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The Association Between Kidney Stone Disease and the Incidence of Genitourinary Cancers

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ABSTRACT

Kidney stone disease (nephrolithiasis) is a common urological condition with rising global prevalence over the past three decades. Data support a correlation between kidney stones and genitourinary malignancies, particularly renal cell carcinoma (RCC), bladder cancer, and prostate cancer. This study examines epidemiological and pathophysiological links between nephrolithiasis and these cancers, based on extensive cohort studies and molecular insights. Bladder cancer, one of the most common urinary tract malignancies, occurs more frequently in individuals with a history of kidney stones, with significantly elevated odds ratios reported. Prostate cancer, the most prevalent male malignancy, is also more common in stone formers, especially with concurrent urinary tract infections. For RCC, the relationship appears subtype-specific, with papillary RCC showing the strongest correlation. Shared risk factors—such as obesity, metabolic syndrome, hypertension, poor diet, tobacco use, age, and sex—contribute to both nephrolithiasis and cancer development. Chronic inflammation and epithelial injury from recurrent stones may create a carcinogenic environment in the urinary tract. However, Mendelian randomization studies are not yet supportive of a direct causal relationship between genetics, suggesting that environmental and physiological processes are more central to the relationship. Finally, kidney stone disease may be a risk marker for genitourinary cancer. Identification of this association is essential for prevention and early detection in high-risk groups.

Keywords: Kidney stones, Genitourinary cancer, Prostate cancer, Bladder cancer

1. INTRODUCTION

In the last few decades, a rising incidence of kidney stone disease all over the world has been observed. Kidney stones constitute a frequent urologic ailment in which crystals are deposited in the urinary tract under normal circumstances and are usually composed of calcium oxalate (Stamatelou and Goldfarb, 2023). The surge in kidney stone formation is associated with contemporary lifestyle patterns, dietary patterns, increasing rates of obesity, and the metabolic syndrome (Scelo and Larose, 2018). This condition is prevalent in both developed countries, where improved diagnostic tools contribute to more frequent detection, as well as in developing

regions, where malnutrition and dehydration are more prominent contributing factors (Stamatelou and Goldfarb, 2023).

Simultaneously, the incidence of genitourinary cancers—including prostate cancer, bladder cancer, and upper tract urothelial carcinoma (UTUC)—has been steadily increasing (Dyrskjøet et al., 2023; Pernar et al., 2018). These malignancies have multifactorial etiologies, involving both genetic predisposition and environmental exposures such as cigarette smoking, occupational contact with carcinogenic substances, and chronic inflammation. Growing evidence points to a possible link between the presence of kidney stones and increased risk of developing cancers within the urinary system (Mihalopoulos et al., 2022).

This study aims to assess whether there is a relationship between kidney stone disease and the incidence of genitourinary cancers. In particular, the study will examine whether a history of kidney stones is a significant risk factor for the development of prostate cancer, bladder cancer, and cancers of the upper urinary tract.

