These areas are known for varying geological compositions, which influence the mineral content of groundwater sources such as boreholes and wells. High concentrations of calcium, oxalates, and other minerals in the local water supply contribute to an increased risk of crystal formation in the urinary tract. Over time, these crystals can aggregate to form calculi, especially in individuals who have inadequate fluid intake, dietary habits that promote stone formation, or genetic predispositions. The control group of 10 patients, who are not exposed to the same environmental factors, will provide a baseline for comparison, helping to better isolate the role of water composition and regional risk factors in the pathogenesis of urinary calculi in these rural populations.
Moreover, the findings serve as a valuable resource for the fields of Nephrology and Urology, offering important guidance for the early identification and management of urinary calculi. This study not only enhances our understanding of the disease in a regional context but also reinforces the importance of environmental health as an integral part of medical and public health planning in the Polog Valley.

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