URINALYSIS AS PREDICTOR OF UPPER-TRACT URINARY STONE ON COLIC PAIN PATIENTS: SINGLE-CENTER COHORT STUDY

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ABSTRACT

Objective: *There was no study in our country especially in our hospital that studied correlation between urinalysis and upper tract urinary stone on colic pain patients, so we conducted the study.* ***Material & Methods:*** *We collected patients' data with colic abdomen from January 2018 to January 2020 then divided into hematuria and non-hematuria group respectively. We excluded patients with lower-tract urinary stones, DJ-stent insitu, BPH, and malignancy. All patients had urinalysis and abdominal ultrasound, then continued with non-contrast abdominal CT-Scan or Intravenous Urography. Retrospective and prospective cohort study was performed to collect data: age, sex, serum ureum and creatinine, urinalysis results (pH, specific gravity, nitric, leucocyte, erythrocyte, crystal, and bacteria), stone number, site, and size, then analysed the relationship between urinalysis results with upper-tract urinary stone incidence using point biserial correlation.* ***Results:*** *We found 235 colic patients, 115 and 120 patients in hematuria and non-hematuria group respectively. Male patients were higher, 137 (58.3%). The highest incidence was in the range 41-50 years-old (30.6%), mean 46.53±13,53 years-old. Stone incidence was 55.7% in all colic patients. Stone was proven 78.3% and 34.2% in hematuria and non-hematuria group respectively. There was significant association between upper-tract urinary stone and haematuria compared to non-haematuria patients ($p<0.05$). Relative-risk (RR) was 2.29, CI 95%.* ***Conclusion:*** *Hematuria increases two-folds probability of upper-tract urinary stone. It is necessary to expand population data and follow-up center to make this representative.*

Keywords: *Colic, hematuria, stone.*

ABSTRAK

Tujuan: *Tidak ada penelitian di negara kami terutama di rumah sakit kami yang mempelajari korelasi antara urinalisis dan batu saluran kemih bagian atas pada pasien nyeri kolik, sehingga kami melakukan penelitian.* ***Bahan & Cara:*** *Kami mengumpulkan data pasien kolik abdomen dari Januari 2018 hingga Januari 2020 kemudian dibagi menjadi kelompok hematuria dan non-hematuria. Kami mengeksklusi pasien dengan batu saluran kemih bawah, DJ-stent insitu, BPH, dan keganasan. Semua pasien menjalani urinalisis dan USG abdomen, dilanjutkan dengan CT-Scan abdominal non-kontras atau Intravenous Urografi. Studi kohort retrospektif dan prospektif dilakukan untuk mengumpulkan data: umur, jenis kelamin, ureum serum dan kreatinin, hasil urinalisis (pH, berat jenis, nitrat, leukosit, eritrosit, kristal, dan bakteri), jumlah batu, lokasi, dan ukuran, kemudian dianalisis hubungan antara hasil urinalisis dengan kejadian batu saluran kemih atas menggunakan korelasi point biserial.* ***Hasil:*** *Kami menemukan 235 pasien kolik, 115 dan 120 pasien pada kelompok hematuria dan non-hematuria. Insiden pasien laki-laki lebih tinggi sebanyak 137 (58.3%). Insiden tertinggi pada rentang usia 41-50 tahun (30,6%), rerata usia 46.53±13.53 tahun. Insiden batu adalah 55.7% pada semua pasien kolik. Persentase batu pada masing-masing kelompok hematuria dan non-hematuria adalah 78.3% dan 34.2%, terdapat hubungan yang signifikan antara batu saluran kemih atas dan kejadian hematuria dibandingkan dengan pasien non-hematuria ($p<0.05$). Risiko relatif (RR) adalah 2.29, CI 95%.* ***Simpulan:*** *_Hematuria meningkatkan kemungkinan dua kali lipat terjadinya batu saluran kemih atas. Perlu adanya perluasan data populasi dan tindak lanjut agar hasil lebih representatif.*

Kata kunci: *Kolik, hematuria, batu.*

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INTRODUCTION

Upper tract urinary stones are a clinical problem that is often an indication of hospitalization in the Emergency Department.[1] As many as 5-15% of the world's population suffer from urinary tract stones.[2] Upper tract urinary stones are stones that deposit in the kidneys and/or ureters.[3] The incidence of upper tract urinary stones reaches 11% in the male population, while in women it has an incidence of 7%.[4] In Asian countries, the incidence varies between 5-19.1% and more prevalent in South and South-East Asia because of the higher average temperature.[5] Indonesia is one of South-East Asian country.

