Ultrasound Findings Of Patients With Microscopic Hematuria Considering The Patients' History Through Questionnaire

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ABSTRACT
Purpose: This study was performed to determine the sonographic findings of urinary system to clarify the prevalence of disease as determined by age, sex and the degree of haematuria at presentation in patients with microscopic hematuria attending to Amiralmomenin Hospital (Tehran, Iran) in 2016 and 2017.
Methods: In this observational study that was performed as a cross-sectional comparative descriptive survey, 216 consecutive patients with microscopic hematuria attending to Amiralmomenin Hospital in 2016 and 2017 were enrolled and the sonographic findings of urinary system were determined.
Results: The findings revealed that sonography was positive in 98.1%. The findings were as stone, cyst plus stone, and others in 80.7%, 13.7%, and 5.6%, respectively. The findings were in kidney, ureter, and bladder in 84.8%, 1.9%, 1.9% and 11.4% more than one location, respectively. It was in left side, right side, and bilateral in 23.7%, 19.3%, and 57%, respectively. Age was the only related factor and was higher in those with mass.
Conclusions: According to the obtained results in this study, it may be concluded that majority of patients with microscopic hematuria would have positive sonography that stone is the most common.

Keywords: Ultrasound, Microscopic hematuria, Amiralmomenin hospital, Sonography, Stone.

1. Introduction

Microscopic hematuria is defined as the presence of three or more red blood cells per microscopic HPF [1]. This disorder can be caused by a range of causes including trivial and transient causes to serious causes [1]. Therefore, careful examination and determination of its etiology is very important; because in 13% of cases of microscopic hematuria, causes requiring treatment such as urothelial and kidney malignancies and urinary stones are observed in people [2]. Therefore, diagnostic evaluations such as imaging studies and cystoscopy, etc., in patients with microscopic hematuria, are very important in determining the cause and treatment course of patients [1, 2]. In addition, in some patients who have malignancy of the administrative system or who have undergone a kidney transplant, microscopic hematuria can be used as an important marker in the follow-up of patients [3]. However, despite the necessary investigations and in accordance with the guidelines, it is not performed in the majority of patients [4]. Isolated hematuria without proteinuria, other cells, or casts often indicates bleeding from the urinary tract. According to the definition, hematuria is the presence of 2 to 5 red cells in each microscopic field with high magnification, which can be determined by a paper strip (dipstick) test. A paper strip test may be false positive (no red cells are seen under the microscope) due to myoglobinuria that occurs due to rhabdomyolysis. The common causes of isolated hematuria are: stones, neoplasms, tuberculosis, trauma and prostatitis. The presence of macroscopic hematuria with blood clots almost never indicates glomerular bleeding, but suggests a postrenal origin in the urine collection system. The presence of hematuria in a complete urine test is a common problem that may be caused by menstruation, viral disease, allergies, exercise or mild trauma. Persistent or significant hematuria (more than 3 red cells per high-magnification field on three urinalysis or one urinalysis with more than 100 red cells or macroscopic hematuria), indicative of significant urologic or renal lesions in 19.0% of patients. Suspicion of genitourinary neoplasms increases with age in patients with discrete, painless hematuria with undeformed RBCs. Neoplasms are rare in children, and in this group of patients isolated hematuria

