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ORIGINAL ARTICLE

The Association Between Urinalysis and Urine Culture Results in Children Aged 3-6 Years Who Applied to A Pediatric Emergency Clinic at A University Hospital

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ÖZET

Amaç: İdrar yolu enfeksiyonu (İYE) çocukluk çağının sık enfeksiyonlarındandır. Tanıda altın standart idrar kültüründe etken patojenin üretilmesidir, ancak özellikle birinci basamak sağlık kuruluşlarında idrar kültürü olanağının kısıtlı olması, idrar kültürünün geç sonuçlanması farklı tetkiklerle hastayı değerlendirmeyi gerektirir. Bu durumda tam idrar tetkiki ve idrar mikroskopisinin hekimlere yol gösterici olabileceği düşünülmektedir. Bu çalışmada tam idrar tetkiki ve idrar mikroskopisinin idrar yolu enfeksiyonu tanısındaki yerinin ortaya konması amaçlanmıştır. **Yöntem:** Araştırmaya 01.01.2016-31.12.2016 tarihleri arasında Adnan Menderes Üniversitesi Uygulama ve Araştırma Hastanesi Çocuk Acil Polikliniğine başvuran, aynı muayenede tam idrar tetkiki ve idrar kültürü istenmiş ve her iki numuneyi de verebilmiş olan 3-6 yaş arası, toplam 728 hasta alındı. Hasta dosyaları Hastane Bilgi Yönetim Sisteminden geriye yönelik tarandı, veriler SPSS 18.0 İstatistik Paket Programı ile değerlendirildi. **Bulgular**: Çalışmaya 425 (%58,4) kız, 303 (%41,6) erkek hasta alındı. İdrar kültüründe üreme olan hastaların %69,5'i kız, %30,5'i erkekti. Tam idrar tetkiki sonuçlarının idrar kültürü ile ilişkisi istatistiksel olarak anlamlı bulundu (p<0,01). Lökosit esteraz, %63,1 ile en yüksek duyarlılığa sahipti. Lojistik regresyon analizinde dizüri varlığının idrar yolu enfeksiyonu olasılığını 3,15 kat, idrarda lökosit varlığının 2,52 kat, nitrit varlığının 19,76 kat, bakteri varlığının 13,43 kat artırdığı görüldü. **Sonuç:** İdrar yolu enfeksiyonlarının tanısında tam idrar tetkiki ve idrar mikroskopisi yol gösterici bilgiler vermektedir.
Anahtar kelimeler: İdrar Yolu Enfeksiyonu, Lökosit Esteraz, Nitrit, Tam İdrar Tetkiki

ABSTRACT

Aim: Urinary tract infection (UTI) is one of the most common infections of childhood. The generation of the causing pathogen in urine culture is the gold standard in diagnosis. However, due to the low likelihood of urine culture, particularly in primary healthcare facilities, and the prolonged results of urine culture, the patient must perform different examinations. In this case, it is thought that urinalysis and urine microscopy may guide physicians. In this study, it is aimed to reveal the role of urinalysis and urinary microscopy in the diagnosis of urinary tract infection. **Methods:** In this study, 728 children between the ages of 3-6 who applied to the pediatric emergency clinic at a university hospital over a 12-month period and were able to deliver both samples for urinalysis and urine culture were included. Retrospective patient file screening was done using the Hospital Information Management System, and Statistical Software SPSS 18.0 was used to assess the data. **Results:** 425 (58.4%) female and 303 (41.6%) male patients were included in the study. Patients with urine culture reproduction comprised 30.5% male and 69.5% female. The relationship between urinalysis and urine culture results was found to be statistically significant (p<0.01). Leukocyte esterase had the highest sensitivity with 63.1%. In the logistic regression analysis, it was seen that the presence of dysuria increased the likelihood of urinary tract infection by 3.15 times, the presence of leukocytes in the urine by 2.52 times, the presence of nitrites by 19.76 times, and the presence of bacteria by 13.43 times. **Conclusion:** Urinalysis and urine microscopy provide guiding information in the diagnosis of urinary tract infections.
Keywords: Urinary Tract Infection, Leukocyte Esterase, Nitrite, Urinalysis

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INTRODUCTION

Urinary tract infection (UTI) is an infection that typically arises from bacteria in the normally sterile urinary system (1). Among childhood infections, UTI is the second most common occurrence after respiratory tract infections (2). In studies, the frequency of UTI in children was determined as 2-8% (3,4).