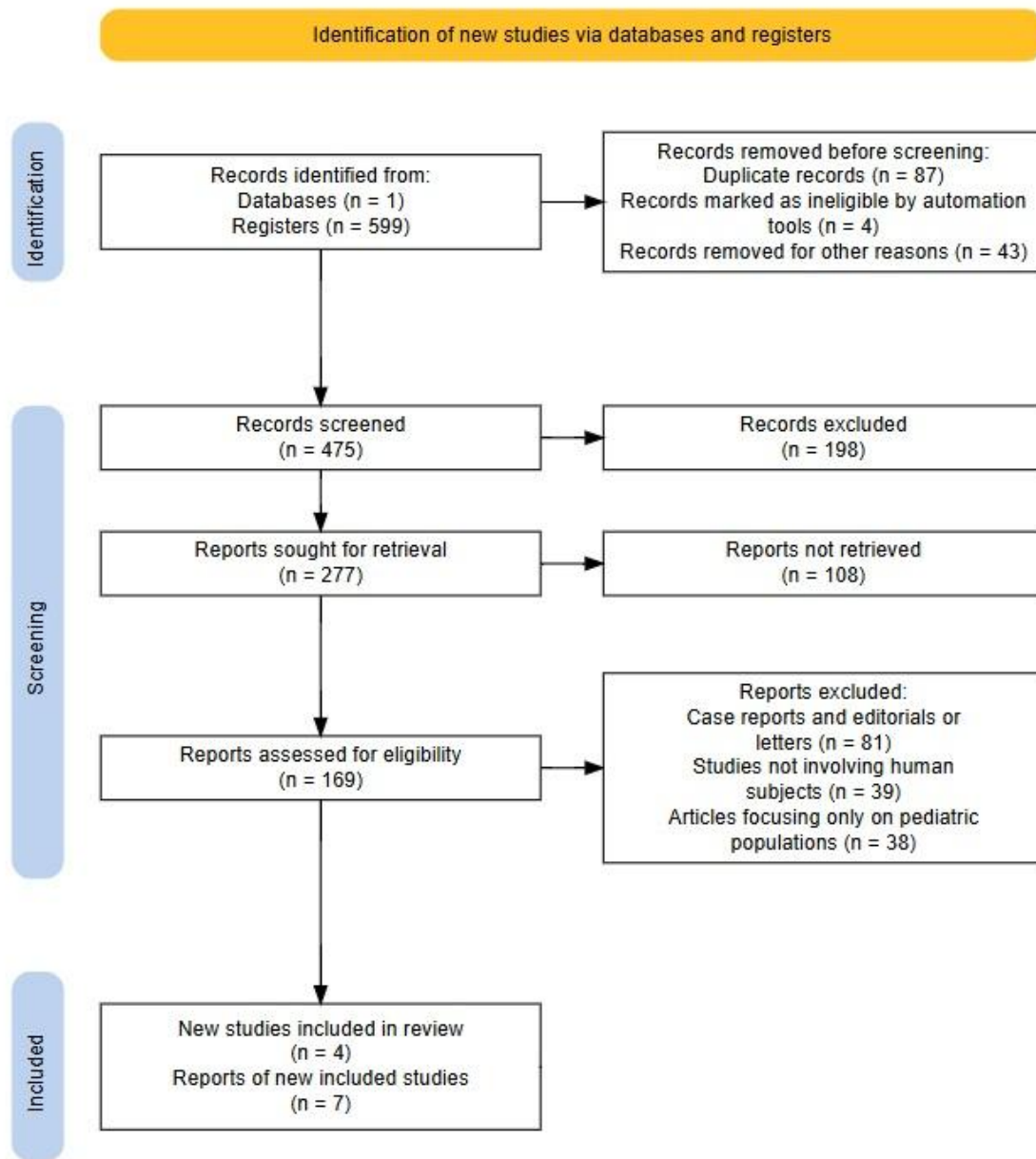


Figure 1. PRISMA Chart. Methodology

2. REVIEW METHODS

We searched open-access medical databases, primarily PubMed, for articles published between January 2011 and May 2025. The search was conducted using the keywords “kidney stones”, “nephrolithiasis”, “urolithiasis”, and “cancer” in various Boolean combinations (e.g., “kidney stones AND cancer”, “urolithiasis AND genitourinary neoplasms”).

In total, 242 articles were initially identified and screened based on their titles and abstracts. We applied the following inclusion criteria: original research articles or meta-analyses, full text available in English, studies involving adult human populations, and research focused on the association between kidney stone disease and genitourinary or systemic cancers.

Exclusion criteria included case reports, editorials, or letters, studies not involving human subjects, articles focusing only on pediatric populations, and publications with insufficient statistical analysis. Ultimately, 11 studies met all inclusion criteria and were included in this review (figure 1).

