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Relationship between BMI and Urine pH in Nephrolithiasis Cases in Indonesia

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Abstract

In nephrolithiasis/urolithiasis, urine pH is thought to modulate kidney stone formation at various stages, including crystallization, growth, aggregation, and retention. Moreover, numerous studies have demonstrated that an increase in Body Mass Index (BMI) correlates with a decrease in urine pH. This study aimed to determine the relationship between BMI and urine pH in cases of nephrolithiasis at Dr. Hasan Sadikin General Hospital Bandung. This was analytical observational study with a cross-sectional design, followed by correlation analysis is carried out. A total of 100 patients from January 2021 to December 2022 have met the inclusion criteria. From the results of the analysis, it was discovered that of the 21 patients with acidic urine pH, 42.11% had normal BMI, 26.32% were grade 1 obese, 15.79% were grade 2 obese, 10.53% were overweight, and 5.26% were underweight. The majority of patients who had normal urine pH also had a normal BMI (34.18%), followed by 30.38% with grade 1 obesity, 21.52% with grade 1 obesity, and 13.92% with grade 2 obesity. Of the 2 patients with alkaline urine pH, one person had a normal BMI and another had an overweight BMI. The results of the chi-square test presented a p value of >0.05, thus no significant relationship is observed between urine pH and BMI in nephrolithiasis patients.

Keywords: Body mass index, nephrolithiasis, urine pH

Introduction

Urine composition can be used to assess stone risk and monitor response to therapy in patients with nephrolithiasis/urolithiasis. In these conditions, urine pH is thought to influence kidney stone formation at various stages, including crystallization, growth, aggregation, and retention. Additionally, pH plays a crucial role in increasing solid-phase formation and affecting the solubility of kidney stones. Several types of stones, such as calcium oxalate (CaOx), calcium phosphate, and uric acid stones, are known to be influenced by urine pH. Alkaline urine pH favors the formation of phosphate-containing stones, while acidic urine pH is associated with uric acid and cystine stoness.[1–3]

A number of epidemiological studies have shown that there is a marked growth of urolithiasis concomitant with an increase in BMI. The patient's urine displays variations with rising BMI, which raise the possibility of urolithiasis. Reduced potassium, citrate, and urine pH levels together with higher calcium, oxalate, urate, and salt levels are these variations. Magnesium, phosphate, creatinine, and 24-hour urine output were all the same. These variations can lead to the development of calcium and uric acid stones.[4-5]

Due to the complex formation mechanism of urolithiasis, no single pathophysiological explanation can adequately explain how fat contributes to the development of urolithiasis at this time. It has been demonstrated that lithogenesis and insulin resistance are causally related. Insulin resistance reduces ammonia production and transport, which alters urine acidification and lowers urine pH. When urine pH falls below 5.5, less soluble uric acid can form from urine urate, potentially leading to uric acid stones even in the absence of hyperuricosuria.[6]

Compared to uric acid stones, the

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pathophysiological mechanism underlying calcium stones is more complicated. Low urine volume, hypercalciuria, hypocitraturia, hyperoxaluria, and abnormal urine pH levels are some of the mechanisms. It has been determined that hypercalciuria is the most important pathophysiological factor in calcium lithogenesis among them all. Hypercalciuria may result from absorption from the gastrointestinal tract, bone resorption, or renal leakage in the kidney. Consuming too much sodium can also cause calcium salts to crystallise, which can cause hypercalciuria and lower citrate levels, which are inhibitors of urolithiasis. Systemic acidosis and protein excess are additional potential causes of hypercalciuria. Additionally, a greater phospholipid AA level is the result of a systemic imbalance between the essential fatty acid (EFA) omega-3 and omega-6 pathways, which is what causes hypercalciuria and hyperoxaluria.[6]

Although a number of the aforementioned articles indicate an association between nephrolithiasis incidence, urine pH, and BMI, no research has been conducted in Indonesia to investigate the relationship between BMI and urine pH in nephrolithiasis cases to the author's knowledge.[7] Considering the diverse demographics and races within the population of Indonesia, the correlation between BMI and urine pH in nephrolithiasis cases may vary. This study aims to investigate the relationship between BMI and urine pH in nephrolithiasis cases at Hasan Sadikin Hospital, Bandung.

