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The relationship between the severity of pain and stone size, hydronephrosis and laboratory parameters in renal colic attack

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ABSTRACT

Objective: In this study, we investigated the relationship between the severity of pain level and hydronephrosis, hematuria and pyuria presence in the acute renal colic attack and whether there was a correlation between the stone size and inflammatory markers.
Methods: The patients' pain scores determined by Visual Analog Scale (VAS), CRP, WBC and NLR levels from the laboratory results, hematuria and pyuria presence in the urine analysis and hydronephrosis presence in the imaging methods were recorded. Moreover, stone size was measured for the patients for whom computed tomography (CT) method was applied.
Results: Mean age of the 275 patients was 41.0 ± 14.9 and 61.1% of them were male. The patients' mean VAS score was 73.3 ± 16.5.The mean VAS score of the groups of which hematuria and pyuria were positive and which have hydronephrosis finding was statistically higher than those whose were negative.
The mean stone size was 5.2 ± 2.1 mm, and those with signs of hydronephrosis on their CT (n = 66) were 5.4 ± 2.3 mm, while those with no signs of hydronephrosis (n = 57) were 4.9 ± 1.7. No statistical difference was found in stone size between patients with hydronephrosis and those without. Not any correlations were determined between the stone size and VAS pain score of the cases.
Conclusions: We detected that the pain level was not correlated with the stone size and big stones were not statistically riskier in the hydronephrosis development. However, we think that the risk of complications such as hydronephrosis is higher in the patients whose pain level are higher and the infection may be accompanied by this group.

1. Introduction

In the management of pain, which is an unpleasant, distressed situation for the patient, physicians determine the cause and level of pain with a systematic, comprehensive evaluation. A renal colic attack constitutes a substantial part of those patients appearing in the emergency department complaining of acute and severe pain [1,2]. The blockage of urine flow by a stone, the pressure increase on the urinary tract wall, ureteral smooth muscle spasms and edema, and increased inflammation around the stone are the primary mechanisms of the pain in renal colic patients. The patients generally define renal colic pain as the most severe pain of their lives [3].

While clinicians provide palliative pain relief for the renal colic attack, they also try to reach a differential diagnosis with urine analysis, laboratory tests, and imaging methods such as ultrasonography (US) or computed tomography (CT). Stone size and location, perinephric stranding, and the presence of hydronephrosis–hydroureter can be detected by the CT, which is the gold standard in diagnosis. However, more importantly, the differential diagnosis allows the exclusion of other risky circumstances such as aortic dissection and appendicitis. The US is very important in renal colic diagnosis and management as it is a bedside treatment, easy to deliver, and does not involve any radiation. However, even though the presence of hydronephrosis may be easily determined by the US, its sensitivity is low in determining the stone size and location [4].

According to published literature, while hematuria is frequently detected in renal colic attacks, there is not enough information about the incidence of pyuria, but it is low [5-7]. The C-reactive protein (CRP) and neutrophil lymphocyte ratio (NLR) are very significant for the diagnosis, follow up, and treatment because these are the systemic inflammatory response markers for many

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inflammatory circumstances such as infections, malignancies, and tissue damage [8,9].

In light of this information, this study investigated the relationship of the pain level with hydronephrosis, hematuria, or pyuria during the acute renal colic attack and whether it showed a correlation with the stone size and inflammatory markers (white blood cell (WBC), CRP and NLR). To our knowledge, no previous study has been carried out in relation to this subject in published literature.

2. Materials and method

2.1. Study design

This prospective, double-centered study was carried out between March 1, 2018 and September 31, 2018 in the Van Training and Research Hospital and Van Yuzuncu Yil University Hospital where approximately 400,000 and 150,000 visitors present to the emergency department per year. The study group consisted of patients who were admitted to the emergency department and suspected a renal colic attack. The patients were requested to score the pain level at the time of presentation with the help of the Visual Analog Scale (VAS) (0: none, 100: the highest) and recorded on a study form. The patients' diagnoses and treatments were then continued to completion. The treatments received by the patients were completely left to the doctors' own clinical decisions and then recorded. The CRP, WBC, and NLR levels from the patients' laboratory results, whether hematuria and pyuria were detected in the urine analysis, or the presence of hydronephrosis was detected by the imaging methods, were then recorded on the study form. In addition, the stone size was measured and recorded for the group who underwent a CT scan. The CT and ultrasonography findings were interpreted by the radiologists. The hematuria was defined as $\geq$5 red blood cells per high power field (RBC/HPF) and pyuria as>10 white blood cells per high power field (WBC/HPF) [10,11]. The presence of hydronephrosis was recorded based on its presence or not regardless of its grade.