is more "idiopathic" or related to a congenital abnormality. Hematuria with pyuria and bacteriuria is characteristic of infection and should be treated with antibiotics after appropriate cultures. Acute cystitis or urethritis in women may cause macroscopic hematuria. Also, increased urinary calcium and uric acid in both children and adults are among the risk factors for unexplained isolated hematuria. In some of these patients (50 to 60 percent), reducing the excretion of calcium and uric acid through dietary interventions can cause microscopic hematuria to disappear [5-8]. Therefore, painless hematuria of any degree in adults should be regarded as a symptom that is suspicious for malignancy until proved otherwise. Cystoscopy is considered the gold standard in the evaluation of hematuria [9]. This technique directly visualizes lower urinary tract anatomy and macroscopic pathology, which may be responsible for the clinical picture under evaluation. However, cystoscopy is invasive, time-consuming and expensive [10]. Currently, modern sensitive transducers have improved imaging of the urinary tract and therefore transabdominal ultrasound is more effective in visualizing intraluminal filling defects in the bladder than it was in the past. Moreover, ultrasonography is a non-invasive, well accepted, and cost effective diagnostic procedure. Systematic use of ultrasonography has been proposed as the initial test for detection of bladder carcinomas in patients presenting with hematuria [11]. Blood in urine can be originated from any part of the urinary tract system, attributed to either glomerular or nonglomerular origins. Glomerular hematuria almost always arises from a medical cause and diagnosis is made by histologic or serologic examinations. Thus, imaging modalities are of no diagnostic value [12, 13]. Nonglomerular hematuria is mainly the sign of renal and bladder tumors, urinary tract infections, tuberculosis, trauma, urinary tract calculi, arteriovenous fistula, and renal vessels thrombosis. Intravenous urography (IVU) is the first diagnostic step and, in a sense, the standard method for the evaluation of patients with hematuria [1, 12]. Its low cost and objective results, when compared with CT scan, has made IVU the popular method used in most studies [1]. However, some conditions, such as hypersensitivity to contrast media, moderate or severe kidney dysfunction, diabetes mellitus, multiple myeloma, congestive heart failure, and pregnancy limit the use of IVU or are accompanied by a high risk [13-15]. Furthermore, this test has a low sensitivity in the diagnosis of small kidney and bladder neoplasms and is not able to differentiate cystic from solid masses [1]. Transabdominal ultrasonography (US) is a non-invasive tool with an acceptable accuracy in evaluation of the kidney, vessels, prostate, and bladder anatomy [16]. Since it is not dependent on contrast media excretion, US can be used regardless of the kidney function [14]. Ultrasonography is currently the method of choice for the evaluation of children with congenital anomalies of the urinary tract system. It can be used to differentiate solid and cystic masses [13, 17]. Notwithstanding its many advantages, US is not recommended in the assessment of the urothelium and diagnosis of transitional cell carcinoma of the renal pelvis or the ureters [1]. Although in patients with hematuria, ultrasound is a routine test among the diagnostic measures; But in 52% of cases, it does not show any special findings and the results are normal [18]. This statistic can be lower in patients with microscopic hematuria and therefore determining the efficiency of this method can help in its better use in this group of patients. Based on this, in this study, we examined the ultrasound findings of the urinary tract in patients with microscopic hematuria who referred to Amiralmomenin Hospital in 2016-2017.

2. Methods

In this observational study, which was conducted as a descriptive-analytical cross-sectional survey, 216 patients with microscopic hematuria referred to Amiralmomenin Hospital in 2016-2017 were selected as available. First, a written questionnaire was used to collect information in the patients' history, then the patients were subjected to ultrasound by a radiologist in the hospital and the findings of ultrasound of the urinary tract were examined in them. The method of data collection was done in the field by using the data collection form and finally after collecting the required information of the study subjects, Age, gender, family history, surgical history, previous trauma, diabetes mellitus, anticoagulant use, smoking status, obesity, ultrasonography findings, ultrasonography findings type, ultrasonography findings location, ultrasonography findings side, ANOVA table, cross tab and chi-square tests were extracted from medical Figs. We analyzed the data and used SPSS version 13 statistical software. The statistical tests used in this study were (Chi-Square) and Fisher and independent t, the results for categorical variables are presented as percentage analyzed using Fisher’s exact test or chi-square test whenever appropriate and the level of significance was considered to be 0.05. Also the personal information of the investigated persons was not disclosed.

3. Results

Age frequency distribution of examined patients.
The average age of the examined patients was 51.1 years with a standard deviation of 19.1 years.
Gender frequency distribution of examined patients

49.1% of patients were female and 50.9% were male.
Frequency distribution of family history in examined patients.
Family history was positive in 25.5% of the examined patients.
Frequency distribution of surgical history in the studied patients.
History of surgery was positive in 3.2% of patients.
Frequency distribution of previous trauma in examined patients.
2.8% of patients had a history of previous trauma.
Distribution of the frequency of diabetes in the studied patients.
19.4% of patients had diabetes.
Frequency distribution of anticoagulant drug use in the studied patients.
6.5% of patients had a history of taking anticoagulant drugs.
Distribution of the frequency of smoking in the investigated patients.
26.9% of patients had smoking history.
Frequency distribution of obesity in examined patients.
Obesity was observed in 32.4% of the examined patients.
Frequency distribution of ultrasound findings in the examined patients.
Ultrasound had positive findings in 98.1% of patients (Table 1).