UTI can manifest itself in a variety of ways from asymptomatic bacteriuria to complex pyelonephritis. Although it is more benign in adults, it may cause complications such as renal scarring, end-stage renal failure, and hypertension in childhood (5,6). Therefore, it's critical to identify the disease early and to administer the proper care and follow-up. The complaints of the patients differ based on their age, gender, and underlying anatomical or neurological condition. Typical symptoms are usually not observed in infants, and the complaints may consist of more general symptoms including agitation, fever, vomiting, weakness, appetite loss, inability to put on weight, jaundice, etc. Children three years of age and older may have more specific symptoms such as frequent urination, burning when urinating, suprapubic sensitivity, urinary incontinence, and changes in urine color or odor (7).

When the symptoms suggest UTI, urinalysis may be performed to support the diagnosis. The gold standard in diagnosis is the production of the causative pathogen in urine culture (4). However, the inability of urine culture to be performed in every health center and the long-term receipt of the results restrict the use of this examination. Urinalysis is used often in situations where urine culture cannot be performed because it is a straightforward, readily available, and quick result examination in the diagnosis of UTI. In this study, it is aimed to reveal the place of urinalysis in the diagnosis of UTI.

MATERIAL AND METHODS

This study is a cross-sectional study and, 728 children between the ages of 3-6 who applied to the pediatric emergency clinic at a university hospital over a 12-month period and were able to deliver both samples for urinalysis and urine culture were included. Patients with incomplete information for the study in the patient file registered in the Hospital Information Management System were excluded from the study.

The patient files included in the study were scanned retrospectively from the Hospital Information Management System software. First complaint, further symptoms, age, gender, results of urine microscopy, urinalysis, and urine culture were all noted. Uric 1600R automatic machine was used to analyze urine samples. When evaluating the urine microscopy, pyuria was defined as the presence of 5 or more leukocytes per field, and bacteriuria as the presence of 1 or more bacteria per field in the produced urine for 5 minutes at 2000 cycles. In urine culture, it was considered significant to have 105 CFU or more reproduction after 24 hours of incubation in urine samples taken sterile from patients and

transplanted into a blood agar base (8,9). No distinction was made between upper and lower urinary tract infections in patients whose urine culture findings showed a significant growth. The SPSS 18.0 Statistics Package Software was used to analyze the collected data. P<0.05 was considered statistically significant.

The necessary approval was obtained from the Adnan Menderes University Faculty of Medicine Non-Interventional Research Ethics Committee for the study.

RESULTS

728 patients were included in the study, 303 (41.6%) were male, 425 (58.4%) were female, with a mean age of 4.29±1.12 years. 688(94.5%) patients had at least one symptom suggestive of a UTI. It's found that 303 (41.6%) patients had fever, 299 (41.1%) had nausea, 233 (32%) had abdominal pain, 99 (13.6%) had dysuria, 60 (8.2%) had changed urine color and odor, 30 (4.1%) had a rash, 21 (2.9%) had frequent urination, 13 (1.8%) had urinary incontinence, and 9 (1.2%) had itching and redness in the perineum.

According to the results of urinalysis and urine microscopy, the number of patients with at least one finding suggestive of UTI was 275 (38.7%). Some of the patients had more than one finding. The findings of urinalysis and urine microscopy are given in Table 1.

Table 1. Urinalysis and urine microscopy findings

Parameter	Positive	Negative
Leukocyte	177 (24.3%)	551 (75.7%)
Erythrocyte	123 (16.9%)	605 (83.1%)
Bacteria	14 (1.9%)	714 (98.1%)
Fungus	8 (1.1%)	720 (98.9%)
Nitrite	23 (3.2%)	705 (96.8%)
Leukocyte Esterase	201 (27.6%)	527 (72.4%)
Leukocyte Esterase		
+1	110 (15.1%)	
+2	42 (5.8%)	
+3	49 (6.7%)	

It was determined that 95 (13%) of the patients had reproduction when the urine culture findings were analyzed. Whereas contamination was seen in 17 (2.3%) patients, 616 (84.6%) patients' urine cultures showed no reproduction. Patients with contamination at urine culture were excluded from the analysis.

When the association between gender and urine culture findings was examined, it was determined that 66 (70.2%) of individuals

who had positive urine cultures were girls and 28 (29.8%) were boys. Urine culture positivity was higher in girls than in boys, and this difference was statistically significant ($p<0.05$).