2.2. Selection of participants

The following patients were included in the study:

- patients who had complaints of side pain and were diagnosed with renal colic attack
- patients with stones detected using the imaging methods (CT, US) or who had a history of renal colic in their patient records and had been admitted with the same complaint
- patients at the age of 18 and over who volunteered to participate in the study and signed the consent forms

The exclusion criteria of the study were as follows:

- patients who were not diagnosed with renal colic (e.g., those diagnosed with appendicitis, pyelonephritis, gynecological pathologies, etc.) were excluded from the study
- patients who were pregnant
- patients who had a history of stone surgery or who had only one kidney
- patients under 18 years of age
- patients who had acute abdominal findings
- patients with signs of infection other than in the urinary tract
- patients who were hemodynamically unstable
- patients who had used analgesics, muscle relaxants, or steroids in the last 12 h and whose VAS pain score was below 50.

2.3. Statistical analysis

The data were evaluated using SPSS 22 (Statistical Package for the Social Sciences) software, IBM, USA. Descriptive statistics for the continuous variables (characteristics) were presented as mean and standard deviation (SD), while counts and percentages were used for the categorical variables. The mean and SD values were used to compare the parametric data with published literature, although the data were not normally distributed. The Mann-Whitney *U* test was used for the statistical analysis when two independent groups were compared and the Kruskal-Wallis test was used when >2 independent groups were compared and for which the parametric test assumptions were not met. The Spearman correlation coefficients were calculated to determine the linear relationship between the variables. A p value <0.05 was considered statistically significant.

2.4. Ethics approval

The ethical committee approval with a decision number 01 and dated 16.02.2018 was obtained from the Clinical Research Ethical Committee of Yuzuncu Yil University Medical Faculty.

3. Results

In total we evaluated 364 patients, and 89 were excluded from the study as they did not comply with the criteria (Fig. 1). The mean age of 275 patients included in the study was 41.0 ± 14.9, and there were 168 (61.1%) males and 107 (38.9%) females. The patients' mean VAS score was 73.3 ± 16.5, 73.8 ± 16.9 for the male patients and 72.4 ± 16.0 for the female patients. There was no statistical difference between genders in terms of the mean VAS score ($p = 0.486$).

Hematuria was detected in 209 (76%) of the patients, and the mean VAS score of the patients with hematuria was 75.5 ± 15.8, while the mean VAS score for patients without hematuria was 66.4 ± 16.8. The mean VAS scores of the patients with hematuria were statistically higher than those without hematuria ($p < 0.001$). The mean VAS score of the patients testing positive for pyuria was statistically higher than those who tested negative ($p = 0.003$). The mean VAS score of the patients with hydronephrosis was statistically higher than those without hydronephrosis ($p < 0.001$) (Table 1).

The mean stone size for 123 patients who underwent CT imaging method, with signs of hydronephrosis on their CT ($n = 66$), and with no signs of hydronephrosis ($n = 57$) were 5.2 ± 2.1 mm, 5.4 ± 2.3 mm, and 4.9 ± 1.7, respectively. No statistical difference was found in stone size between patients with hydronephrosis and those without ($p = 0.127$). There was no correlation between stone size and VAS pain score ($r = 0.079$, $p = 0.123$) (Table 2).

When the correlation between the patients' inflammatory markers and pain levels was investigated, there was a positive, weak, and linear relationship ($r = 0.276$, $p < 0.001$) between the CRP level and VAS score and a very weak linear relationship ($r = 0.218$, $r = 0.220$) between the WBC/NLR levels and the VAS score (Table 2).