3. RESULTS AND DISCUSSION

3.1. Kidney Stones Epidemiology

Kidney stones (KS), also referred to as nephrolithiasis or urolithiasis, are a prevalent urological disorder characterized by the development of crystalline structures inside the urinary tract. The term is derived from the Greek words nephros (kidney), uro- (urinary), and lithos (stone). The most common type of kidney stones worldwide consists of calcium compounds, primarily calcium oxalate.

The prevalence of kidney stones is highly diverse worldwide and is influenced by geographic location, socioeconomic status, climate, and individual characteristics like age, sex, race, and diet. Among some of the most significant risk factors are obesity and metabolic syndrome, both of which are extremely closely linked to the development of calcium oxalate stones.

They are also associated with an increased risk of several systemic diseases, including diabetes, cardiovascular disease, bone fractures, and chronic kidney disease. These conditions often share underlying risk factors with kidney stones, also known as nephrolithiasis.

Over the past three decades, the global incidence of kidney stones has risen considerably. In developed countries, this trend is attributed to changes in diet and improved diagnostic capabilities, while in developing regions, contributing factors include water scarcity and malnutrition (Stamatelou and Goldfarb, 2023).

3.2. Genitourinary system cancer types

3.2.1. Bladder Cancer

Bladder cancer is one of the most common malignancies of the urinary tract, typically originating in the epithelial lining of the bladder. The primary cause of bladder cancer is cigarette smoking, which is responsible for over half of all cases. In addition to smoking, exposure to industrial chemicals, particularly aromatic amines found in the dye and rubber industries, significantly increases the risk. Persistent bladder inflammation, such as that caused by prolonged catheter use or infections like *Schistosoma haematobium* in certain regions of Africa and the Middle East, also contributes to the development of cancer (Yohana et al., 2023). Bladder cancer occurs more frequently in men than women, with men being three to four times more likely to develop the disease. Diagnosis is most common among individuals aged 60 and above (Dyrskjøet et al., 2023)

3.2.2. Kidney cancer

Kidney cancer, which is dominated by renal cell carcinoma (RCC), is the cause of the vast majority of adult kidney cancers, with clear cell RCC being the most common subtype. The cancer is of renal parenchymal origin and exhibits extensive worldwide variation in incidence due to environmental, geographic, and demographic variables. It ranks as the 13th most common cancer worldwide and is of much higher frequency in high-income countries like Europe, North America, and some Asian countries. Men are affected approximately twice as often as women, and incidence increases steadily with age, peaking around 75 years. The etiology of kidney cancer remains largely unknown, though several risk factors have been established. Tobacco smoking modestly increases the risk, as does excessive body weight, which shows a clear dose-response relationship with RCC (Scelo and Larose, 2018). Hypertension is another consistent and independent risk factor, potentially due to the renal damage it causes. Chronic kidney disease also contributes significantly to risk, particularly in populations with higher prevalence, such as Black Americans (Lipworth et al., 2011)

3.2.3. Prostate cancer

Prostate cancer is the leading cancer diagnosis in men worldwide and ranks among the top causes of cancer-related mortality. In 2020, over 1.4 million new cases and 375,000 deaths were reported globally (Leslie et al., 2024). The incidence of prostate cancer exhibits significant geographical variation, being notably higher in developed countries. Excess body weight and an increase in body mass have been tied to an increased risk of advanced forms of prostate cancer, whereas regular physical activity is linked to a lower risk. Smoking has been connected to increased mortality from prostate cancer. Dietary factors, such as high consumption of calcium and dairy products, may elevate risk.

In contrast, the intake of lycopene-rich foods such as tomatoes and fish, as well as vitamin D and statins, may offer protective effects (Pernar et al., 2018). The disease typically advances at a slow pace and may be asymptomatic during its initial stages. When symptoms arise, they may include fatigue resulting from anemia, bone pain, paralysis from spinal metastases, and renal failure resulting from bilateral ureteral obstruction (Leslie et al., 2024).