Patient's complaints regarding upper tract urinary stones can vary, ranging from no complaints, mild to severe colic, hematuria, and anuria.[6-7] Colic pain is defined as sharp pain caused by blockage, smooth muscle spasm, or the rotating of a hollow organ.[8] The incidence related to urolithiasis in acute abdominal pain was 31.18%.[9] Hematuria is a condition of the presence of red blood cells in the urine (≥ 4/HPF)[10], can be appeared in conditions of upper tract urinary stones due to friction between the stone surface and the urinary tract mucosa. The sensitivity of hematuria as a predictor of urinary tract stones ranged from 75-84% [1,11] and could be a screening tool that increased efficiency in diagnosis, so abdominal CT-Scan as a gold standard[12] should be more selectively performed and the cost was reduced.[13]

OBJECTIVE

There was no study in our country especially in our hospital that studied correlation between urinalysis and upper tract urinary stone on colic pain patients, so we conducted the study.

MATERIAL & METHODS

The study was conducted at Dr. Saiful Anwar General Hospital, Malang, East Java, Indonesia in the periode of January 1st, 2018 to January 31st, 2020. We collected patients's data with colic abdomen that was consulted to Urology Department. We excluded patients with lower-tract urinary stones, DJ-stent insitu, Benign Prostate Hyperplasia (BPH), and malignancy because those conditions can caused hematuria.[10] All patients had urinalysis then divided into group 1 and 2 as hematuria and non-hematuria group respectively. Hematuria was defined as ≥ 4 erythrocyte in urinalysis result.[10] Furthermore all patients had been performed abdominal ultrasound, then continued with non-contrast abdominal CT-Scan or Intravenous Urography according to creatinine serum level. Patients with evidence of abnormalities such as upper tract urinary stones and/or hydronephrosis had been performed surgery depends on the indication. Then the results obtained as upper tract urinary stones or ureteral stenosis. Single centre cohort study followed retrospectively and prospectively was performed to collect data: age, sex, serum ureum and creatinine, urinalysis results (pH, specific gravity, nitric, leucocyte, erythrocyte, crystal, and bacteria), stone number, site, and size, then analysed to determine relationship between urinalysis results with upper-tract urinary stone incidence using point biserial correlation. All of the study scheme showed at Figure 1.

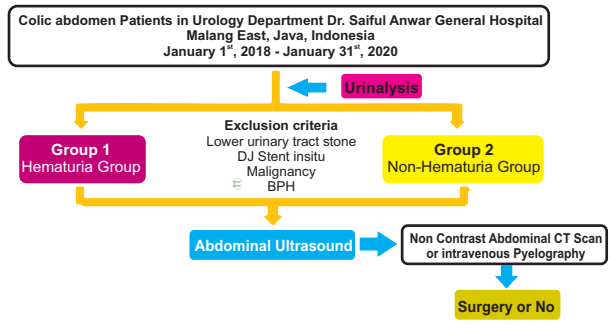

Figure 1. The Scheme of the Study.

RESULTS

There were 256 patients with colic pain obtained, then 21 patients were excluded so that 235 patients were sampled. Demographic data showed that 137 patients (58.3%) were male and 98 (41.7%) were female (Table 1).

The highest incidence of upper tract urinary stones occurred in the age range 41-50 years, as many as 72 patients (30.6%) with a mean age of 46.53 ± 13.53 years. Upper tract urinary stones showed an incidence rate of 55.7% of the total sample size. From the data obtained, single stones had a higher incidence than multiple stones, 61.8%, and unilateral stones were more than bilateral stones, which was 72.5%. A total of 46.6% of samples with stones had a stone size of 1.1-2.0 cm, while stones

with a size of 0.5-1.0 cm had an incidence of 28.2%, and stones with a size of >2.0 cm had an incidence rate of 25.2% (Table 1).

