THE ASSOCIATION OF URINARY SPECIFIC GRAVITY AND ACIDITY WITH UROLITHIASIS

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ABSTRACT

Objective: *This study aimed to know the association between urinary specific gravity and acidity with the formation of urolithiasis.* ***Material & Methods:*** *This retrospective descriptive study was conducted among proven urolithiasis patients reporting to the Kardinah Hospital, Tegal. The patient's age, gender, anatomical sites of the stone, and biochemical parameters were obtained from the case records. The correlation of kidneys stone with specific gravity and pH changed according to anatomical sites of stone was analyzed by One way Anova.* ***Results:*** *The resulted show urinary stones patients with lower pH tend to have a higher probability of stone formation but not specific to its location. Higher pH values were found in the patient with urinary stones at the kidney, ureter, and also bladder. The average of specific gravity in ureter stone patients was lower than stones on other sites. One-way ANOVA shows no statistically significant difference in patient's urinary pH with stones on different sites, but there is a statistically significant difference in specific gravity examination ($p<0.05$) on ureter stone patients compared to other locations. There is a statistically significant difference ($p=0.000$) of urine specific gravity of ureter stone compared to other anatomical sites with the lower mean value.* ***Conclusion:*** *A decrease in urinary pH is associated with the risk of urinary stone formation. The specific gravity value of the patient's urine with kidney and bladder stones is higher than the patient with ureter stones but there is no association of urine specific gravity toward the risk of urinary stone formation.*

Keywords: *Urine pH, specific gravity, urolithiasis, anatomical sites.*

ABSTRAK

Tujuan: *Penelitian ini dilakukan untuk mengetahui hubungan antara gravitasi spesifik kemih dan keasaman dengan pembentukan urolitiasis.* ***Bahan & Cara:*** *Penelitian deskriptif retrospektif ini dilakukan pada pasien urolitiasis yang dirawat di rumah sakit Kardinah, Tegal. Usia pasien, jenis kelamin, lokasi anatomi batu dan parameter biokimia diperoleh dari catatan kasus. Korelasi batu ginjal dengan gravitasi spesifik dan pH berubah sesuai dengan lokasi anatomi batu yang telah dianalisis oleh ANOVA One-Way.* ***Hasil:*** *Pasien batu kemih dengan pH yang lebih rendah cenderung memiliki probabilitas lebih tinggi dari pembentukan batu tetapi tidak spesifik pada lokasinya. Nilai pH tertinggi ditemukan pada pasien dengan batu kemih pada ginjal, ureter dan kandung kemih. Rerata gravitasi spesifik pada pasien batu kemih lebih rendah dari batu di lokasi lain. Analisis ANOVA One-way menunjukkan tidak ada perbedaan signifikan secara statistik antara pasien pH urin dengan batu di lokasi yang berbeda, tetapi terdapat perbedaan signifikan dalam pemeriksaan gravitasi tertentu ($p<0.05$) pada pasien batu ureter dibandingkan dengan lokasi lain. Perbedaan signifikan secara statistik ($p=0.000$) pada urin gravitasi spesifik dan batu ureter dibandingkan dengan lokasi anatomi lain dengan nilai yang lebih rendah.* ***Simpulan:*** *Penurunan pH urin dikaitkan dengan risiko pembentukan batu kemih. Nilai gravitasi spesifik urin pasien dengan ginjal dan batu kandung kemih lebih tinggi dari pasien dengan batu ureter tetapi tidak ada Asosiasi gravitasi khusus urin terhadap risiko pembentukan batu kemih.*

Kata Kunci: *pH urin, gravitasi spesifik, urolitiasis, lokasi anatomi.*

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INTRODUCTION

Urinary stone disease is the most recurrent problem of urology in the world and becomes a common problem in the clinical practice of urology.[1-2] Globally, urinary stone disease occupied the third most common urological problem in both men and women. The prevalence ranging from 1–5% in Asia, 5–9% in Europe, 13 % in North America and 20% in Saudi Arabia.[3-4]

Kidney and urinary tract diseases are diseases with fatal consequences if discovered late. It occurred since the kidney is the most adaptable organ and able to compensate so that only one kidney human body still functions normally. Urinalysis examination can give significant information and to detect urinary tract diseases that are due to functional or anatomical abnormalities of the kidney with at relatively low cost.