Table 1. Ultrasonography Findings.

	Frequency	**percent**	**Valid percent**	**Cumulative percent**
Valid Neg	4	1.9	1.9	1.9
Pos	212	98.1	98.1	100.0
Total	216	100.0	100.0	

Frequency distribution of the type of ultrasound findings in the examined patients.
The findings of the sonographer were in 80.7% stones, 13.7% cysts with stones and in the remaining 5.6%, there were other diagnoses (Table 2).

Table 2. Ultrasonography Findings Type.

	Frequency	**Valid percent**
Valid Stone	171	80.7
Cyst+Stone	29	13.7
Unknown	2	.9
Stone+Mass	1	.5
Maas	1	.5
Collectasia	1	.5
Cyst Alone	7	3.3
Total	212	100.0

Frequency distribution of ultrasound findings in examined patients.
The location of ultrasound findings were 1.9% ureter, 1.9% bladder and 11.4% more than one location (Table 3).

Table 3. Ultrasonography Findings Location.

	Frequency	**Valid percent**
Valid kidney	179	84.8
Ureter	4	1.9
Bladder	4	1.9
>1	24	11.4
Total	211	100.0

Frequency distribution of ultrasound findings in examined patients.
Ultrasound findings in 23.7% were on the left side, 19.3% were on the right side, and 57% were bilateral.
Frequency distribution of ultrasound findings based on age in the investigated patients.
The mean age was significantly higher in patients with Mass (P=0.0001) (Table 4).

Table 4. Age.

Ultrasonography	Mean	Std. Deviation
Stone	47.76	18.138
Cyst+Stone	66.93	14.827
Unknown	39.50	45.962
Stone+Mass	70.00	.
Maas	60.00	.
Collectasia	50.00	.
Cyst Alone	71.29	10.626

Frequency distribution of ultrasound findings based on gender in the examined patients.
There was no statistically significant difference in the frequency distribution of ultrasound findings based on gender in the investigated patients ($P > 0.05$).
Frequency distribution of ultrasound findings based on family history in the examined patients.
The frequency distribution of ultrasound findings based on family history in the studied patients had no statistically significant difference ($P > 0.05$).
Frequency distribution of ultrasound findings based on surgical history in examined patients.
The frequency distribution of ultrasound findings based on the history of surgery in the examined patients had no statistically significant difference ($P>0.05$).
Frequency distribution of ultrasound findings based on history of trauma in examined patients.
The distribution of the frequency of ultrasound findings based on trauma in the studied patients had no statistically significant difference ($P>0.05$).
Frequency distribution of ultrasound findings based on diabetes in the studied patients.
The frequency distribution of ultrasound findings based on diabetes in the examined patients had no statistically significant difference ($P > 0.05$).
Frequency distribution of ultrasound findings based on the use of anti-anxiety drugs.
The distribution of the frequency of ultrasound findings based on the use of anti-inflammatory drugs was not statistically significant ($P > 0.05$).
Frequency distribution of ultrasound findings based on smoking in the examined patients.
The frequency distribution of ultrasound findings based on smoking in the studied patients had no statistically significant difference ($P > 0.05$).
Frequency distribution of ultrasound findings based on obesity in the examined patients.
The frequency distribution of ultrasound findings based on obesity in the studied patients had no statistically significant difference ($P > 0.05$).
Age frequency distribution of examined patients the average age of the examined patients was 51.1 years with a standard deviation of 19.1 years (Fig. 1).