Of the 235 samples with colic pain had been performed urinalysis examination, then the samples were grouped into two groups as mentioned above. There were 115 patients classified into group 1 and 120 patients into group 2. All patients underwent ultrasound examination (USG) of the upper urinary tract and it was found that 93 patients in group 1 showed abnormal ultrasound results (80.9%), while in group 2 there were 47 patients (39.2%) with abnormal ultrasound results. The results of further investigation (CT scan Abdomen without contrast or IVU) showed the incidence of stones in group 1 was 78.3% and 34.2% in group 2. These results were showed at Figure 2.

Table 1. Demographic Data of the Samples.

		n	%	
Sex	Male	137	58.3	
	Female	98	41.7	
Age	≤20 yrs	7	3.0	
	21-30 yrs	23	9.8	
	31-40 yrs	48	20.4	??46.53
	41-50 yrs	72	30.6	± 13.53
	51-60 yrs	45	19.1	
	61-70 yrs	28	11.9	
	> 70 yrs	12	5.1	
Stone number		131	55.7	
	Single	81	61.8	
	Multiple	50	38.2	
Stone location	Unilateral	95	72.5	
	Bilateral	36	27.5	
Stone size	0.5-1.0 cm	37	28.2	
	1.1-2.0 cm	61	46.6	
	>2.0 cm	33	25.2	

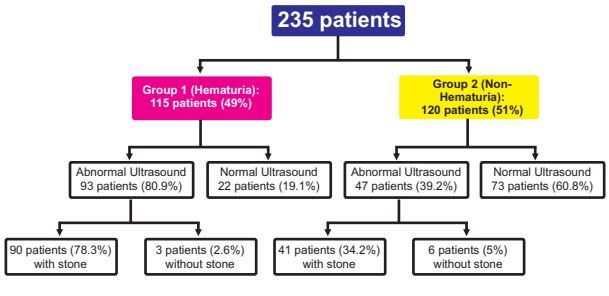

Figure 2. Stone Incidence in the Study.

The results of the urinalysis which consisted of pH (acidity), specific gravity, nitrite levels, leukocytes, erythrocytes, epithelium, cylinders, crystals, and bacteria were analyzed for the relationship with the incidence of stones using the biserial point correlation because it was an interval scale test with a nominal scale. Correlation test showed a significant relationship between levels of nitrite, leukocytes, erythrocytes, and epithelium in urine with the incidence of upper tract urinary stones with a p-value of 0.012; 0.000; 0.002; and 0.001 respectively. Then the β coefficient was calculated and the results were revealed 0.164 for nitrite, 0.235 for leukocytes, 0.196 for erythrocytes, and 0.221 for epithelium. A correlation test was also conducted on the results of leukocytes and erythrocytes with dipstick examination of the incidence of upper tract urinary stones and both showed a significant relationship with each p-value of 0.000. Then the β coefficient was calculated and the results were revealed 0.285 for dipstick leukocytes and 0.680 for dipstick erythrocytes. Then the study proceed with the calculation of the t-value on the variable with a p-value <0.05 and the results were revealed 2.539 for nitrite, 3.684 for leukocytes, 3.057 for erythrocytes, 3.464 for epithelium, 4.537 for dipstick leukocytes, and 14.170 for dipstick erythrocytes. The results were showed at Table 2.

Table 2. Results of Variables Correlation Analysis.

Variable	Biserial Point Correlation (*p*)	β Coefficient	*t*
pH	0.473	-0.047	X
Specificgravity	0.946	0.004	X
Nitrite	0.012	0.164	2.539
Leukocyte (microscopic)	0.000	0.235	3.684
Erythrocyte (microscopic)	0.002	0.196	3.057
Epithel	0.001	0.221	3.464
Cylinder	0.066	0.120	X
Crystal	0.442	0.050	X
Bacteria	0.696	0.026	X
Leukocyte (dipstick)	0.000	0.285	4.537
Erythrocyte (dipstick)	0.000	0.680	14.170

To determine the relative risk between the incidence of upper tract urinary stones and the findings of erythrocytes in the urine, a calculation was performed as in table 3 and the result was 2.29. This indicates that the presence of upper tract urinary stones will increase the risk of increasing erythrocyte levels in urine by 2.29 times.