3.3. The impact of kidney stone disease on the incidence of genitourinary cancers

3.3.1. Correlation between the frequency of kidney stone disease and prostate cancer

The EPICAP study found a statistically significant link between a history of kidney stones and elevated prostate cancer risk. Specifically, men with a history of kidney stones had a 46% higher likelihood of developing prostate cancer compared to those without (OR: 1.46; 95% CI: 1.13–1.90). This association was most pronounced for low-grade prostate cancer (OR: 1.49) but was not significant for high-grade tumors (OR: 1.16). Furthermore, the association between kidney stones and prostate cancer was particularly robust in those men with a history of pyelonephritis, also suggesting chronic inflammation as a possible mechanism in cancer development. In such cases, the odds ratio increased markedly to 5.43. The findings suggest that kidney stones may contribute to prostate cancer risk through mechanisms involving chronic urinary tract inflammation (Sawaya et al., 2025).

Another study, based on 13,013 adult participants from the U.S. National Health and Nutrition Examination Survey (NHANES), was conducted between 2007 and 2020. Participants provided self-reported information on kidney stone history and cancer diagnoses. Multivariate logistic regression models, which accounted for potential confounders by adjusting for variables such as age, sex, race, socioeconomic status, body mass index, and pre-existing medical conditions, were used to assess the statistical relationship between kidney stones and renal cell carcinoma (RCC).

The results demonstrated a statistically significant association between a history of kidney stones and the risk of RCC, with an odds ratio (OR) of 1.01 and a 95% confidence interval (CI) of 1.00–1.03 following full adjustment. Although the strength of this association was modest, its statistical significance suggests a potential link between prior kidney stone disease and an increased risk of renal cell carcinoma incidence (Zhong et al., 2025).

In conclusion, this research supports the notion that kidney stone disease may contribute to a higher likelihood of developing prostate cancer, especially in the presence of kidney infections, indicating that inflammation might be a key factor in prostate carcinogenesis (Sawaya et al., 2025).

3.3.2. Correlation between the frequency of kidney stone disease and upper tract urothelial carcinoma

In 2019, researchers used data from the Netherlands Cohort Study to examine the connection between kidney stone history and the risk of two types of cancer: renal cell carcinoma (RCC) and upper tract urothelial carcinoma (UTUC). This was an extensive prospective cohort study involving over 120,000 participants aged 55–69, followed for more than 20 years.

The study's findings indicate that prior episodes of kidney stones are strongly associated with an increased risk of both renal cell carcinoma and UTUC. Specifically, individuals with a history of kidney stones had a 39% higher risk of RCC compared to those without stones. This association was influential for papillary renal cell carcinoma (pRCC), where the risk was more than tripled; however, it was not significant for clear-cell renal cell carcinoma (ccRCC) (van de Pol et al., 2019).

Regarding UTUC, the study found a 66% increased risk in participants with a history of kidney stones. This elevated risk applied to both UTUC subtypes—renal pelvis and ureter cancer, with no significant difference between their associations. The study also found that an earlier diagnosis of kidney stones (before age 40) was associated with a higher risk of developing both RCC and UTUC later in life.

In conclusion, the study supports a positive correlation between kidney stone history and increased incidence of upper tract urothelial carcinoma. It suggests that chronic irritation and inflammation caused by stones may contribute to the development of these cancers. Early-life stone formation could be particularly relevant in cancer risk (Mihalopoulos et al., 2022).

3.3.3. Correlation between the frequency of kidney stone disease and bladder cancer

The study titled “Association between kidney stones and urological cancers: results from the NHANES 2007–2020 and Mendelian randomization study” provides evidence of a statistically significant correlation between a history of kidney stone disease and the incidence of bladder cancer. According to the analysis of epidemiological data from 13,013 adult participants, individuals with a history of nephrolithiasis exhibited an increased risk of bladder cancer, with an odds ratio (OR) of 1.60 and a 95% confidence interval (CI) of 1.58–1.62, taking into consideration confounding factors like age, sex, and race, body mass index, comorbidities, and socioeconomic status (Zhong et al., 2025).

