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The relationship between urine specific gravity, urine pH, and blood uric acid levels to the type of urinary stones of patients with urolithiasis at Sanglah Hospital, Bali, Indonesia



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ABSTRACT

Background: Urine specific gravity, urine pH, and blood uric acid levels are risk factors for urinary tract stones. The urinary tract stones are formed due to the concentration of a solute exceeds its ability to remain in solution, resulting in supersaturation and crystallization. This study aims to determine the relationship between urine specific gravity, urine pH, and blood uric acid levels to the urinary stone's types in patients with urolithiasis at Sanglah Hospital

Methods: A retrospective cross-sectional study was conducted among 95 subjects by using secondary data from the medical records in the period June 2017-2018 at Sanglah Hospital. The urolithiasis patient who met the inclusion and exclusion criteria were enrolled in this study. Data were analyzed by the Mann-Whitney Test and Kruskal-Wallis Test using SPSS version 17 for Windows.

Results: The average age was 55±11 years old. Most of respondents were male (70.5%), normal Body Mass Index (BMI) (89.5%), urine pH <7 (75.7%), and mixed type of urinary stones (48.4%). There was a statistically significant relationship between the type of uric acid stone (p=0.029), blood uric acid levels (p=0.003), phosphate stone type (p=0.026), and magnesium stone (p=0.010) with urine pH. Besides, there was a statistically significant relationship between ammonium stone and blood uric acid levels types (p=0.022). A statistically significant difference was also found between stone types based on urine pH (p=0.013) in multivariate analysis.

Conclusion: There is a significant relationship between urine pH and stone type on the incidence of urolithiasis in Sanglah Hospital in June 2017-2018, thereby increasing the incidence of urolithiasis.

Keywords: Urinary tract stones, urine pH, urine specific gravity, blood uric acid

Cite This Article: Kalembang, J., Oka, A.A.G., Widiana, I.G.R. 2020. The relationship between urine specific gravity, urine pH, and blood uric acid levels to the type of urinary stones of patients with urolithiasis at Sanglah Hospital, Bali, Indonesia. *Intisari Sains Medis* 11(2): 566-570. DOI: 10.15562/ism.v11i2.744

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INTRODUCTION

Urinary stones or urolithiasis is a pathological state for their mass as hard as a rock formed along the urinary tract.¹ It can cause pain, bleeding or infection in the urinary tract.^{1,2} Globally, urolithiasis is the third most common urological disease found in men and women.³ It has been reported that the prevalence of kidney stone disease is 1 to 5% in Asia, 5 to 9% in Europe, 13% in North America.⁴

Based on previous research conducted at Sanglah Hospital, the highest proportion of urolithiasis was ≥ 50 years old, which was 53.2%, more often than men compared to women with a ratio of 3:1.⁵ The highest proportion of urinary tracts originating from the kidneys is 59.6%. The composition of urinary tract stones is as follows Calcium Oxalate 72.3%, Calcium Phosphate 42.5%, Uric Acid 17%, Cystine 34.7%, Struvite 67.4%, and others 17%.⁵

Individual risk for experiencing urinary tract stones can be analyzed from biochemical factors such as urine volume, urine pH and blood uric acid levels.⁶ Urinary tract stones are formed when

the concentration of a solute exceeds its ability to remain in solution (solubility balance).⁶ Stone settles in the urinary tract when there is an excess amount of substances in the urine. This situation is called supersaturation which is the most important cause in the process of the stone.⁷ Changes in urine pH toward more acidic or more alkaline will encourage the formation of different types of stones.⁷

Factors such as increased calcium excretion, lower urine output, dehydration, diet, low urine citrate, genetic factors, and environmental disorders (ambient temperature) can contribute to increased supersaturation of urine salt, lower urine pH, and decreased urine volume, which in ultimately causes crystallization.⁸ In addition, the condition of hyperuricemia is related to age, male sex, hypertension, diabetes mellitus, hypertriglyceridemia, obesity, and insulin resistance. Some of these conditions are factors that can affect the decrease in urine pH.⁸

Based on the explanation above, this study aims to determine the relationship between urine specific

Received: 2020-04-08

Accepted: 2020-06-30

Published: 2020-07-19

gravity, urine pH, and blood uric acid levels to the type of urinary stones of patients with urolithiasis at Sanglah Hospital, Bali, Indonesia.

