Environmental and Geographical Determinants of Nephrolithiasis: An Ecological Study in Kabupaten Kebumen

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Abstract

Background:
Nephrolithiasis is a significant public health concern influenced by environmental, metabolic, and lifestyle factors. This study aimed to investigate the incidence of nephrolithiasis and its associated risk factors in karst and non-karst zones, focusing on demographic characteristics, water sources, comorbidities, and geographic variability. Understanding these determinants is crucial for developing targeted prevention strategies.

Methods:
A cross-sectional study was conducted from January 2025 to February 2025, involving 98 participants (35 from a karst zone and 63 from a non-karst zone). Data were collected through structured interviews, medical record reviews, and laboratory assessments, following the STROBE guidelines. Variables included age, gender, water source, daily water consumption, urinary habits, comorbidities, and occupational environment. Statistical analyses were performed using RStudio, with Mann-Whitney U tests for continuous variables and logistic regression for categorical variables. Nephrolithiasis incidence rates were calculated per 100,000 population and visualized using a heatmap.

Result:
District-specific incidence ranged from 10,989.0 (Ayah, karst; Karanganyar, non-karst) to 1,098.9 (Prembun, non-karst) per 100,000 population. Unadjusted risk-ratio (RR) estimates (95 % CI) included: female sex RR 1.52 (0.52–4.42); groundwater vs distilled water RR 1.65 (0.43–6.35); municipal vs distilled water RR 0.26 (0.03–2.12); fluid intake < 2,500 mL vs ≥ 2,500 mL RR 0.96 (0.32–2.81); urine retention RR 1.07 (0.38–3.03); outdoor vs indoor work RR 1.52 (0.52–4.42); scale present on boiling water RR 3.27 (0.88–12.24). None of the adjusted models reached statistical significance.

Conclusions:
This study underscores the multifactorial etiology of nephrolithiasis, emphasizing the role of geological, metabolic, and lifestyle factors. Targeted interventions, including community screening, dietary modifications, and improved water quality, are essential for reducing disease burden. Future research should explore causal relationships and refine preventive strategies through longitudinal studies and larger cohorts. These findings contribute to a deeper understanding of nephrolithiasis and inform region-specific public health measures.

Introduction

Nephrolithiasis, commonly known as kidney stone disease, is a significant global health concern due to its high prevalence, recurrent nature, and associated morbidity.[1] It is a multifactorial condition influenced by genetic, dietary, environmental, and geographical factors.

Over the past few decades, the incidence of nephrolithiasis has been rising worldwide, with notable increases reported in both developed and developing countries.[1] This upward trend is particularly concerning in low- and middle-income countries (LMICs), where limited access to healthcare, poor dietary habits, and environmental stressors exacerbate the burden of the disease.[2]

In Indonesia, nephrolithiasis is a growing public health issue, with regional variations in prevalence that are likely linked to differences in environmental and lifestyle factors.[3] The country's diverse geography, which includes extensive karst regions, presents unique challenges in understanding the epidemiology of kidney stone disease. Karst landscapes, characterized by limestone bedrock and specific hydrogeological conditions, have been hypothesized to influence the prevalence of nephrolithiasis due to their impact on water quality, mineral content, and dietary practices.[4] However, there is limited research exploring the relationship between karst ecosystems and nephrolithiasis incidence, particularly in Indonesia.

Globally, LMICs face a disproportionate burden of nephrolithiasis compared to high-income countries. Factors such as inadequate healthcare infrastructure, limited awareness of preventive measures, and exposure to environmental risk factors contribute to this disparity.[5] In these settings, nephrolithiasis often leads to severe complications, including chronic kidney disease and renal failure, further straining already overburdened healthcare systems. Despite the growing recognition of nephrolithiasis as a public health priority, there remains a paucity of data on its epidemiological distribution and determinants in LMICs, particularly at the subnational level.[5]

Kabupaten Kebumen, located in Central Java, Indonesia, provides an ideal setting to investigate the interplay between environmental and geographical factors in nephrolithiasis incidence. The region encompasses distinct zones, including karst areas (e.g., Buayan, Ayah, Rowokele) and non-karst urban areas (e.g., Gombong, Kebumen, Alian). These zones differ not only in their geological characteristics but also in terms of socioeconomic conditions, water sources, and dietary patterns, all of which may influence the prevalence of kidney stone disease. Understanding the spatial distribution of nephrolithiasis in Kabupaten Kebumen can provide valuable insights into the role of environmental determinants and inform targeted public health interventions.

