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Association between age, urine pH, and urinary stone incidence in Kardinah Tegal General Hospital, Indonesia

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ABSTRACT

Introduction: An increase in the incidence of urolithiasis at age > 15 years in Indonesia provides increased morbidity and medical costs. The study aims to determine the association between age, urine pH, and urinary stones incidence in Kardinah Tegal General Hospital, Indonesia.

Method: There were 240 subjects from July to August 2019, with urolithiasis in Kardinah Tegal General Hospital who never received any previous treatment for urolithiasis. Subjects were divided into 120 subjects in case group and 120 subjects in control group. Medical records were assessed and reviewed for age, gender, urinalysis (including urine pH), urinary tract infection (UTI), and urinary stones incidence. Kolmogorov-Smirnov was used to assess data distribution of age and urine pH, and Chi-square test was used to evaluate the association between each age category and urinary pH.

Results: Subject's mean age between urolithiasis and non-urolithiasis groups were 47.68 ± 11.74 and 55.49 ± 15.72 years old, respectively There are no significant differences in stone incidence according to urinary pH in both groups. Stone incidence was found to be highest in age group of 50-59 years old in acidic urinary pH. No age group and urinary pH were associated with stone incidence. The odds of urinary stones occurrence would be 0.689 times more likely to happen with the increase of urinary pH.

Conclusion: There was significant difference of age between urolithiasis and non-urolithiasis groups. No age group and urinary pH were found associated with stone incidence, however the increase of age and urinary pH, increase the odds of developing urinary stones.

Keywords: age; gender; urine pH; urolithiasis; non-urolithiasis

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INTRODUCTION

Urinary stones or urolithiasis is one issue that is considered as a health problem in life. The incidence of urolithiasis is estimated at 10-15% of the global population.[1] Urolithiasis cases in North America are estimated around 7-13%, 5-9% in Europe, and 1-5% in Asia. In South Korea, the prevalence of urolithiasis from the year 1998 to 2013 increased from 3.5% to 11.5%.[2] In developing countries such as India, Thailand, and Indonesia, the prevalence ranges around 2%-15%, this is due to the effect of the economic development of those countries.[3,4]

In Indonesia, the exact number of urolithiasis prevalence is still unknown. However, there were an estimated 170,000 cases each year. According to Riskesdas 2013, the incidence of urolithiasis in people age>15 years in West Java was at top 5 from 33 provinces in Indonesia.[5] Urolithiasis cases in Cipto Mangunkusumo Hospital 1997 – 2002 were increased. In 1997 there were 182 cases, and then increased to 847 cases in 2002.[6]

Some risk factors lead to stone formation in the urinary tract, one of which is pH. Acid-base plays a role in the creation of stones in the urinary tract. Normal urine pH ranges from 4.6 to 8.0. A decrease in pH can occur due to the consumption of high protein, drugs such as methionine ammonium chloride, and both metabolic and respiratory acidosis, while an increase in urine pH can occur due to the consumption of drugs such as sodium bicarbonate, potassium citrate, and acetazolamide.[7] Urine pH is a determinant of stone formation in the urinary tract. Urea splitting bacteria such as *Klebsiella sp., Proteus sp*., and *Pseudomonas sp.*can increase the pH of urine and form magnesium-ammonium phosphate stone. Low urine pH often triggers the formation of uric acid stones and calcium-oxalate stone.[8]

Age is one intrinsic factor of urinary tract stones formation. Urinary tract stones are formed more common in the age 30-60.[9] A study conducted by Ratu et al. stated that most patients with urinary tract stones are in the range 31 - 45 age. Besides, urinary tract stones are also found in children aged <15 years, the age of the youngest is two years old, and the oldest is 86, with an average value 49.5.[10] The aim of this study is to determine the association

between age, urine pH, and urinary stones incidence in Kardinah Tegal General Hospital, Indonesia.

MATERIAL AND METHODS

Subject and Data Collection

The target populations for this study were all adult patients (18 years old) with urolithiasis in Kardinah Tegal General Hospital who never received any previous treatment for urolithiasis. The exclusion criteria for this study were patients with anatomical abnormalities and congenital defects in the urinary tract. All patients' data were collected from medical records starting from July to August 2019. During period of enrollment, there were 240 subjects, divided into 120 subjects in case group and 120 subjects in control group. Medical records were assessed and reviewed for age, gender, urinalysis (including urine pH), urinary tract infection (UTI), and urinary stones incidence.