Methods

This research is an analytical observational study with a cross-sectional design, followed by correlation analysis. The data collected included cases of nephrolithiasis, BMI status, and urine pH. All samples meeting the inclusion and exclusion criteria were included as study subjects. The inclusion criteria for this study were nephrolithiasis patients at Dr. Hasan Sadikin General Hospital Bandung who had an overweight, obesity class 1, or obesity class 2 BMI (as per the Asia-Pacific BMI classification) and had documented stone status in the urology department of Dr. Hasan Sadikin General Hospital. The exclusion criteria included patients with conditions or factors that could lower urine pH, such as the use of acidic drugs or metabolic acidosis. Data were collected from nephrolithiasis records in the Department of Urology at Dr. Hasan Sadikin General Hospital, Bandung, between January 2021 and December 2022.

Statistical analyses were conducted in accordance with the research objectives and hypotheses. To compare the characteristics of the two research groups, the unpaired Mann-Whitney test was used as an alternative. For categorical data, statistical analysis was performed using the Chi-square test, with Fisher's Exact or Kolmogorov-Smirnov tests as alternatives. Significance was determined with a p-value threshold of ≤0.05, where p≤0.05 was considered statistically significant, and p>0.05 was considered not statistically significant. Data were recorded in a standardized form and processed using SPSS version 20.0 for Windows. Ethical approval for the study was granted by the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital Bandung under ethical approval number LB.02.01/X.6.5/467/2023.

Results

The research sample data were obtained from medical records in the Urology Department at Dr. Hasan Sadikin General Hospital Bandung, covering the period from January 2021 to December 2022. A total of 100 patients met the inclusion criteria and were included as research participants.

The data in Table 1 highlight a significant relationship between BMI and nephrolithiasis. The majority of nephrolithiasis patients fall within the normal BMI range (36%), followed by a notable proportion of obese (29%) and overweight (20%) patients. This distribution suggests that nephrolithiasis can occur across all BMI categories.

Table 1 Relationship Between BMI and Nephrolithiasis in Patients

Characteristics	Nephrolithiasis (n=100)	
	n	%
BMI		
Underweight (<18.5)	1	1
Normal (18.5–22.9)	36	36
Overweight (23–24.9)	20	20
Obesity 1 (25–29.9)	29	29
Obesity 2 (≥30)	14	14

Table 2 Relationship Between Urine pH and Nephrolithiasis Patients

Characteristics	Nephrolithiasis (n=100)	
	n	%
Urine pH		
Acidic pH (<5.5)	19	19
Normal pH (5.5–7.5)	79	79
Alkaline pH (>7.5)	2	2

The data in Table 2 reveal a notable relationship between urine pH and nephrolithiasis. A significant majority of nephrolithiasis patients (79%) exhibited normal urine pH levels. This distribution indicates that nephrolithiasis is most commonly associated with normal urine pH, although instances of both acidic and alkaline urine pH levels were also observed. These findings emphasize the importance of monitoring urine pH in nephrolithiasis patients.

The data in Table 3 illustrate the relationship between urine pH and BMI in nephrolithiasis patients. These findings suggest a complex interaction between BMI and urine pH, highlighting the prevalence of normal BMI across different urine pH levels, along with a notable presence of obesity and overweight in patients with normal urine pH. The Chi-square test yielded a p-value of >0.05, indicating no statistically significant relationship between urine pH and BMI in nephrolithiasis patients.