The rationale for this ecological study lies in addressing critical gaps in the existing literature. While previous studies have examined nephrolithiasis at broader levels, few have focused on the impact of specific environmental and geographical factors, such as karst topography, on disease prevalence. By comparing nephrolithiasis incidence rates between karst and non-karst zones in Kabupaten Kebumen, this study aims to elucidate the potential role of these factors in shaping the epidemiological landscape of kidney stone disease. The findings could have important implications for policymakers, healthcare providers, and communities in designing effective prevention and management strategies tailored to local contexts.

Material And Methods

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Ethics Committee of Dr. Soedirman Regional Public Hospital, ensuring adherence to ethical guidelines for human subject research. Informed consent was obtained from all participants prior to data collection, and confidentiality of personal information was strictly maintained throughout the study. Ethical principles outlined in the Declaration of Helsinki were followed to ensure participant safety and data integrity.

Study Design and Data Collection

This cross-sectional study was conducted between January 2025 and February 2025, adhering to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines to ensure methodological rigor and transparency. Participants were recruited from two distinct

geographic zones: a karst zone and a non-karst zone. A total of 98 individuals (35 from the karst zone and 63 from the non-karst zone) were included based on predefined inclusion criteria, which required participants to be adults residing in the respective zones for at least five years

The inclusion criteria required participants to be adults aged 18 years or older, residents of the respective zones for at least five consecutive years, willing to provide informed consent, and available for medical assessments such as blood tests for hyperuricemia and urine analysis. Exclusion criteria encompassed individuals with a history of nephrolithiasis prior to residing in their current geographic zone, pregnant women due to potential physiological changes affecting urinary habits and metabolic profiles, individuals with incomplete or unreliable data, and those unwilling or unable to participate in structured interviews or provide necessary biological samples.

Data were collected through structured interviews. Demographic variables included age, measured as a continuous variable in years, and gender, classified as a categorical variable with male or female categories. Water source was categorized into three types: groundwater, obtained from wells or natural springs; municipal supply, provided through public utilities; and distilled water, purified through distillation. Daily water consumption was measured in milliliters (mL) per day and grouped into three categories: less than 1,000 mL, 1,000–2,500 mL, and greater than 2,500 mL. Urinary retention habits were defined as the tendency to delay urination for extended periods and were categorized as either "Yes" or "No." Comorbid conditions were assessed based on specific clinical criteria. Hypertension was identified as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medications. Hyperuricemia was defined as serum uric acid levels exceeding 7.0 mg/dL for males and 6.0 mg/dL for females. Diabetes mellitus was diagnosed if fasting blood glucose levels were ≥126 mg/dL or if participants were using antidiabetic medications. Obesity was determined by a body mass index (BMI) of ≥30 kg/m². The occupational environment was classified into two categories: outdoor work, which included employment primarily conducted outside (e.g., agriculture, construction), and indoor work, which involved employment primarily conducted inside (e.g., office work, retail). Scale formation during water boiling was recorded as "Yes" if participants reported observing mineral deposits after boiling water, and "No" otherwise. Finally, nephrolithiasis incidence was calculated as the number of new cases per 100,000 population within each district, providing a standardized measure for comparing disease prevalence across geographic zones.

Statistical Analysis

Statistical analyses were conducted using RStudio with a particular focus on addressing the non-parametric distribution of the data. Descriptive statistics were employed to summarize the demographic and clinical characteristics of the study population, providing a clear overview of the sample.

For the comparison of continuous variables, such as age and water consumption, the Mann-Whitney U test was utilized. This non-parametric test is well-suited for analyzing ordinal or skewed data. Categorical variables and risk factor analysis were addressed through logistic regression. This method was used to assess the association between categorical variables—such as water source, urinary habits, and comorbidities—and the likelihood of nephrolithiasis occurrence. Both unadjusted and adjusted risk ratios (RRs) were calculated, with adjustments made for potential confounders such as age, gender, and comorbid conditions.