Data Analysis

We used Kolmogorov-Smirnov to assess data distribution of age and urine pH. Normally distributed data were presented as mean and standard deviation while median, minimum, and maximum value. Mean differences between categorical and numeric variables were identified using the Unpaired-T test for normally distributed or Mann-Whitney U-test for not normally distributed data. To assess association between each age category and urinary pH, we used Chi-square test. We further performed multivariate analysis using logistic regression method. All statistical analysis was performed using SPSS version 25.0. (SPSS Inc., Chicago, IL. USA). All values considered significant if $p<0.05$.

RESULTS

In this study, we collected data from 240 subjects, with 120 subjects in each group. Data regarding age, gender, presence of crystalluria and UTI, type of crystal, urinary pH, specific gravity, and urinary stones incidence were gathered. The subjects characteristics were shown in Table 1.

The majority of subjects in both groups were male, with male and female ratio in urolithiasis group and non-urolithiasis were 77 vs. 43 and 88 vs. 29. Subjects' mean age between urolithiasis and non-urolithiasis groups were quite different, 47.68 ± 11.74 and 55.49 ± 15.72 years old, respectively. Urolithiasis was observed to mostly occur in patients between 50-59 years old (Figure 1). More than half (58.3%) subjects with urolithiasis had UTI. Urinary

Table 1 Characteristics of subjects

Variable	Case (n=120)	Control (n=120)	p-value*
Gender (n)			
Male	77	91	-
Female	43	29	-
Age in years (mean ± SD)	47.68 ± 11.74	55.49 ± 15.72	0.068
Stone location (n)			
Ureter	38	-	-
Renal	61	-	-
Bladder	15	-	-
UPJ	2	-	-
UVJ	1	-	-
Pyelum	3	-	-
UTI (n)			
Present	70	47	-
Absent	50	73	-
Proteinuria (n)			
Present	37	30	-
Absent	83	90	-
Urinary pH (median [min-max])	5.0 (5.0-8.0)	5.0 (5.0-9.0)	<0.001
Specific gravity (median [min-max])	1.010 (1.000-1.030)	1.010 (1.000-1.030)	<0.001

*normality test of numeric variable was performed using Kolmogorov-smirnov
Abbreviations: UPJ, ureteropelvic junction; UVJ, ureterovesical junction; UTI, urinary tract infection.

Table 2 Association between age, urinary pH, and stone incidence

Variable	Case (n=120)	Control (n=115)	MD (95% CI)	p-value
Age (years)	47.68 ± 11.74	55.49 ± 11.72	7.81 (4.26 – 11.37)	<0.001t
Urinary pH	5.0 (5.0-8.0)	5.0 (5.0-9.0)	-	0.266[m]

t) Unpaired T-test; m) Mann-Whitney U-test; MD (mean difference; 95% confidence interval)

Table 3 Association of urinary pH, age group, and stone incidence

	Urinary pH						
	Acidic≤ 5.5		Normal 5.6-6.4		Alkaline≥ 6.5		
Age (yr)	Case (%)	Control (%)	Case (%)	Control (%)	Case (%)	Control (%)	p-value*
20-29	2 (3)	4 (6)	1 (5)	2 (4)	1 (4)	3 (9)	0.956
30-39	18 (23)	9 (13)	6 (32)	1 (7)	8 (35)	5 (14)	0.527
40-49	23 (29)	11 (16)	4 (21)	2 (14)	4 (17)	4 (11)	0.671
50-59	**24 (31)**	12 (17)	4 (21)	1 (7)	7 (30)	7 (20)	0.283
60-69	12 (15)	26 (37)	2 (11)	2 (14)	3 (13)	8 (23)	0.705
70+	1 (1)	8 (11)	2 (11)	6 (43)	0 (0)	8 (23)	0.203
Total	78 (100)	70 (100)	19 (100)	14 (100)	23 (100)	35 (100)	0.168

*P-value was estimated using Chi-square test

Table 4 Multiple logistic regression model for prediction of urinary stones

Variable	OR	95% CI	p-value
Age (years)	0.961	0.942-0.980	0.059
Urinary pH	0.689	0.506-0.938	**0.018**