There was no statistically significant correlation between urine culture positivity and symptoms like high fever, abdominal pain, nausea/vomiting, frequent urination, urinary incontinence, itching-redness of the perineum, rash, and reproduction in urine culture. Among the 97 patients with dysuria, 29 (29.9%) had reproduction, while 68 (70.1%) had no growth ($p<0.01$). There was growth in urine culture in 17 (28.8%) of the 59 patients with urinary abnormalities, but not in 42 (71.2%) of them ($p<0.01$).

There was a statistically significant relationship between positive findings in urinalysis/urine microscopy and urine culture positivity (Table 2). Leukocyte esterase (LE) was grouped as one positive, two positives, and three positives according to density. The effect of LE density on urine culture positivity is given in Table 2. In addition, 12 out of 13 patients (92.3%) whose nitrite and three positive leukocyte esterase tests were together, exhibited reproduction in urine culture.

Table 2. The relationship between urinalysis/urine microscopy and urine culture results

		Urine Culture		p
		Positive	Negative	
Urinalysis	Had findings	69 (25.8%)	198 (74.2%)	<0.01
	No findings	26 (5.9%)	418 (94.1%)	
Leukocyte	Yes	56 (32.7%)	115 (67.3%)	<0.01
	No	39 (7.2%)	501 (92.8%)	
Erythrocyte	Yes	33 (27.5%)	87 (72.5%)	<0.01
	No	62 (10.5%)	529 (89.5%)	
Bacteria	Yes	12 (92.3%)	1 (7.7%)	<0.01
	No	83 (11.9%)	615 (88.1%)	
Nitrite	Yes	20 (90.9%)	75 (10.9%)	<0.01
	No	2 (9.1%)	614 (89.1%)	
LE*	Yes	60 (31.1%)	133 (68.9%)	<0.01
	No	35 (6.8%)	483 (93.2%)	
LE*	+1	21 (19.6%)	86 (80.4%)	<0.01
	+2	10 (25%)	30 (75%)	
	+3	29 (63%)	17 (37%)	

*LE: Leukocyte esterase

Symptoms that significantly increase the frequency of reproduction in urine culture; dysuria and urine changes were evaluated together with urinalysis/urine microscopy findings (Table 3, Table 4).

Table 3. The relationship between urinalysis findings and urine culture in patients with dysuria

		Urine Culture		p
		Positive	Negative	
Urinalysis	Had findings	24 (51.1%)	23 (48.9%)	<0.01
	No findings	5 (10%)	45 (90%)	
Leukocyte	Yes	23 (57.5%)	17 (42.5%)	<0.01
	No	6 (10.5%)	51 (89.5%)	
Erythrocyte	Yes	15 (65.2%)	8 (34.8%)	<0.01
	No	14 (18.9%)	60 (81.1%)	
Bacteria	Yes	5 (100%)	0 (0%)	0.002
	No	24 (26.1%)	68 (73.9%)	
Nitrite	Yes	10 (90.9%)	1 (9.1%)	<0.01
	No	19 (22.1%)	67 (77.9%)	
LE*	Yes	24 (57.1%)	18 (42.9%)	<0.01
	No	50 (9.1%)	5 (90.9%)	

*LE: Leukocyte esterase

Table 4. Relationship of urinalysis findings with urine culture in patients with urinary changes

		Urine Culture		p
		Positive	Negative	
Urinalysis	Had findings	15 (41.7%)	21(58.3%)	0.006
	No Findings	2 (8.7%)	21 (91.3%)	
Leukocyte	Yes	14 (53.8%)	12 (46.2%)	<0.01
	No	3 (9.1%)	30 (90.9%)	
Erythrocyte	Yes	9 (39.1%)	14 (60.9%)	0.162
	No	8 (22.2%)	28 (77.8%)	
Bacteria	Yes	2 (100%)	0 (0%)	0.024
	No	15 (26.3%)	42 (73.7%)	
Nitrite	Yes	5 (83.3%)	1 (16.7%)	0.002
	No	12 (22.6%)	41 (77.4%)	

LE*	Yes	15 (51.7%)	14 (48.3%)	<0.01
	No	2 (6.7%)	28 (93.3%)	

*LE: Leukocyte esterase

Regression analysis was performed to investigate the effect of the signs and symptoms on the urine culture result. (Table 5).