The subsequent treatment of patients was solely based on the doctors' own clinical decision. One hundred and thirty (47.3%) patients were treated with intramuscular (IM) or intravenous (IV) non-steroidal, anti-inflammatory drugs (NSAIDs) on their own, 63 (22.9%) of them with IV paracetamol, 42 (15.3%) of them with IV opioids and NSAIDs, 21 (7.6%) of them with IV opioids, and 19 (6.9%) of the patients were treated with IV opioids and IV paracetamol. The mean VAS score of the groups treated with only

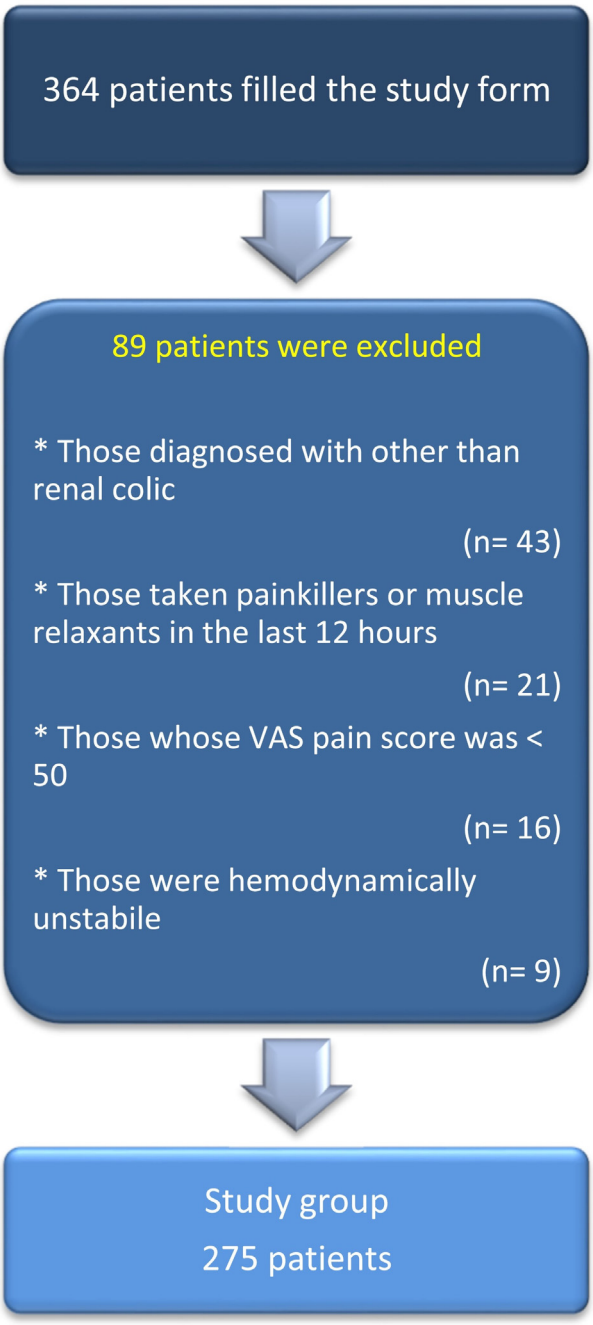

Fig. 1. Patient flow chart.

Table 1
Relationship of the pain levels with the urine analysis and hydronephrosis findings

	n (%)	VAS score	p value
Hematuria			
Positive	209 (76%)	75.5 ± 15.8	<0.001
Negative	66 (24%)	66.4 ± 16.8	
Pyuria			
Positive	129 (46.9%)	76.4 ± 15.3	0.003
Negative	146 (53.1%)	70.6 ± 17.1	
Hydronephrosis			
Positive	106 (38.5%)	82.1 ± 14.8	<0.001
Negative	169 (61.5%)	67.2 ± 14.5	

Table 2
The relationship between VAS scores and inflammatory markers and stone size.

	VAS score-CRP	VAS score-WBC	VAS score-NLR	VAS score-stone size
r	0.276	0.218	0.220	0.079
p value	<0.001	<0.001	<0.001	0.123

r = Pearson correlation coefficient, VAS = Visual analog scale.
CRP = C-reactive protein, WBC = White blood cell

Table 3
Drugs administered in the treatments.

	n (%)	VAS score	p value
NSAID	130 (47.3%)	66.9 ± 14.1	<0.001
Paracetamol	63 (22.9%)	66.6 ± 14.9	
NSAID + Opioid	42 (15.3%)	88.7 ± 10.7	
Opioid	21 (7.6%)	87.33 ± 10.1	
Paracetamol + Opioid	19 (6.9%)	89.5 ± 8.5	

non-steroidal, anti-inflammatory drugs and only paracetamol was significantly lower than the other 3 treatment groups (Table 3).

4. Discussion

The study investigated the relationship of renal colic pain level with hydronephrosis, laboratory parameters, and stone size. This is the first study performed on this subject in the literature. And, it was found that the pain was significantly higher for patients diagnosed with hydronephrosis and for those with hematuria and pyuria diagnosed by urine analysis among patients suffering a renal colic attack.