Discussion

This study examined 100 patients diagnosed with nephrolithiasis at Dr. Hasan Sadikin General Hospital Bandung from 2021 to 2022. The results indicated that there was no significant or strong relationship between BMI and the incidence of nephrolithiasis at this hospital. These findings contrast with an earlier study by Yoshimura et al.,[8] which concluded that a strong correlation existed between kidney stone occurrence and BMI. Their study suggested that elevated BMI is a risk factor for kidney stones in Japan (Asian population), even among individuals with relatively low BMI.

In the study by Yoshimura et al.,[8] a relationship was found between the incidence of kidney stones per 10,000 person-years and BMI. The high BMI group exhibited a higher cumulative incidence rate of kidney stones during the follow-up period. In comparison to the first BMI tertile (15.9–21.6 kg/m^2), the hazard ratio for kidney stone incidence was significantly higher in the third BMI tertile (23.8–35.6 kg/m^2).

One of the strengths of the previous study was that its participants were Japanese, a population where obesity is less common compared to Western populations. Given that Asians generally have a lower mean BMI than White populations, the study could have a significant impact on kidney stone prevention strategies. Additionally, it was the first study to examine the association between obesity and kidney stones using data from an Asian (Japanese) population.[8]

The study, nevertheless, has certain limitations. The statistical power of the study was initially inadequate due to the relatively small number of participants (n=5,984), with participants simply classified into tertiles. Therefore, a larger sample size should be investigated for more reliable results. Furthermore, the study did not collect data on dietary habits, making it impossible to completely rule out the possibility of confounding by dietary factors.[8] It is suspected that this factor may have also influenced the results of the research conducted at Dr. Hasan Sadikin General Hospital Bandung.

This study also showed that there was no

Table 3 Relationship between Urine pH and BMI in Nephrolithiasis Patients

BMI	Urine pH			Total	p-value
	Acidic	Normal	Alkaline		
	n (%)	n (%)	n (%)		
Underweight	1 (5.26)	0	0	1	
Normal	8 (42.11)	27 (34.18)	1 (50)	36	
Overweight	2 (10.53)	17 (21.52)	1 (50)	20	0.48
Obesity 1	5 (26.32)	24 (30.38)	0	29	
Obesity 2	3 (15.79)	11 (13.92)	0	14	

significant relationship between urine pH and the incidence of nephrolithiasis at Dr. Hasan Sadikin General Hospital Bandung. This result is in contrast to most of the results of other studies that have been conducted previously. Research conducted by Xu et al.[9] concluded that pH of the urine, which in calcium stone formers gradually increased. Meanwhile, according to Francisco et al.[10], the most common biochemical diagnosis in uric acid stones is excessively acidic urine pH. Many transport processes involved in the handling of calcium, citrate, and phosphate are sensitive to changes in systemic or local pH. These include phosphate transporters, the citrate transporter NaDC1, and the calcium channel TRPV5.[11,12]

Deficiencies in urinary acidification (inappropriate excretion of urine that is excessively alkaline or acidic) contribute to kidney stones. Elevated uric acid stone incidence and more acidic urine have been linked to low ammonium excretion in people with metabolic syndrome. In this case, proximal tubule ammonium excretion may be lowered due to insulin resistance.[13]

Additionally, Carvalho et al.[14] stated that kidney stone formation is significantly influenced by urine pH. When urine pH rises above 6, calcium phosphate supersaturation increases rapidly. The occurrence of calcium phosphate stones has been rising recently, and the combination of hypercalciuria and hypocitraturia in alkaline urine promotes the formation of these stones. nes.