Table 5. Effect of symptoms and urinalysis signs on reproduction in urine culture

	B	*p*	*OR*
Gender	0.439	0.076	1.552
Dysuria	1.148	0.000	3.153
Color and odor change in urine	1.098	0.001	2.997
Leukocyte	0.927	0.003	2.526
Erythrocyte	0.261	0.414	1.298
Bacteria	2.597	0.031	13.430
Fungus	1.391	0.059	4.017
Nitrite	2.984	0.000	19.762
LE* +3	1.358	0.002	3.888

*LE: Leukocyte esterase

DISCUSSION

UTI is one of the common infectious diseases in childhood. Although it is more common in uncircumcised boys in the first year of life, it is more common in female of all other ages than in male (7). In our study, 13% of the patients had urine culture reproduction, 66 (69.5%) of the patients with reproduction were females and 29 (30.5%) were males, these findings are consistent with the literature according to age group. Pouladfar et al, their study in Iran, found that females grew urine cultures at a rate of 70.3%, which is twice as often as males, similar to our findings (9).

As in similar studies; fever, abdominal pain, nausea, vomiting, burning during urination, color and odor changes in urine, frequent urination, urinary incontinence, urinary tract infection was accepted as suggestive findings (9-11). Of the patients included in the study, 41.6% had fever, 41.1% had nausea-vomiting, 32% had abdominal pain, 13.6% had burning while urinating, 8.2% had changes in urine color and odor, 4.1% had the rash, 2.9% had frequent urination, 1.8% had urinary incontinence, 1.2% had itching-redness.

To diagnose UTI, the complaints of the patients should point to the UTI and give an idea to the physician about this. In this respect,

we compared whether there was a correlation between the symptoms of the patients included in our study and urine culture. When we excluded 17 patients with urine culture contamination and evaluated the remaining 711 patients, there were 672 patients who presented to our emergency department with at least one symptom. Only 14% of patients with at least one symptom had reproduction, which suggests that the presence of symptoms was insufficient for the diagnosis of UTI. Nevertheless, the rate of reproduction in urine culture was significantly higher in patients presenting with at least one symptom than in patients without symptoms. When we evaluated the symptoms individually, nearly half of the patients with high fever, one quarter of the patients with abdominal pain and nausea/vomiting had urine culture growth. There was no statistically significant association between fever and UTI. The fact that we included patients between the ages of 3-6 in our study may have caused this result. UTI symptoms vary according to age, fever, loss of appetite, nausea-vomiting, fever are the symptoms mostly seen in UTI between the ages of 0-2 (12). Fever is often not expected in uncomplicated UTI and lower urinary tract infections (13).

Two symptoms that we have seen significantly increase the likelihood of reproduction in urine culture are dysuria and a change in urine color and odor. Almost one-third of patients with dysuria and changes in color and odor in urine have seen reproduction in urine culture. This data is an expected finding in terms of UTI symptoms seen in children aged 2-5 years (14).

In patients who have applied with suspicion of UTI, urinalysis and urine microscopy may be guiding in cases where urine culture cannot be performed or if it is desired to start treatment without waiting for the result of the culture. Leukocyte esterase and nitrite in urinalysis, leukocytes, erythrocytes, or bacteria in the microscopic examination is evaluated in favor of UTI. In our study, urinalysis, urine microscopy, and urine culture were performed on all patients. Urine cultures were positive in 25.8% of the patients who had any positive urinalysis results. This data is statistically significant, and it demonstrates that urinalysis can help with the diagnosis of UTI.

Bacterial growth was observed in 32.7% of patients with leukocytes detected in the urine in our study. It was found that those with leukocytes in the urine were 4.5 times more likely to have a UTI than those who did not have leukocytes. The sensitivity of the test was 59%; specificity was calculated as 81.3 %. According to these data, the absence of leukocytes in the urine distracts the physician from the diagnosis of UTI, but positive values are insufficient in diagnosis. Positive findings need to be supported by urine culture. In different two studies, the sensitivity of leukocytes was 73.3% and 96% (15,16).