Although Inci et al. [12] determined a positive relationship between stone size and hydronephrosis in their study, they did not find a relationship between stone size and microhematuria. Metford et al. [13] showed a significantly higher ratio of hydronephrosis in the presence of stone sizes of 5 mm or more. Although the mean stone size of the patients with hydronephrosis was larger than those without hydronephrosis, this difference was not statistically significant ($p = 0.127$) due to the lower patient numbers. These findings may suggest that bigger stones lead to more obstructive complications, and urological consultation may be necessary for patients with bigger stones. In addition, the severity of pain was significantly higher in patients with hydronephrosis. We assume that high ureteral pressure and high backflow, which play a major role in the development of hydronephrosis, cause severe pain. Although we have investigated the relationship between stone size and pain level, we could not find a significant correlation. This result indicates that the location of the stone and increase in ureteral pressure are the important determinants of pain level rather than the stone size.

In a study investigating pyuria and urine cultures in renal colic patients, hematuria was found in 74.9% of a total of 339 patients and pyuria was found in 14.2% [5]. In a study performed on patients with urolithiasis, Metford et al. [13] determined that hematuria was associated with it in 82% of cases. In a study performed on 100 patients with renal colic [7], urinalysis detected bacteria in 36% of cases. In a more comprehensive study, pyuria was observed in 21% to 34% of patients with renal colic [14]. In our study, while the rate of hematuria (76%) was similar to other studies, the rate of pyuria (46.9%) was found to be higher. Hematuria in renal colic is caused by mucosal damage during passage of the stone [12]. Also in this study, patients with hematuria had

significantly more severe pain, which may be due to difficulties caused by the passage of the stone and associated mucosal damage. The presence of pyuria detected by urine analysis in terms of infection is not as significant as a leukocyte esterase and/or nitrite positive test [15,16]. However, in this study, the severity of pain in patients with pyuria may be coincidental or may be due to the presence of infection.

The acute phase reactants, such as WBC and CRP, rapidly increase under inflammatory circumstances such as infection and trauma [17]. NLR is one of the markers frequently used to evaluate the inflammatory circumstances, and it has been shown to be a strong diagnostic marker in the classification of mortality in cardiac events [18,19], some cancers [20,21], and in infectious or inflammatory circumstances [22]. The study also investigated whether there was a correlation between pain level and increase in inflammatory markers such as WBC, CRP, and NLR. However, the study determined a weak relationship with CRP and a very weak relationship with WBC and NLR.

The non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are the drugs frequently used in acute renal colic pain in emergency departments [3]. Although the rapid effect of opioids is a big advantage at the beginning, some clinicians do not think that opioids should be the first choice due to their side effects, such as hypotension, vomiting, and dizziness [23]. A recent study showed that IV paracetamol was as effective as IV opioids in renal colic attacks [24]. In our study, the patients' treatments were left entirely to the doctor's own clinical decisions. A substantial number (47.3%) of patients were only treated with IM or IV NSAIDs. The mean VAS score of the patients treated only with NSAIDs, or only with IV paracetamol, was lower than the group receiving only IV opioids or a combined treatment. This suggests that clinicians prefer IV opioids in the event of severe pain or when the first treatment is not sufficiently effective.

5. Limitations

The main disadvantage of the study was that we did not grade hydronephrosis. Also, accepting the sonographic findings in terms of hydronephrosis may be a disadvantage, when CT is the gold standard. The acute phase reactants and imaging results may be different in chronic diseases such as malignancy, chronic kidney failure, heart failure, and diabetes. Including patients with chronic diseases might have affected the results.

6. Conclusion

In conclusion, this study found that the pain level experienced by the patients was not related to the stone size in renal colic attacks, and big stones could pose an increased risk in the development of hydronephrosis. The results indicated that the risk of complications such as hydronephrosis is higher in patients with severe pain and that it may be accompanied with infection.

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Informed consent

Informed consent was obtained from all individual participants included in the study.

Prior presentations

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Contributors' list

Contributorship and data collection: MİŞ and VK.; Served as scientific advisors: MİŞ and VK. Writing and statistical study: MİŞ.

Declaration of Competing Interest

Muhammed İkbal Şaşmaz, and Vedat Kırpat do not have any conflict of interest.

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