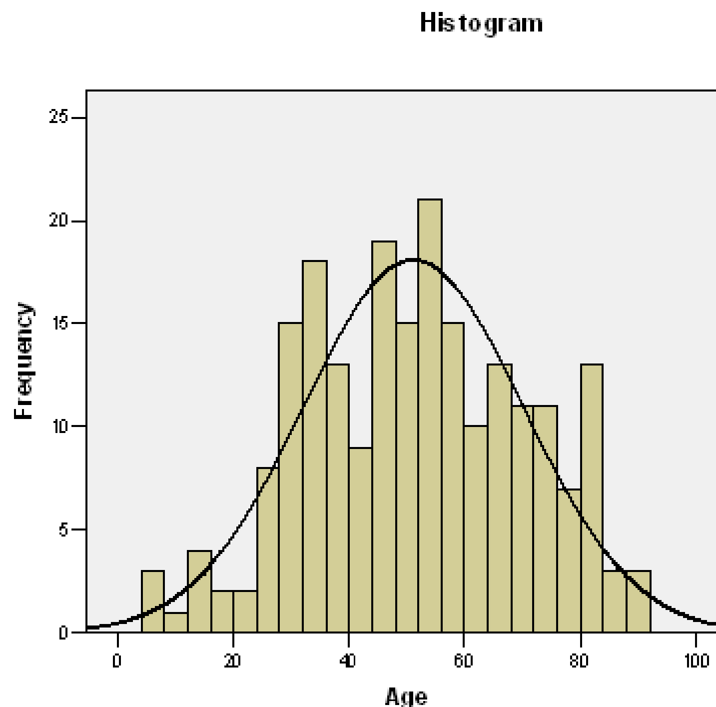

Fig. 1 Histogram _ Age

Gender frequency distribution of examined patients
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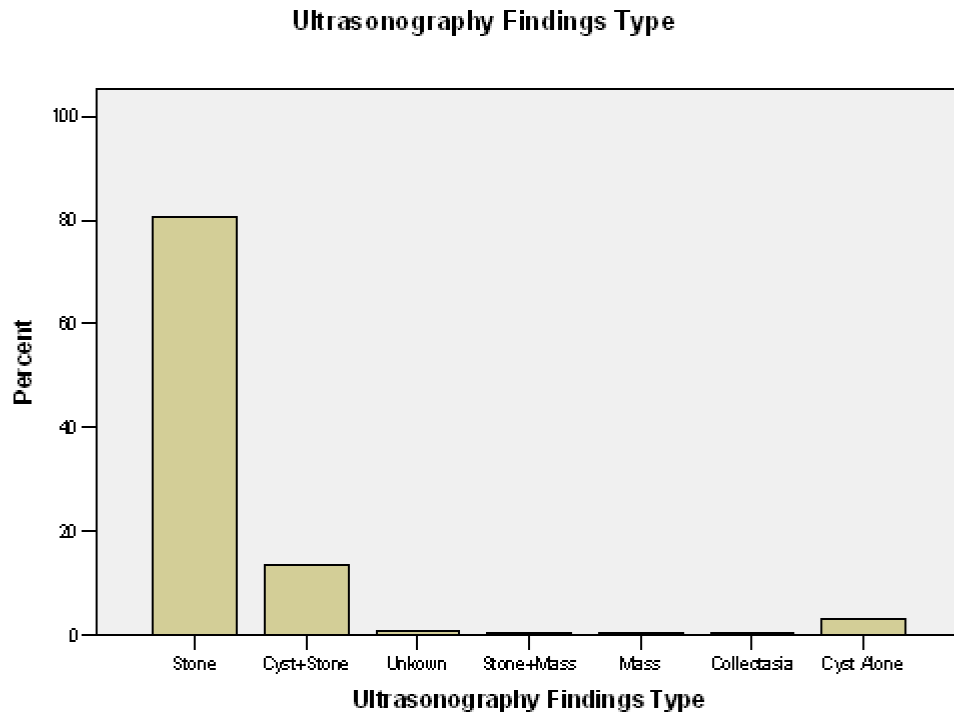

Fig. 2 Ultrasonography Findings Type
Frequency distribution of ultrasound findings in the studied patients.
The location of ultrasound findings is 1.9% ureter, 1.9% bladder and 11.4% more than one location.
Frequency distribution of ultrasound findings in the examined patients.
Ultrasound findings in 23.7% were on the left side, 19.3% were on the right side, and 57% were bilateral.