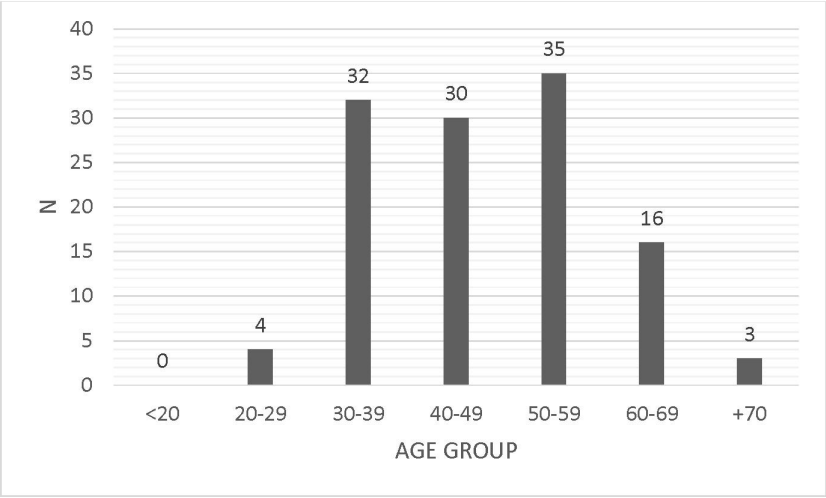

Figure 1 Incidence of stones according to age group

pH and specific gravity between both groups were found quite similar. Proteinuria was observed to be more frequent in urolithiasis group compared to control, 37/83 vs. 30/85. Furthermore, we used Unpaired T-test or Mann-Whitney U-test to identify mean difference (MD) between both groups. The mean difference of age between urolithiasis group and non-urolithiasis group was found to be significant (p<0.001) with MD of 7.81 (4.26-11.37). Differences in stone incidence according to urinary pH in both groups were not statistically significant (p=0.266) (Table 2 and Table 3).

Further association analysis between urinary pH and stone incidence according to each age group was performed using Chi-square. Stone incidence was found to be highest in age group of 50-59 years old in acidic urinary pH. However, no age group and urinary pH were associated with stone incidence. Furthermore, we also observed that with the increase of urinary pH, the odds of urinary stones occurrence would be 0.689 times more likely to happen (p=0.018). (Table 4)

DISCUSSION

In this study, total 240 subjects were divided into two groups, 120 in urolithiasis group and 115 in non-urolithiasis group. The majority of subjects in both groups were male (64.2% and 76.5%). Though urolithiasis could occur in both sexes, urolithiasis is frequently found in male compared to female.[11] Therefore, these findings are similar to some previous studies regarding the prevalence of urolithiasis, especially in developing countries like Indonesia, e.g. Iran (1.15:1), Thailand (1.6:1), Iraq (2.5:1), and Saudi Arabia (5:1).[12-15]

The mean age of subjects in both groups was also different, which were 47.68 ± 11.74 (urolithiasis group) and 55.49 ± 11.72 (control group). These findings were quite similar with Mat et al., who observed that the highest incidence of urinary stones

occurred in 40–49 years old males and 50–59 years old females respectively.[16] Trinchieri in his systematic review state that there are dietary risk factors that differ in terms of age and age. In younger women, consumption of calcium, phytate, and fluid intake has a relationship with a reduced risk of the stone formation while animal protein and sucrose increase the incidence of stone. In older populations, there is no relationship between calcium consumption and stone formation. On the other hand, magnesium, potassium, and fluid intake will reduce the risk of symptomatic nephrolithiasis, while total vitamin C intake has the opposite effect.[17]

In patients with suspected UTI, alkaline urine (pH>7.5) describes infection with microorganisms that produce urea, such as Proteus. Bacteria that produce urea convert ammonia into ammonium ions which can significantly increase urine pH and cause precipitation of calcium crystals from magnesium ammonium phosphate. Massive crystallization can produce kidney stone. Urine pH usually tends to be acidic in patients with gout or cystine stones, where urine alkalinization is an essential therapy for both conditions.[18] Even though, from the theory urinary pH could affect stone formation, we found differences between urinary pH in both groups were not significant. Since we did not perform specific stone analysis, we assumed that the type of stone might be difficult to assess based on pH for we were not able to distinguish whether stones were formed in acidic or alkalinized condition. Therefore, we suggest this finding needs to be further investigated to objectively match stones and their formation.

CONCLUSION

According to this study, there was significant difference of age between urolithiasis and non-urolithiasis group. No age group and urinary pH were found associated with stone incidence, however the increase of age and urinary pH, increase the odds of developing urinary stones.

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ETHICAL CONSIDERATION

Current study has been approved by Ethical Committee Kardinah Tegal General Hospital, Indonesia with ethical clearance reference number 12/KEPK/RSUK/VII/2019.

DISCLOSURE

The author reports no conflict of interest in this work.

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