The ggplot2 package was used for data visualization, while the stats package facilitated hypothesis testing, and the rms package supported logistic regression modeling. A significance level of $p < 0.05$ was applied consistently across all analyses to ensure the reliability and validity of the findings.

Result

The karst-zone subgroup comprised 20 participants, whereas the non-karst subgroup comprised 71 participants (Table 1). Mean age was 51.2 years (range 27–80) in the karst zone and 54.73 years (29–80) in the non-karst zone. Sex distribution in the karst zone was 14 males and 6 females; the non-karst zone contained 39 males and 24 females. Regarding water source, karst households reported 2 using distilled water, 17 using groundwater wells, and 1 connected to a municipal supply. In the non-karst zone, 5 households used distilled water, 53 used groundwater wells, and 13 relied on a municipal supply. Daily fluid intake ≥ 2,500 mL was documented in 6 karst participants and 22 non-karst participants, while intake < 2,500 mL was recorded for 14 and 49 participants, respectively. Habitual urine retention was reported by 13 karst participants and 45 non-karst participants; 7 and 26 participants, respectively, denied the practice. Comorbidity counts in the karst zone were: hypertension 2, hyperuricemia 3, obesity 0, diabetes mellitus 2. Corresponding counts in the non-karst zone were: hypertension 17, hyperuricemia 22, obesity 1, diabetes mellitus 16. Work setting was classified as indoor for 6 karst and 28 non-karst participants, and outdoor for 14 karst and 43 non-karst participants. Scale formation when boiling water was noted by 17 karst and 45 non-karst participants, with negative responses from 3 and 26 participants, respectively.

Table 1. Demographic and Socioeconomic Characteristics of the Study Population.

Variable	Living area	
	Karst zone (n = 20)	Non-karst zone (n = 71)
Age, years	51.2 (27 – 80)	54.73 (29 – 80)
Sex		
Male	14 (70.0 %)	39 (54.9 %)
Female	6 (30.0 %)	24 (33.8 %)
Water source		
Distilled water	2 (10.0 %)	5 (7.0 %)
Groundwater (well)	17 (85.0 %)	53 (74.6 %)
Municipal water supply	1 (5.0 %)	13 (18.3 %)
Total water consumption		
≥ 2,500 mL	6 (30.0 %)	22 (31.0 %)
< 2,500 mL	14 (70.0 %)	49 (69.0 %)
Retaining urine habits		
No	7 (35.0 %)	26 (36.6 %)
Yes	13 (65.0 %)	45 (63.4 %)
Comorbid		
Hypertension	2 (10.0 %)	17 (23.9 %)
Hyperuricemia	3 (15.0 %)	22 (31.0 %)
Obesity	0 (0 %)	1 (1.4 %)
Diabetes Mellitus	2 (10.0 %)	16 (22.5 %)
Working environment		
Indoor	6 (30.0 %)	28 (39.4 %)
Outdoor	14 (70.0 %)	43 (60.6 %)
Scale appears when boiling water		
No	3 (15.0 %)	26 (36.6 %)
Yes	17 (85.0 %)	45 (63.4 %)

Incidence of nephrolithiasis per 100,000 population in karst districts was 10,989.011 in Ayah, 5,494.505 in Buayan, and 5,494.505 in Rowokele. Non-karst incidence values were: Karanganyar 10,989.011; Sempur 7,692.308; Kebumen 7,692.308; Gombong 7,692.308; Kuwarasan 6,593.407; Karanggayam 6,593.407; Sruweng 6,593.407; Puring 4,395.604; Adimulyo 4,395.604; Petanahan 4,395.604; Sadang 3,296.703; Alian 2,197.802; Klirong 2,197.802; Prembun 1,098.901 (Table 2; Figure 1).

Table 2. Geographical Distribution and Incidence Rates of Nephrolithiasis per 100,000 Population.