4. Discussion

In an analytical cross-sectional study conducted by Stamatiou et al. in Greece and the results of which were published in 2009, by examining 173 patients with microscopic hematuria, it was announced that only 20% had positive findings in ultrasound, which compared to cystoscopy, indicates sensitivity. 87.1% and specificity was 98.1% [19], in this study 98% had positive findings. In a review study conducted by McDonald and colleagues in America and the results of which were published in 2006, it was announced that in patients with microscopic hematuria, different diagnostic evaluations are needed, among which the most important of them is ultrasound [20]. That is why we investigated ultrasound in this study. In a prospective study conducted by Khadra et al. in England and the results of which were published in 2000, after examining 2200 patients with microscopic hematuria, it was announced that 14 patients (0.7%) had important diseases including stones in ultrasound. were urinary and malignant, only 4 patients had microscopic hematuria [21], which is lower than the statistics obtained in this study.In a cross-sectional study conducted by Feld et al. in America and the results of which were published in 1998, by examining 325 patients with microscopic hematuria, it was announced that 18 people (5.5%) of them had positive findings in ultrasound [22]. Compared to this study, it is a lower figure which can be caused by the difference in the devices used in the two studies. In a study conducted by Mokulis et al. in America and the results of which were published in 1995, by examining 101 patients with microscopic hematuria, it was announced that 20% of the patients had a positive ultrasound [23], and in this study, this rate was 98% was achieved. Hematuria, either gross or microscopic, may be indicative of a serious disease of the genitourinary tract. In a study conducted by Gerber GS and Brendler CB showed that hematuria is more frequent in men than in women. They found no explanation for this sign in 40% of the patients. Kidney and ureteral calculi were the most common causes of hematuria, followed by bladder and kidney neoplasms with a much lower frequency. In agreement with the literature [12], so we examined patients with microscopic hematuria in this study. In a retrospective study by Eshed and Witzling, it was shown that CT scan, when carried out after US, could not provide additional information in children with kidney calculi aged 1 to 15 years. They suggested that US be used as the first step and CT scan be used only when US results are not normal or not definite [24]. Some investigators have defined 2 to 3 red blood cells per HPF as significant microhematuria [25, 26]; other investigators have a more rigid definition of greater than or equal to 1 red blood cell per HPF as significant hematuria [23, 27-30]. In other studies, significant microhematuria was defined as 6 or more red blood cells per HPF [31, 32]. In our study, microscopic hematuria is reported in patients based on urine testing.

Asymptomatic hematuria is a common problem with numerous causes, including prostate disease and kidney stones; however, the most worrisome cause is malignancy. A recent meta-analysis showed a 3.3% risk of urinary tract malignancy in patients with asymptomatic microscopic hematuria without stratification for age or other risk factors [33]. An additional risk factor for malignancy is age. Typically, age older than 35, 40, or even 50 years has been considered a threshold for placing a patient in a higher risk category classification. Finally, male sex and occupational and other environmental risk factors, such as tobacco use, analgesic abuse, and cyclophosphamide intake, have all been reported to increase the risk of urinary tract malignancy, accordingly in this study patients with microscopic hematuria were investigated. Regardless of the risk factors associated with microscopic hematuria, most cases will not have a specific cause identified even after a thorough evaluation[21], however, in our study various causes including the presence of stone, cyst, mass, cyst with stone and stone with mass were observed that stones were most common reason with 80.7%. In fact, transabdominal ultrasonography is a simple and quick examination that can be safety performed on all individuals with no restrictions (for example, the elderly and handicapped patients that cannot undergo cystoscopy, and septic patients and those with renal failure that are contraindicated for intravenous pyelography). Ultrasonography is also easily available, cost- effective, and non-invasive, requiring no special preparation, and provides images of both the upper and lower renal tract. In the past, the accuracy of ultrasound devices in the diagnoisis of superficial bladder tumors was less than that of the current devices and this led to an underestimation of the value of ultrasound; thus, ultrasonography has been accused of not always being an appropriate method for the diagnosis of bladder cancer. Technological evolution has rendered current scanners, which combine several different transducers and color or spectral Doppler imaging facilities, more accurate in the visualization of intraluminal filling defects of the bladder. In fact, detection rates for bladder carcinoma have been increased from 82% to 95% [34, 35], therefore we used ultrasound method in our study. In general, based on the results of this study and their comparison with other studies, it is concluded that ultrasound is abnormal in most patients who have microscopic hematuria, and urinary stones are the most common cause. In the end, it is suggested that more studies should be conducted in order to confirm the findings obtained in this study, with a larger sample size and also by examining the effect of other factors on ultrasound findings in patients.

5. Conclusions

The results obtained in sonography had positive findings in 98.1% of patients. The findings of the sonography in 80.7% were stones, 13.7% were cysts with stones and in the remaining 5.6% of other diagnoses. The location of ultrasound findings was 84.8% kidney, 1.9% ureter, 1.9% bladder and 11.4% more than one location. Ultrasound findings in 23.7% were on the left side, 19.3% were on the right side, and 57% were bilateral. Age was the only factor associated with ultrasound findings, and the age of patients with Mass was higher.

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