Table 3. Relative Risk between Upper Tract Urinary Stones and Increases Urine Erythrocyte Levels.

	Stone	Without Stone	Total
Erythrocyte in urine	90	25	115
Without erythrocyte	41	79	120
Total	131	104	235

$$\frac{\frac{A}{A+B}}{\frac{C}{C+D}} = \text{RR } 2.29$$

DISCUSSION

Previous research conducted by Simerville, 2005, proved that urinalysis can predict the occurrence of upper tract urinary stones. The parameters that become the emphasis were hematuria and leukocyte esterase induced by infection[14] consistent with the findings obtained in this study, there is a significant correlation between erythrocytes and leucocytes in patients with upper tract urinary stones with a fairly high β coefficient, 0.680 for dipstick erythrocytes and 0.285 for dipstick leukocytes. Because of a large differential diagnosis of hematuria and leukocyturia, it remains to be confirmed by radiological investigations or diagnostic endourological procedures.[14]

Some medical conditions that can cause hematuria are urinary tract infections, urinary tract stones (urolithiasis), malignancy, benign prostate hyperplasia (BPH), and nephropathy and nephritis. Further examination is needed to determine the cause of the hematuria in the patient. The tests that can be done are laboratory tests which include blood urea nitrogen, creatinine serum, and glomerular filtration rate to show the patient's kidney function. Hematological status examinations such as PTT (Prothrombin Time) and INR (International Normalized Ratio) can also seen the presence of coagulopathy and the degree of hematuria in the patient.[10]

Hematuria can appear in conditions of upper tract urinary stones due to friction between the stone surface and the urinary tract mucosa. This friction arises from the urge of urine to flow out, but there is an irregularity and turbulence in the urinary tract due to the urinary tract stones. When stones occur in the kidneys, massive hematuria can occur, because the kidneys are rich in vascularity and high sensitivity. The rough and sharp surface of the stone facilitates hematuria in patients with urolithiasis. Previous studies have shown that hematuria can be a predictor of urinary tract stones. The sensitivity of hematuria as a predictor of urinary tract stones ranged from 75-84%.[1,11] Our study compared hematuria with the presence of urinary tract stones in gold standard examinations such as intravenous urography (IVU), abdominal CT scan, macroscopic stone collection, and other clinical evidence and revealed the sensitivity of hematuria was 78.3%.

Another study showed that there are 10-20% of patients with urinary tract stones are not accompanied by hematuria.[1] Hematuria may not occur in urinary tract stone patients with obstructive uropathy. One hypothesis that could explain this phenomenon is the presence of large urinary tract stones that block the ureter and cause red blood cells to not flow until urine leaves the body. Several other factors that can influence the presence or absence of hematuria in patients are dehydration, menstruation, stone position, and the time interval between pain onset and urine sample collection.[15-16] According to previous studies, patients who have a single urinary tract stone without hematuria may be at risk for moderate-severe hydronephrosis, when compared to a similar group of patients with hematuria.[17]

The study presented by Moreira et al., 2013 revealed that the 24-hours urinalysis cannot accurately predict the type of stone, but it can predict the stone diagnosis and stone composition with the help of other variables.[18] Therefore, it is important to review the history, physical examination, and other investigations in the form of radiological or other diagnostic procedures in patients with a large suspicion of stones. Elton and colleagues in 1993 showed that patients with hematuria have a 3.9-fold greater risk of being diagnosed with upper tract urinary stones than those without hematuria[19], which mean similar from the relative risk obtained in our

study, 2.29. But it is important for us to assess not only one factor but also in combination with other tests to determine the diagnosis of urinary tract stones.

The results showed that the erythrocyte and leukocyte dipstick β coefficients were quite high. This could be due to severe condition of the samples, and leukocyte may be because of concomitant or related infection. Until now there has been no study that explains the possibility of dipstick hematuria findings for the diagnosis of upper tract urinary stones, which have always been used so far microscopic findings from urinalysis. However, in a further retrospective study over 3.5 years of 587 patients showed urinalysis in the diagnosis of urinary tract stones had a sensitivity of 84% and about 46% of urinary tract stones showed no hematuria.[1] This result had similarity with our study, about 34.2% of patients diagnosed with upper tract urinary stones were not followed by hematuria.