Rank	District(s)	Incidence rate per 100,000 population
Karst zone		
1	Ayah	10,989.011
2	Buayan	5,494.505
3	Rowokele	5,494.505
Non-karst zone		
1	Karanganyar	10,989.011
2	Sempor	7,692.308
3	Kebumen	7,692.308
4	Gombong	7,692.308
5	Kuwarasan	6,593.407
6	Karangayam	6,593.407
7	Sruweng	6,593.407
8	Puring	4,395.604
9	Adimulyo	4,395.604x
10	Petanahan	4,395.604
11	Sadang	3,296.703
12	Alian	2,197.802
13	Klirong	2,197.802
14	Prembun	1,098.901

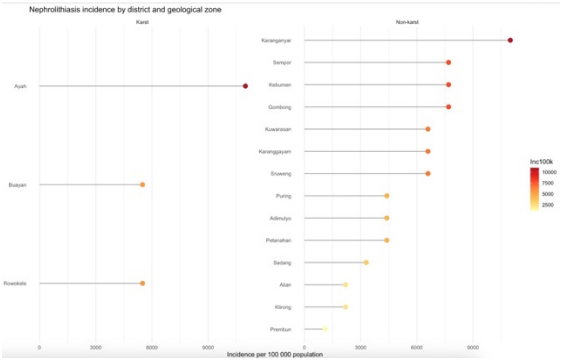

Figure 1. Lollipop Diagram Depicting Spatial Variability in Nephrolithiasis Incidence Across Villages.

Unadjusted RR estimates with 95 % confidence intervals (CI) and p-values were: female sex vs male RR 1.519 (0.522–4.422), p = 0.443; groundwater use vs distilled water RR 1.648 (0.428–6.345), p = 0.467; municipal supply vs distilled water RR 0.259 (0.032–2.123), p = 0.208. For total fluid intake < 2,500 mL vs ≥ 2,500 mL, RR 0.955 (0.324–2.812), p = 0.933. Urine retention yes vs no yielded RR 1.073 (0.380–3.030), p = 0.894. Hypertension, hyperuricemia, and diabetes mellitus produced RRs of 0.353 (0.074–1.678), 0.393 (0.104–1.418), and 0.382 (0.080–1.824) with p-values 0.190, 0.168, and 0.228, respectively. Outdoor vs indoor work gave RR 1.519 (0.522–4.422), p = 0.443. The appearance of scale when boiling water had an unadjusted RR 3.274 (0.876–12.243), p = 0.078 (Table 3).

Table 3. Unadjusted and Adjusted Odds Ratios for Risk Factors Associated with Nephrolithiasis in Karst and Non-Karst Zones.

Variable	Unadjusted	Adjusted
	RR (95% CI); p-value	
Age, years	-	-
Sex		
Male	Ref	Ref
Female	1.519 (0.522 – 4.422); 0.443	-
Water source		
Distilled water	Ref	Ref
Groundwater (well)	1.648 (0.428 – 6.345); 0.467	-
Municipal water supply	0.259 (0.032 – 2.123); 0.208	-
Total water consumption		
≥ 2,500 mL	Ref	Ref
< 2,500 mL	0.955 (0.324 – 2.812); 0.933	-
Retaining urine habits		
No	Ref	Ref
Yes	1.073 (0.380 – 3.030); 0.894	-
Comorbid		
Hypertension	0.353 (0.074 – 1.678);0.190	-
Hyperuricemia	0.393 (0.104 – 1.418); 0.168	-
Obesity	-	-
Diabetes Mellitus	0.382 (0.080 – 1.824);0.228	-
Working environment		
Indoor	Ref	Ref
Outdoor	1.519 (0.522 – 4.422); 0.443	-
Scale appears when boiling water of patient drinking water from the well		
No	Ref	Ref
Yes	2.142 (1.215 – 8.701); 0.033	1.157 (1.092 – 5.273); 0.041

Discussion

The findings of this study provide valuable insights into the relationship between geographic zones, environmental factors, and nephrolithiasis incidence. Notably, the prevalence of nephrolithiasis was observed to be higher in certain districts within both karst and non-karst zones, suggesting that geological and environmental characteristics may play a significant role in disease development. For instance, the karst zone, characterized by limestone-rich terrain, exhibited a higher frequency of scale formation during water boiling, which is indicative of mineral-rich water.[6] This observation aligns with existing literature suggesting that hard water, containing elevated levels of calcium and magnesium, may contribute to kidney stone formation.[7–9] Similarly, the non-karst zone demonstrated higher rates of comorbidities such as hyperuricemia and diabetes mellitus, which are known metabolic risk factors for nephrolithiasis. These findings underscore the complex interplay between environmental exposures and individual health conditions in shaping disease outcomes.