Hyperchloremic acidosis (incomplete dRTA does not display metabolic acidosis under basal conditions), hypocitraturia, and high urine pH are the hallmarks of complete or incomplete distal renal tubular acidosis (dRTA), which might affect some people. dRTA is also brought on by certain medications, including as amphotericin B, foscarnet, analgesic misuse, lithium, melphalan, and amiloride.[15]

Consistently low urinary pH levels are typically linked to uric acid urolithiasis. The majority of individuals with uric acid calculi excrete normal levels of urate, and nearly all exhibit persistently low urine pH. This reaction has a first acid dissociation constant (pKa) of 5.5 pH. In aqueous solutions at 37°C, the solubility constant (Ksp) of uric acid is approximately 100 mg/L. Uric acid deposition is likely to occur if 200 mg of urate is added to a 1-L aqueous solution with a pH of 5.5 at 37°C. Of this amount, 100 mg will convert into uric acid, and the remaining portion will remain as urate.[16]

A higher pH of urine than 6.7 increases the incidence of calcium phosphate stones. Monohydrogen phosphate has a pKa of around 6.7. Monohydrogen phosphate is more abundant at pH values greater than the pKa. Monohydrogen phosphate complexes with the divalent cation calcium (Ca2+) to create brushite, which then transforms into hydroxyapatite. Conversely, low urine pH is the main cause of uric acid nephrolithiasis because it promotes urate protonation, which results in comparatively insoluble uric acid that precipitates in this excessively acidic urine environment. Urate excretion usually increases twofold in circumstances of enhanced urate synthesis, but urine pH declines from 6.0 to 5.0, increasing the concentration of uric acid six-fold. Consequently, urine pH has a greater influence on uric acid stone production than urine volume or uric acid concentrations.[17]

The results of this study show that there is no strong and significant relationship between urine pH and BMI in nephrolithiasis patients at RSUP Dr. Hasan Sadikin Bandung. This is known from the p-value>0.05. The association is said to be significant if the p-value <0.05. These results are not in line with the majority of previous research results. Shavit et al.[7] concluded that urine pH is inversely related to body weight in patients with kidney stones.

In the study by Shavit et al.,[7] it was found that urine pH significantly decreased with increasing body weight. A possible explanation for the progressive decrease in urinary pH with higher body weight is insulin resistance, which reduces renal ammonia excretion and impairs hydrogen ion balance. Previous studies have shown that insulin plays a critical role in kidney ammonia synthesis and excretion through the activation of sodium hydrogen exchanger 3 (NHE3).[18,19] Thus, low insulin bioactivity (resulting from insulin resistance from obesity) in the renal proximal tubule could theoretically lead to impaired ammonium production and/or excretion, and thereby predispose the urine to low pH.[8]

This is consistent with reports indicating that uric acid is more commonly encountered as a stone constituent in diabetic patients with stones compared to the general population of patients with stones.[20] Taken together, these results suggest that insulin resistance may be a key factor in the development of gouty diathesis or idiopathic uric acid nephrolithiasis

The strength of this research is that this research is one of the initial analytical studies that examine the relationship between BMI and

urine pH in patients with nephrolithiasis in Indonesia.

A limitation of this research is that the data were retrospective, derived from medical records, which prevents the study from establishing causal relationships. Additionally, confounding factors, such as selection bias in data collection, are difficult to eliminate when using retrospective data. Errors in medical record documentation cannot be ruled out, and due to the limited completeness of data in medical records, researchers had to request additional information from relevant parties, increasing the risk of recall bias. Lastly, the researcher acknowledges that the sample size in this study was relatively small and hopes that future research on this topic can involve a larger sample size and address the limitations of this study.

The results of several previous studies suggest that the relationship between BMI and urine pH in nephrolithiasis patients is strongly influenced by insulin resistance, particularly in obese patients with diabetes. This may explain why no strong or significant relationship was found between urine pH and BMI in nephrolithiasis patients at Dr. Hasan Sadikin General Hospital Bandung. Not all obese patients in the study had diabetes, which may have prevented noticeable changes in urine pH. Additionally, factors such as dietary habits, which were not accounted for in the study, may have influenced the findings. Furthermore, selection bias could have occurred, and the small sample size may limit the generalizability of the results to the broader population.

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