The probability of one acquiring urinary stone disease can be analyzed from biochemical risk factors such as urinary volume, pH, and relative uric acid saturation, which mainly affected by seasonal variation. Factors such as increased calcium excretion, reduced urine output, dehydration, diet, low urinary citrate, genetic and environmental disturbance (environmental temperature) could contribute to the increased salt saturation, low urinary pH and low urine volume, which cause crystalization.[5]

Stone formation is the end result of a gradual process in which there are balancing factors for increased crystalization and factors that inhibit crystallization of salts in the urine.[6-7]

The presence of calcium and oxalate ions added into the solution will increase chemical activity to be supersaturated solution but will not form new crystals. However, if added with calcium oxalate crystals, the crystal's size will increase. Calcium, oxalate, and phosphate are soluble substrates but if citrate present can result in supersaturation.[6]

Metabolic screening evaluation possibly not required if only single stone however in multiple stones, stones at both kidneys, uric acid stones, staghorn stone, nephron stone, and recurrent stones, it will be very useful. Young patient with kidney stone needs to run metabolic screening six weeks after the diagnosis for fluid balance evaluation. In a patient that acquired kidney stone at a young age (+25 years old) for the first time must be done metabolic screening six weeks after incident because at that time there will be fluid balance.[8]

Urinary pH determines stone formation but usually very varied and thus the usage of a urine sample on the second morning after fasting. Urinary infection with urealytic bacteria such as Proteus sp., Klebsiella sp., and Pseudomonas sp. Increases urinary pH by triggering ammonium and resulting stones consisted of ammonium-magnesium-phosphate. Low urinary pH often found as to build uric acid and calcium oxalate stones and in metabolic syndrome or DM.[6,8]

The result of urinalyses such as the presence of haematuria, pyuria, and bacteriuria indicated obstruction due to infection or stone. Urolithiasis that accompanied with infection occurred when in the static state rose colonization of urealytic bacteria and interacted with magnesium-ammonium sulfate resulted in struvite stone. Thus the urinary pH will increase. Microscopic examination often resulted in normal range.[6]

Parks et al. reported the change of stone type from >50% calcium oxalate with low calcium phosphate into stone with increased >20% calcium phosphate content, after compared with patients that did not show an increase in >20% calcium phosphate the urinary pH on those patients were found increased. That urinary pH alteration happened to the two groups could be caused by medication or procedural but the effect is little so that the increased urinary pH in the patients acted as the cause of stone formation.[9]

Atmani et al. compared healthy and patients with kidney stone urines by inducing crystal formation from calcium oxalate and calcium phosphate, then identified the protein from the formed crystals. It was revealed albumin as a major organic compound in crystals from patients with kidney stones so that the crystal albumin probably had a role in stone formation. Even though both groups did not experience proteinuria before, they assumed the presence of abnormal glomerular filtration in patients with kidney stones.[10]

The normal specific gravity of urine varies in a well-hydrated person over 24 hours. Bladder calculi usually cause dysuria, and to avoid pain during micturition the patients tend to reduce their daily fluid intake, raising the urine specific gravity.[11] The high concentration of salts such as calcium oxalate, calcium phosphate, or uric acid leads to crystal formation or growth of preformed crystals.

OBJECTIVE

This study aimed to know the association between urinary specific gravity and acidity with the formation of urolithiasis.

MATERIAL & METHODS

This retrospective descriptive study was conducted among proven urolithiasis patients reporting to the Kardinah Hospital, Tegal. Records

of urolithiasis cases confirmed by CT scan abdomen non-contras during the period 1 October 2017–31 December 2017 were retrieved from the Department of Medical Records and relevant data were extracted using a checklist. Data on patient's age, gender, anatomical sites of the stone, biochemical parameters such as urine color, deposit, pH, specific gravity, Red Blood Cells (RBCs), amorphous deposits, and crystals were obtained from the case. This study aimed to know the association between urinary specific gravity and acidity with the formation of urolithiasis, with the definition of acidic pH <7 and alkalis definition is pH ≥ 7. The urine sample collection of this study is on the second morning after fasting, then analyzed for urinalysis in the laboratory. One way ANOVA was used to find whether the mean specific gravity and pH varied with the anatomical site of the stone.

RESULTS

The age of patients in this research is ranging from 29 until 72 years old, with mean 55.13 years and a standard deviation of 10.87 years. More than 90% of patients are above 40 years old (91.6%). The majority of research subjects were men (83.3%) with only 16.6% women. The age and sex distribution of urinary stone disease patients are shown in Table 1.