Hyperuricemia emerged as a particularly significant risk factor for nephrolithiasis, with multivariable logistic regression analysis revealing a fourfold increase in the odds of developing the condition among affected individuals. This finding is consistent with prior research highlighting the role of elevated serum uric

acid levels in promoting the crystallization of uric acid stones.[10] The adjusted RR further confirmed the independent contribution of hyperuricemia after controlling for potential confounders such as age, gender, and other comorbidities. Interestingly, while other comorbid conditions like hypertension and diabetes mellitus were more prevalent in the non-karst zone, they did not demonstrate statistically significant associations with nephrolithiasis in this study. This discrepancy may be attributed to the relatively small sample size or regional variations in disease etiology, warranting further investigation in larger cohorts.

The geographical analysis of nephrolithiasis incidence rates revealed notable spatial variability, with certain districts exhibiting significantly higher rates than others. For example, Tambak in the non-karst zone had the highest incidence rate, surpassing even the highest rates observed in the karst zone. This suggests that factors beyond geology—such as lifestyle, dietary habits, or access to healthcare—may also influence disease prevalence. The heatmap visualization effectively highlighted these disparities, enabling comparisons between high-risk and low-risk districts. Overlapping incidence rates between some districts in the karst and non-karst zones further indicate shared risk factors, such as reliance on groundwater or similar occupational environments. These findings emphasize the importance of adopting a multidimensional approach to understanding nephrolithiasis, considering both environmental and sociodemographic determinants.

From a public health perspective, the results of this study have important implications for targeted interventions aimed at reducing nephrolithiasis burden. For instance, Ayah District showed the highest incidence rate in this study. Residents in this area are advised to avoid using groundwater for daily consumption due to its high mineral content, which may contribute to stone formation. If groundwater use is unavoidable, it is recommended to let the water sit for at least 24 hours to allow minerals to settle before consumption, thereby reducing the potential lithogenic risk.[11] These strategies, tailored to the unique characteristics of each geographic zone, could contribute to a more effective and equitable approach to nephrolithiasis prevention.

Limitations

Despite its contributions, this study has several limitations that should be acknowledged. First, the cross-sectional design precludes the establishment of causal relationships between identified risk factors and nephrolithiasis incidence. Longitudinal studies are needed to explore temporal associations and validate the findings. Second, the relatively small sample size, particularly in the karst zone, may limit the generalizability of the results and the statistical power to detect significant associations for subgroup analyses.[12] Third, reliance on self-reported data for variables such as water consumption and urinary habits introduces the potential for recall bias, which could affect the accuracy of the findings. Additionally, serum uric acid testing was not performed systematically because this laboratory test is not consistently reimbursed by the national health insurance (BPJS Kesehatan); consequently, hyperuricemia and uric acid–related stone cases may have been underascertained, introducing possible misclassification and selection biases.[13] Finally, the study focused primarily on two geographic zones, which may not fully capture the diversity of environmental and lifestyle factors influencing nephrolithiasis across broader populations. Future research incorporating larger, more diverse cohorts and employing advanced methodologies, such as biomarker analysis, will be essential to address these limitations and further elucidate the multifactorial etiology of nephrolithiasis.

Conclusion

This study contributes valuable insights into the multifactorial etiology of nephrolithiasis and highlights the importance of adopting a multidimensional approach to disease prevention. By integrating environmental, metabolic, and

lifestyle considerations, healthcare providers and policymakers can develop more effective and equitable strategies to mitigate the burden of nephrolithiasis in high-risk populations. Future research should build on these findings by incorporating larger, more diverse cohorts and employing longitudinal designs to establish causal relationships and refine preventive measures.

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