METHODS

A retrospective cross-sectional study has been conducted to determine the relationship between urine specific gravity, urine pH and blood uric acid levels with urinary tract stone types in patients with urolithiasis in Sanglah General Hospital. A thorough observation of the 95 patient's medical records at the Medical Records installation of Sanglah General Hospital in Denpasar during June 2017-2018 was carried out.

The inclusion criteria were those who had stones in the urinary tract recorded confirmed by X-ray or ultrasound results during the study period. Urinary Stone Type is divided into Acid type stones (urine pH <7), Alkaline type stones (urine pH > 7) and mixed stones (consisting of a combination of acid and base stone components). The results of urine pH levels are categorized into acidic pH (<7) and alkaline pH (> 7). Urine Specific Gravity is divided into <1,003 and > 1,035. Blood Uric Acid levels are divided into <3.5 mg/dl and > 7 mg/dl in men and <2.5 mg/dl and > 5.7 mg / dl in woman. The Body Mass Index (BMI) is divided into normal/ideal (18.5-25.0 kg/m²), overweight (25.1-29.9 kg/m²), underweight (<18.5 kg/m²), and obese (>30 kg/m²).

The data collected was analyzed by univariate, bivariate and multivariate analysis. The univariate analysis describes the characteristics of the subjects and research variables. The bivariate analysis was assessed by the Mann-Whitney Test due to data was not normally distributed. The multivariate analysis was conducted to determine the differences in stone types based on urine pH, urine specific gravity and blood uric acid by Kruskal-Wallis Test. The level of significance is determined if the p-value <0.05. The data obtained were analyzed with SPSS version 17 for Windows.

RESULTS

The characteristics of respondents can be depicted in Table 1, where the average age of respondents was 54.6 ± 11.39 years. Most of the respondents were male (70.5%) compared with the female (29.5%). Also, most of respondent's Body Mass Index (BMI) is in the normal category (89.5%), followed by urine pH in the acidic category (<7) (75.7%), normal urine specific gravity (93.7%), uric acid levels high (57.9%), and have mixed type stones (48.4%) (Table 1).

Characteristics of urinary tract stones can be seen in Table 2, where acid stones are a type of uric

acid stone, calcium phosphate, and cystine stones. Alkaline stones are calcium oxalate stones, struvite stones, and ammonium urate stones. Mixed stone, is a rock consisting of acidic and basic elements. Oxalate stones were obtained more than other stones, namely (72.6%), phosphorus stones (56.8%) uric acid stones 46 (48.4%), magnesium stones 17 (17.9%) and ammonia stones 5 (5.3%) (Table 2).

Table 3 shows a significant relationship between urine pH and blood uric acid based on uric acid stone type with (p=0.029 and 0.003, respectively) while urine specific gravity is not significantly different. Based on the type of oxalate stone urine pH, urine specific gravity and blood uric acid with p-value > 0.05, which means there is no significant relationship (Table 3). Based on the type of phosphate stone urine pH obtained (p=0.026), which means there is a relationship between urine pH based on the type of phosphate stone. In contrast, urine specific gravity and blood uric acid has no significant association (Table 3).

Based on the type of ammonium stone found a significant relationship with uric acid (p=0.022) while the urine pH and urine, specific gravity did not have a significant relationship. Based on the type of magnesium stones found a significant correlation with urine pH (p=0.010) while the specific gravity of urine and blood uric acid had no significant relationship (Table 3).

Table 4 shows that there is only a significant relationship between stone types based on urine pH (p=0.013). In comparison, there is no significant relationship between urine specific gravity to the type of stones (p=0.779) and blood uric acid levels (p=0.640) (Table 4).