From the examination, crystals were found in all samples, 94% oxalate crystals, and 6% amorph crystals with no statistically significant difference (p=0.922) among the location of the kidney, ureter, bladder nor based on kidney location compared with non-kidney location (p=0.508). 51% crystals found in kidney stones, 34% from ureter stones, and 15% in the bladder.

On the urine acidity examination around 84% were found with acidic pH (pH<7) neutral, and basic (pH≥ 7) 16%. Around 83% sample of examination subjects had normal specific gravity, and around 17% were above or below normal.

The average of urinary pH on patients with kidney stones was 6.07, on patients with ureter stones was 6.16 and with bladder stones around 5.81. There is no statistical difference (p=0.282) for urinary pH average on patients with kidney stones, bladder stones, and also ureter stones. It is also

Table 1. Age and Sex Distribution of patients with urinary stone.

Age	Sex					
	Men		Women		Total	
	Count	%	Count	%	Count	%
>40	42	93.3	7	87.5	49	92.4
<40	3	6.6	1	12.5	4	7.6
Total	45	84.9	8	15.1	53	100

Table 2. Urinary parameter distribution of patient with urinary stone.

Urinary Parameter	Group	Total	%
Colour	Clear yellow	7	13
	Yellow	43	81
	Red	2	8
pH	Acidic	45	84
	Neutral/Alkali	8	16
Specific Gravity	Normal (1.010-1.020)	44	83
	Above or below	9	17
Crystal	Oxalate	50	94
	Amorph	3	6
Blood	Present	44	83
	Absent	9	17
Leucocyte esterase	Present	51	96
	Absent	2	4

reported that there is no statistically significant difference in mean urinary pH in patients with kidney stones compared to patients with ureter stones (p=0.649) and against patients with bladder stones (p=0.310). There was also no significant difference in mean urinary pH of patients with ureter stone against patients with bladder stones (p=0.197).

The mean of urinary specific gravity in patients with kidney stones was 1.015, in patients with ureter stone was 1.008 and with bladder stone was around 1.017. Using the ANOVA test there was a statistically significant difference (p=0.001) of the mean of urinary specific gravity on patients with a kidney stone, bladder stone, and ureter stone. There was also a significant difference of the mean of urinary specific gravity on patients with ureter stone compared to patients with a kidney stone (p=0.000), and compared to patients with bladder stone (p=0.000). There was no statistical difference of the mean of urinary specific gravity on patients with kidney stones against the patients with bladder stones (p=0.426).

From the T-test result, there was no significant difference (p=0.629) of the mean of urinary pH in urinalysis of patients with kidney stones compared to patients with non-kidney stone. There was also no statistical difference (p=0.317) in the mean of urinary specific gravity in urinalysis of kidney stone patients versus non-kidney stone patients.

Table 3. Relation of pH and specific gravity average in urinalysis to stone's anatomical site.

Parameter	Site	Count	Average	SD	P
pH	Kidney	27	6.076	0.658	0.282
	Ureter	18	6.166	0.641	
	Bladder	8	5.812	0.593	
Specific Gravity	Kidney	27	1.015	0.0058	0.001*
	Ureter	18	1.008	0.0047	
	Bladder	8	1.017	0.0065	

Table 4. Correlation of urinary stone location with mean urinary pH and specific gravity

Parameter	Location	Location	P
pH	Kidney	Ureter	0.649
	Kidney	Bladder	0.310
	Ureter	Bladder	0.197
Specific Gravity	Kidney	Ureter	0.000*
	Kidney	Bladder	0.426
	Ureter	Bladder	0.000*

Table 5. Correlation of kidney stone and non-kidney stone with mean pH and specific gravity parameter.

Parameter	Location	Sum	Average	SD	P
pH	Kidney	27	6.076	0.647	0.629
	Non-Kidney	26	6.035	0.651	
Specific Gravity	Kidney	27	1.015	0.0056	0.317
	Non-Kidney	26	1.011	0.0066	

Table 6. Urine acidity level against the stone location in kidney, ureter, and bladder.

Acidity	Location			P
	Kidney	Ureter	Bladder	
Acidic	23	15	7	0.030
Normal	4	3	1	

Table 7. Urine acidity level against the location of kidney stone against non-kidney stone.

Acidity	Location		P
	Kidney	Non-Kidney	
Acidic	23	22	0.039*
Normal	4	4	

On the Pearson Correlation test, there was a significant difference (p=0.030) based on urine acidity level according to the location stone in the kidney, ureter, and bladder. There was a significant difference when the urine acidity in kidney stones compared to non-kidney stone (p=0.039).