Another study, aiming at the same highlights, says that there is consistent epidemiological evidence supporting a positive correlation between a history of kidney stone disease and an increased risk of bladder cancer. The review compiles findings from several large-scale population studies that highlight this association. For example, data from a Swedish national registry demonstrated that individuals hospitalized for kidney stones exhibited a notably higher incidence of bladder cancer compared to the general population (Mihalopoulos et al., 2022).

These findings suggest that a prior diagnosis of kidney stones may be associated with a higher likelihood of developing bladder cancer. However, the Mendelian randomization (MR) component of the study, which utilized genome-wide association study (GWAS) data, did not support a genetic causal relationship between kidney stones and bladder cancer. The MR estimates lacked statistical significance and demonstrated wide confidence intervals, indicating that the observed association is unlikely to be explained by shared genetic predispositions (Zhong et al., 2025). Instead, the biological plausibility of this relationship is supported by the hypothesis that chronic irritation and inflammation induced by kidney stones may promote a carcinogenic microenvironment in the bladder. Repeated epithelial injury and subsequent regenerative processes in the bladder lining could lead to hyperplasia and, over time, malignant transformation (Mihalopoulos et al., 2022).

Table 1. The impact of kidney stone disease on the incidence of genitourinary cancers: summary

Cancer Type	Authors	Association with Kidney Stones (OR, 95% CI)	Notes / Biological Mechanism
Prostate cancer	Sawaya et al., 2025	OR: 1.46 (1.13–1.90) Low-grade: OR: 1.49 High-grade: OR: 1.16 (ns)	Stronger association in cases with pyelonephritis (OR: 5.43); chronic inflammation is likely involved
Renal cell carcinoma (RCC)	Zhong et al., 2025	OR: 1.01 (1.00–1.03)	Weak but statistically significant link
Papillary RCC (pRCC)	van de Pol et al., 2019	>3-fold increased risk	Association specific to pRCC subtype; not significant for clear-cell RCC
Upper tract urothelial carcinoma (UTUC)	Mihalopoulos et al., 2022	OR: 1.66	Increased risk for both renal pelvis and ureter cancers; higher if stone formation occurs before age 40
Bladder cancer	Zhong et al., 2025	OR: 1.60 (1.58–1.62)	No genetic causality (MR); likely due to chronic irritation and inflammation
Bladder cancer	Mihalopoulos et al., 2022	No specific OR reported	Registry data confirms increased incidence; repeated epithelial injury may promote carcinogenesis

3.4. Common Risk Factors Linking Kidney Stone Disease and Genitourinary Cancers

Based on the analysis of current literature, several common risk factors have been identified that may contribute both to the development of kidney stone disease (nephrolithiasis) and malignancies of the genitourinary tract, including renal cell carcinoma (RCC), bladder cancer, and prostate cancer (Table 1).

3.4.1. Obesity and Metabolic Syndrome

Obesity ranks among the most critical risk factors that can be altered through behavioral changes that significantly increase the likelihood of developing both kidney stones and genitourinary cancers. An elevated body mass index (BMI) promotes lithogenesis due to enhanced renal excretion of calcium, oxalate, and uric acid. It simultaneously contributes to carcinogenesis through hormonal dysregulation, insulin resistance, and systemic inflammation. These mechanisms are strongly associated with an increased risk of renal cell carcinoma and advanced prostate cancer (Scelo and Larose, 2018). The burden of metabolic syndrome is also highlighted as a critical component in stone pathophysiology (healthcare-11-00424.pdf) and in the development of prostate neoplasia through altered androgen and insulin signaling (Pernar et al., 2018).

3.4.2. Hypertension and Chronic Kidney Disease

Hypertension and chronic kidney disease (CKD) are frequently coexisting conditions in patients with kidney stones and are independently linked to higher risks of renal malignancies. Chronic tubular damage, oxidative stress, and compensatory hyperfiltration may all contribute to renal carcinogenesis (Scelo and Larose, 2018). Moreover, CKD is commonly observed in recurrent stone formers due to obstructive uropathy and repeated infections (Stamatelou and Goldfarb, 2023).