CONCLUSION

Hematuria increases two folds probability of upper tract urinary stone. So it could be concluded that the use of urinalysis can indeed predict the presence of upper tract urinary stones, but it is not a certainty for the diagnosis of urinary tract stones, which must be combined with a further comprehensive examination.

REFERENCES

1. Luchs JS, Katz DS, Lane MJ, et al. Utility of Hematuria Testing in Patients with Suspected Renal Colic: Correlation with Unenhanced Helical CT-results. Adult Urol. 2002; 59: 839-42.
2. Moe OW. Kidney Stones: Pathophysiology and Medical Management. Lancet. 2006; 367(9507): 333-44.
3. Pfau A, Knauf F. Update on Nephrolithiasis: Core Curriculum 2016. Am J Kidney Dis. 2016; 68(6): 973-85.
4. Scales CD, Smith AC, Hanley JM, et al; Project Urologic Diseases of America Project. Prevalence of Kidney Stones in the United States. Eur Urol. 2012; 62: 160-5.
5. Liu Y, Chen Y, Liao B, Luo D, Wang K, et al. Epidemiology of Urolithiasis in Asia. Asian J Urol. 2018; 5: 205-14.
6. Engeler DS, Schmid S, Schmid HP. The Ideal Analgesic Treatment for Acute Renal Colic – Theory and Practice. Scan J Urol Nephr. 2008; 42: 137-42.
7. Kenny C, Eragat M, Salahia S, Mulhem W, Hammadeh MY. Diagnosis and Management of Ureteric Colic. ResGate. 2017: 16-21.
8. Shokeir AA. Renal Colic: Patophysiology, Diagnosis, and Treatment. Eur Urol. 2001; 39: 241-9.
9. Cervellin G, Mora R, Ticinesi A, Meschi T, Comelli I., et al. Epidemiology and Outcomes of Acute Abdominal Pain in a Large Urban Emergency Department: Retrospective Analysis of 5,340 cases. Ann Transl Med. 2016; 4(19)362: 1-8.
10. Sing RI, Singal RK. What is Significant Hematuria for the Primary Care Physician? Can J Urol. 2012; 19(Suppl 1): 36-41.
11. Das M, Bardakci O, Yurtseven E, Akman C, Beyazit Y., et al. Diagnostic Utility of Microhematuria in Renal Colic Patients in Emergency Medicine Correlation with Findings from Multidetector Computed Tomography. Med Sci Int J. 2019; 1-5.
12. Li J, Kennedy D, Levine M, Kumar A, Mullen J. Absent Hematuria and Expensive Computerized Tomography: Case Characteristics of Emergency Urolithiasis. J Urol. 2001; 165: 782-4.
13. Bove P, Kaplan D, Dalrymple N., et al. Reexamining the Value of Hematuria Testing in Patients with Acute Flank Pain. J Urol. 1999; 162: 685–7.
14. Simerville JA, Maxted WC, Pahira JJ. Urinalysis: a Comprehensive Review. American fam phys. 2005; 71(6): 1153-62.
15. Inci MF, Ozkan F, Bozkurt S., et al. Correlation of Volume, Position of Stone, and Hydronephrosis with Microhematuria in Patients with Solitary Urolithiasis. Med Sci Monit. 2013; 19: 295-9.
16. Kobayashi T, Nishizawa K, Mitsumori K,. et al. Impact of Date of Onset on the Absence of Hematuria in Patients with Acute Renal Colic. J Urol. 2003; 170(4 Pt 1): 1093-6.
17. Mefford JM, Tungate RM, Amini L., et al. A Comparison of Urolithiasis in the Presence and Absence of Microscopic Hematuria in the Emergency Department. West J Emerg Med. 2017; 18(4): 775-9.
18. Moreira DM, Friedlander JI, Hartman C, Elsamra SE, Smith AD, Okeke Z. Using 24-hour Urinalysis to Predict Stone Type. Journal Urol. 2013; 190(6): 2106-11.
19. Elton TJ, Roth CS, Berquist TH, Silverstein D. A Clinical Prediction Rule for the Diagnosis of Ureteral Calculi in Emergency Departments. J Gen Int Med. 1993; 8(2): 57-62.