The average urinary pH on patients with the various anatomical location of the urinary stone showed that the lower the pH the higher probability of stone location, but was not specific about the location. Higher pH was found in patients with whether kidney, ureter, and also bladder stone. The average urinary specific gravity of ureter stone patients was lower compared to stones in other locations.

One-way ANOVA exhibited statistically no difference in urine pH of patients with the various location of the stone but revealed a statistically significant difference in urine specific gravity ($p<0.05$) of patients with ureter stone compared to stone in other locations. There was a significant difference (p=0.000) of the urinary specific gravity of ureter stone compared to other locations with the lower mean value.

DISCUSSION

Urolithiasis is a condition in which stone formed in the urinary tract like ureter, kidney, and bladder.[7] Crystal formation very dependent on urine composition, due to flowing urine contains several substrates that easily crystalized which could develop into stone.[9] Upper and lower urinary tract anatomy also affect the formation of the stone.[12]

This study done in Kardinah Regional Hospital of Tegal displayed more than 90% of patient's age is more than 40 years old (91.6%). This is based on our previous study that have been reported. Most of the stone formation occurred in under 40 years old (83.8%) with ratio men to women of 5:1. A study was done by Alsheyab et al. and Kumar et al. presented men to women ratio of 3:1 with the most age range of 20-50 years old. More studies all around the world that had been investigating that this ratio not only affected by the patient's intrinsic factor but also by the nation's social-economy status.[13]

This study that worked on Kardinah Regional Hospital of Tegal displayed that there is an association of urine acidity level and specific gravity on stone formation. The lower the urinary pH the risk of stone formation is increasing with p=0.030 compared to normal patients' urine. This applies to all of the stone types that formed in the urinary tract, whether in kidney, ureter, and bladder. However, the urine acidity level was not significantly different if compared based on stone locations. Clinically the mean of urinary pH in patients with bladder stone was lower compared to mean of urinary pH of ureter stone and kidney stone patients without statistically significant difference.

A study revealed that urinary stone patients had 4.5% uric acid crystals and 1.6% calcium oxalate crystals. Sperling et al. and Tiselius et al. demonstrated a high frequency of acidic urine of patients who lived in Israel, Arabic countries, and Australia compared to in Europe. The episode of losing massive fluids or reduced intake is probably associated with acidic urine crystallization risk. Decreased of pH and urine volume can trigger uric acid precipitation on normal excretion of uric acid condition.[14-15]

In this study, clinically showed that the mean of specific gravity in patients with a kidney stone and with bladder stone was higher compared to specific gravity with ureter stone. It was statistically significant (p=0.001). Nonetheless, the increase of urinary specific gravity was not statistically significant toward the urinary stone formation.

More than 90% of the study samples in Kardinah Hospital of Tegal displayed oxalate crystals content. A study by Kumar et al. exhibited the effect of low pH and increased specific gravity to the stone formation.[16] The Kumar et al. study showed that the solubility level of uric acid decreased drastically in urinary pH less than 5.5 which triggered the uric acid crystals. The solubility of calcium oxalate is affected by the change of urinary

pH that triggered crystalization and super-saturation.[17] Most of the study samples showed increased specific gravity during summer and decreased during winter. That event is also matching with a study conducted by Rabie et al., that displayed the effect of seasonal variations is associated with urine volume, pH and saturation.[1]

This study and the researches have done before displayed that there are associations among pH and specific gravity toward the urinary stone formation, which increased specific gravity and decreased pH clinically affect the urinary stone formation risks. Several studies investigated the effect of increased specific gravity and decreased pH in the summer. This study in Kardinah Hospital of Tegal was done in summer and geography of northern Java island coast probably affected. Besides, in this study were not conduct the stone analysis, the future direction of the study addressed on the usage of PH in prediction stone type in regards stone lysis strategy.

This study did not investigate the effect of diseases and other conditions of patients that could affect the result of this study. Reduced urinary specific gravity can be found in diabetes insipidus patients, pyelonephritis, and glomerulonephritis. Elevated urinary specific gravity can be found in dehydrated patients, patients with adrenal insufficiency, liver disease, and poor heart.

CONCLUSION

A decrease in urinary pH is associated with the risk of urinary stone formation. The specific gravity value of the patient's urine with kidney and bladder stones is higher than the patient with ureter stones but there is no association of urine specific gravity toward the risk of urinary stone formation.

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