DISCUSSION

From 95 respondents involved in this study, it was found that the average age in this study was 54.6 years with a male as the predominant gender. Urolithiasis incidence between 120 to 140 per 1000,000 people each year, male/female ratio 3: 1. Several factors are known to influence the incidence of urolithiasis.⁹ The incidence of stone disease is relatively rare before the age of 20, but the peak occurrence occurs in the fourth - sixth decade of life.⁹ Previous studies have shown the bimodal distribution of stone disease, with a second peak of stone disease incidence in the sixth decade of life, according to the onset of menopause.¹⁰ This is associated with the protective effect of estrogen on stone formation in premenopausal women, because it increases renal calcium absorption and reduces bone resorption, coupled with a slightly different metabolism between sexes.¹⁰

In this study, we found a significant relationship between urine pH and stone types. Urine pH

Table 1 Baseline Characteristic of Respondents

Variables	Mean±SD	N=95
Age (Years)	54.65±11.39	
Gender, n (%)		
Male		67 (70.5)
Female		28 (29.5)
Body Mass Index (BMI), n (%)		
Overweight		8 (8.4)
Normal		85 (89.5)
Underweight		2 (2.1)
Urine pH, n (%)	6.107±0.759	
Acid		72 (75.7)
Normal		16 (16.8)
Alkaline		7 (7.5)
Urine Specific Gravity, n (%)	1.010±0.005	
Normal		89 (93.7)
Abnormal		6 (6.3)
Blood Uric Acids, n (%)	7.30±2.10	
Normal		40 (42.1)
High		55 (57.9)
Type of Stones, n (%)		
Acid		38 (40.0)
Alkaline		11 (11.6)
Mixed		46 (48.4)

Table 2 Types of Urinary Stones Based on Stone Analysis

Type of Urinary Stones	n=95
Uric Acid, n (%)	
Negative	49 (51.6)
Positive	46 (48.4)
Oxalate, n (%)	
Negative	26 (27.4)
Positive	69 (72.6)
Cystine, n (%)	
Negative	95 (100.0)
Positive	0 (0.0)
Phosphorus, n (%)	
Negative	41 (43.2)
Positive	54 (56.8)
Ammonium, n (%)	
Negative	90 (94.7)
Positive	5 (5.3)
Magnesium, n (%)	
Negative	78 (82.1)
Positive	17 (17.9)

is a measure of urine hydrogen concentration. A pH below 7 indicates acidic urine and pH above 7 indicates alkaline urine. Excessive acid urine, with a pH lower than 7.0, is excreted by patients on a high protein diet.¹¹ Patients with uncontrolled acidosis and diabetes mellitus secrete urine containing large amounts of acid.¹² Alkaline urine is often excreted after food as a normal response to HCL secretion in the stomach.¹³ Alkaline urine occurs in individuals who consume foods high in vegetables, citrus fruits, milk and milk products.¹³ Certain medications, such as sodium bicarbonate, potassium citrate, and acetazolamide, has been known related to the formation of alkaline urine. Alkaline urine may indicate whether a urinary tract infection or possible bacterial contamination of the specimen.¹⁴ Acidic or alkaline urine will affect the solubility of various metabolites and salts. Alkaline urine decreases the solubility of calcium phosphate products, while acidic urine pH triggers the formation of stones containing uric acid or cystine. Changes in systemic pH homeostasis as in the case of metabolic acidosis will change the concentration of various substances in the urine that play a role in the formation of crystals (e.g. calcium, phosphate) and other substances that prevent the formation of stones (citrate or magnesium).¹⁵ Shaafie et al. found an association between a decrease in urine pH and an increase in urine specific gravity with the formation of urinary tract stones.⁸ However, the uric acid solubility decreases dramatically when the urine pH level decreases <7 and finally triggers the formation of uric acid crystals. The solubility of calcium oxalate is influenced by changes in urine pH which ultimately causes supersaturation and crystallization.¹⁶