3.4.3. Dietary Factors

Diets high in animal protein, sodium, and refined sugars are associated with an increased risk of kidney stone formation. They are suspected to play a role in cancer development, particularly in prostate and bladder malignancies. High calcium intake has been implicated in both conditions: while necessary for health, excessive calcium, especially from supplements, may elevate the risk of prostate cancer (Pernar et al., 2018) and contribute to stone formation by increasing urinary calcium saturation (Stamatelou and Goldfarb, 2023).

3.4.4. Tobacco Use

Tobacco use has been firmly correlated with elevated risk for both bladder cancer and renal cell carcinoma, exerting its carcinogenic effects through DNA adduct formation and chronic inflammation of the urothelium. At the same time, smoking is associated with increased urinary excretion of lithogenic substances, thus promoting nephrolithiasis (Scelo and Larose, 2018). Scientists discuss these effects in the context of prostate cancer risk in patients exposed to tobacco-related oxidative stress (Stamatelou and Goldfarb, 2023).

3.4.5. Age and Sex

Kidney stones and urologic malignancies are more common in older males. This shared demographic arises from the cumulative effects of metabolic and environmental risks that increase with age. Prostate cancer, above other cancers, is predominantly age-related, and the frequency increases substantially after 50 years of age. Kidney stone disease also becomes more frequent with age due to declining renal function and shifts in urinary chemistry (Stamatelou and Goldfarb, 2023).

3.4.6. Chronic Inflammation and Infection

Chronic inflammation caused by recurrent urinary tract infections or stone-related epithelial irritation can lead to carcinogenic transformation, particularly in the bladder and upper urinary tract. Persistent epithelial damage promotes metaplasia and dysplasia, creating a favorable environment for tumor initiation (Scelo and Larose, 2018). This pathway is also relevant in the context of prostate cancer, where chronic prostatitis may contribute to tumor development (Dyrskjøet et al., 2023).

4. CONCLUSIONS

Based solely on the presented analysis, a consistent relationship emerges between the occurrence of kidney stone disease (nephrolithiasis) and the incidence of cancers within the genitourinary system, particularly renal cell carcinoma (RCC), bladder cancer,

and prostate cancer. The epidemiological data discussed indicate that individuals with a history of kidney stones are at an elevated risk of developing these malignancies. This association is most evident in bladder and prostate cancers, where statistically significant increases in risk were observed in extensive cohort studies. For RCC, although the correlation appears more modest, it remains statistically relevant, especially for specific histological subtypes such as papillary RCC.

The potential pathophysiological mechanisms linking kidney stones and cancer development are multifactorial. Chronic inflammation and epithelial injury induced by recurrent stone episodes create a pro-carcinogenic microenvironment in the urinary tract, predisposing to neoplastic transformation. Moreover, shared modifiable risk factors—including obesity, metabolic syndrome, hypertension, smoking, and dietary habits—further support the biological plausibility of a common etiological pathway.

While no definitive genetic evidence of causative connection is present, the consistency of the epidemiological associations, supported by molecular and observational data, suggests that kidney stone disease should be considered a significant risk factor in the general context of urological malignancy. Recognizing nephrolithiasis not only as a urological condition but also as a potential marker for increased cancer susceptibility underscores the importance of integrated preventive strategies and long-term surveillance, particularly among high-risk patient populations.

Author's Contributions

Conceptualization: Szymon Bienia, Sara Hassan

Methodology: Szymon Bienia, Sara Hassan

Formal analysis: Sara Hassan, Szymon Bienia

Resources, data curation: Szymon Bienia, Kamil Hassan

Investigation: Sara Hassan, Aisha Hassan

Writing – original draft: Szymon Bienia, Sara Hassan

Writing – review & editing: Szymon Bienia

All authors have read and agreed with the final, published version of the manuscript.

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Informed consent

Not applicable.

Ethical approval

Not applicable.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data and materials availability

All data associated with this study will be available based on the reasonable request to corresponding author.

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