LE is a parameter that indirectly indicates the presence of leukocytes in the urine and can be measured by dipstick and automatic systems. In our study, urine culture was detected in 31.1% of those who were LE

positive. The sensitivity of the LE test was 63.1%; specificity was found to be 78.4%. Although these data are consistent with the literature, studies indicate that the sensitivity and specificity of LE differ according to the patient's age, gender and the way urine is collected. LE is evaluated according to its density. Urine culture was reproduced in 19.6% of patients with LE +1, in 25% of patients with +2 LE, and in 63% of patients with +3 LE. As LE positivity increases, bacterial reproduction increases. In the groups evaluated by one-way variance analysis test, any positive value increased the rate of reproduction in culture according to the negative result, while there was no significant difference between +1 LE and +2 LE, and it was observed that +3 LE significantly increased reproduction. Any level of LE positivity was observed in 87.5% of patients with reproductive production in urine culture. In Hay et al. research, 5.6% of the study participants were found to have minimal LE, 4% had +1 LE, 5.4% had +2 LE, and 1.8% had +3 LE and 3.9%; 1.8%; 12.8%; 33.3% reproduction in these groups, respectively (17).

The presence of leukocytes and leukocyte esterase in the urine differs according to gender. In our study, the presence of leukocytes and leukocyte esterase in the urine was significantly higher in girls than in boys. In a study conducted with primary school children in Turkey, the rate of pyuria was significantly higher in girls with a rate of 24.9% and 1.5% of boys (18). The possible reason why the pyuria rates were lower than our study may be that this study was conducted in asymptomatic healthy children. In Ercan et al. study (19), LE specificity was 55.9% in women and 83.9% in men. It is thought that this difference may be due to leukocytes, epithelial cells, eosinophils in the urine contained in the vaginal discharge. The high number of false positive LE results in women requires the physician to be careful in this regard. In the suspicion of UTI in women, vaginitis, discharge, perineal problems should be questioned; a physical examination should be performed, and the perineum should be cleaned before taking a urine sample.

The seem of erythrocytes in urine microscopy is not specific to infection, it can also be seen in other diseases of the urinary system, but it may still be a guide in the patient presenting with UTI symptoms. In our study, culture positive results were found in 27.5% of patients with erythrocytes, and culture negative results in 72.5%. The sensitivity of the test was 34.7%; the specificity was 85.8%.

The appearance of bacteria in the urine has high diagnostic power in terms of UTI. In our study, 92.3% of the patients with bacteriuria had reproduction in culture. Bacteriuria sensitivity was 12.6%; specificity was 99.8%. Although false negativities are high, seeing bacteria in the urine strongly supports the diagnosis of UTI. Similar results have been reached in domestic and international studies (15, 20).

Nitrite detected by dipstick or automatic methods is an indirect indicator of the presence of bacteria in the urine. It occurs as a result of Gram-negative bacteria converting dietary nitrate to nitrite. Since the

detection of nitrite in the urine indicates the presence of bacteria, it has a strong effect on the diagnosis of UTI. In our study, 90.9% of 22 patients with nitrite positivity in the urine had reproduction. The sensitivity of nitrite in the diagnosis of UTI was 21%; the specificity is 99.6%. The fact that false negativities and therefore sensitivity are low can be attributed to several reasons. The first is that the bacteria that reduce nitrate to nitrite are gram-negative bacteria. Nitrite positivity is not seen in UTIs caused by gram-positive bacteria. Another reason is that the urine must remain in the bladder for at least 4 hours in order to reduce nitrate. Therefore, taking samples from the first urine in the morning can help reduce false negative results. In addition, nitrate must be taken in the diet in order for nitrite to form.

In our study, UTI was detected in 92.3% of patients with three positive LE and nitrite together. Sensitivity was 12.6% when both tests were positive; specificity was calculated as 99.8%. The combination of the two tests increases selectivity. In Tekin et al. (4) study, the sensitivity of the examination was 56.8% and the specificity was given as 97.4% in cases where nitrite and LE were positive. In a guideline, the sensitivity was given as 30-61% and the specificity as 96-99% in the combination of LE and nitrite positivity (21). The fact that the two tests are positive together supports the diagnosis considerably.

Logistic regression test was used to investigate the contribution of symptoms and signs to reproduction in urine culture. It was found that the reproduction in urine culture increased by 3.15 times in the presence of dysuria and 2.99 times in the presence of urine changes. In urine culture, reproduction increased 2.52 times in the presence of leukocytes, 13.43 times in the presence of bacteria, 19.76 times in the presence of nitrite, and 3.88 times in the presence of +3 LE. Burning while urinating and a change in color, and odor in urine are symptoms suggestive of UTI. LE positivity, nitrite positivity, leukocyte and bacteria give an idea in terms of UTI. Detecting the symptoms with a perfect history and evaluating all the findings of urinalysis and urinary microscopy together and in detail will be guiding the diagnosis of UTI.

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