The results showed the specific gravity of urine was not related to the type of urinary tract stones. This is due to the specific gravity of urine in this study found that most of the results were normal (93.7%). Urine specific gravity is closely related to diuresis, the greater diuresis, the lower specific gravity found, and vice versa.¹⁷ The more concentrated urine, the higher the specific gravity. Urine that has more than normal density can be caused by fever and dehydration.¹⁸ In contrast, urine density less than normal can be caused by excessive fluid intake, hypothermia, alkalosis and chronic kidney failure.¹⁸ Low urine volume is a major factor that plays a role in the formation of uric acid stones because the urine environment will experience supersaturation if there is a uric acid salt.¹⁹

The results of blood uric acid in the study showed as many as 55 respondents were found with high blood uric acid (57.9%) while normal blood uric acid was found as many as 40 respondents (42.1%).

Table 3 The relationship between urine pH, urine specific gravity, and blood uric acid levels with the type of stones

Type of Stones	pH urine		Urine Specific Gravity		Blood Uric Acid	
	Mean Difference	p-value	Mean Difference	p-value	Mean Difference	p-value
Uric Acid						
Positive	41.83	0.029	52.95	0.089	56.70	0.003
Negative	53.80		43.36		39.84	
Oxalate						
Positive	45.88	0.208	47.24	0.660	47.57	0.802
Negative	53.63		50.02		49.15	
Phosphorous						
Positive	53.31	0.026	49.66	0.500	47.09	0.713
Negative	41.00		45.82		49.20	
Ammonium						
Positive	55.40	0.525	70.70	0.058	20.50	0.022
Negative	47.59		46.74		49.53	
Magnesium						
Positive	63.21	0.010	44.18	0.527	36.65	0.061
Negative	44.69		48.83		50.47	

Table 4 Stone Types Based on Urine pH, Urine Specific Gravity, and Blood Uric Acid Levels by Kruskal-Wallis test

Variable	Type of Stones	Mean	p-value
Urine pH	Acid	39.01	0.013
	Alkaline	62.82	
	Mixed	51.88	
Urine Specific Gravity	Acid	45.71	0.779
	Alkaline	51.36	
	Mixed	49.09	
Blood Uric Acids	Acid	50.54	0.640
	Alkaline	41.86	
	Mixed	47.37	

The number of respondents with high blood uric acid is different from normal but not statistically related to the type of stone. Uric acid in urine is more easily dissolved in a higher pH so that under low pH conditions, uric acid crystals are more easily formed.²⁰ The low urine pH is influenced by several things, such as a high animal protein diet, the presence of gout, obesity, and insulin resistance, and diarrhoea.²⁰ Low urine volume can be caused by lack of fluid intake or diarrhoea conditions. At the same time, hyperuricosuria is caused by hyperuricemia. According to a previous study, the condition of hyperuricemia is related to age, male sex, hypertension, diabetes mellitus, hypertriglyceridemia, obesity, and insulin resistance.²¹ Some of these conditions are factors that can affect the decrease

in urine pH. Therefore, hyperuricemia does not directly affect the formation of uric acid stones. The indirect effect of hyperuricemia is caused by its impact on the pH reduction factor. Hyperuricemia conditions will not necessarily immediately make someone suffer from gout. Besides, hyperuricemia is not the only factor influencing the formation of uric acid stones.²²

CONCLUSION

Based on the composition of urinary tract stones, there is a significant relationship between urine pH with the formation of uric acid stones, phosphate stones, and magnesium stones. In addition, this study shows that there is a significant relationship

between blood uric acid and ammonium stone formation. From the multivariate analysis test, it was found that urine pH was significantly related to the type of urinary tract stones.

CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

ETHICS CONSIDERATION

Ethics approval has been obtained from the Ethics Committee, Faculty of Medicine, Universitas Udayana, Sanglah General Hospital, Bali, prior to the study being conducted.

FUNDING

None.

AUTHOR CONTRIBUTION

All of the authors are equally contributed to the study from the conceptual framework, data gathering, data analysis, until interpreting the results of study through publication.

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