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Urine analysis sensitivity and specificity for paediatric urinary tract infections

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RESEARCH

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ABSTRACT

Background
Paediatric urinary tract infection (UTI) is one of the most common infections among children and a reliable method for diagnosis is critical for management. Few studies have discussed the relationship between the number of leukocytes in the microscopic urinalysis and urine culture.

Aims
Our aim was to determine the sensitivity and specificity of pyuria as a predictor of culture- proven UTI in the paediatric age group.

Methods
This retrospective study was conducted between 2015 and 2020 at King Abdulaziz University Hospital. Demographic data, history of congenital anomalies, and microscopic urine analysis of 315 participants (≤14 years old) was analysed. Pyuria was defined as >5 WBC /HPF.

Results
UTI was diagnosed in 115 patients based on urine culture. The most common organism was *Escherichia coli*. Non-*E. coli* UTI are more common with vesicoureteral reflux patients. Pyuria was found to be positive in 134 (42.5 per cent) of the total sample; 80 of them had a confirmed UTI, with sensitivity of 70 per cent and specificity of 73 per cent. Nitrite has a high sensitivity (66 per cent) but a low specificity. The association between pyuria and positive urine culture was strongly and independently significant (P=0.001). Pyuria and nitrite positivity appear to be more sensitive to *E. coli*.

Conclusion
In conclusion, pyuria is a strong predictor for urinary tract infection in the paediatric age group and is a wise initial test.

Key Words
Paediatrics, pyuria, urinary tract infections

What this study adds:

1. What is known about this subject?
Urine analysis is considered as a good initial screening for paediatric patients suspected to have urinary tract infections.

2. What new information is offered in this study?
Pyuria is a strong independent predictor with high sensitivity and specificity for detecting urinary tract infection. In contrast, nitrite has high specificity but low sensitivity.

3. What are the implications for research, policy, or practice?
Empirical treatment can be started in children with suspected UTI alongside detection by urine analysis as a

primary tool. Non-*E. coli* UTI strongly associated with vesicourethral reflex.

Background

Paediatric urinary tract infection (UTI) is one of the most common infections among children; PUTI affects 7 per cent of females and 2 per cent of males.[1] In Saudi Arabia, 18.6 per cent of children were diagnosed with PUTI, and almost 4 per cent of those presented to the emergency department as a complication of PUTI.[2] The presentation of the condition ranges from mild to severe symptoms, including bacteraemia and shock.[3] Studies have shown that UTI can be accompanied by a variety of complications, such as kidney involvement, subsequent renal scarring, and abnormalities. These complications are considered risk factors for the development of future diseases such as hypertension, pre-eclampsia, and end-stage renal failure.[3] Thus, a reliable and accurate diagnosis is a necessary and critical step in UTI management, especially in paediatric patients. Urine culture is the gold standard method for diagnosing UTI, distinguishing between normal colonization and pathological infection and determining the causative agent and its susceptibility to antibiotics.[1] However, the technique is time-consuming and requires many attempts to exclude negative results and identify specific organisms.[4] Moreover, the specimen should be processed and analysed as early as possible to ensure diagnostic accuracy.[1]

Microscopic analysis of the urine sample is another technique for diagnosing UTI. It is based on examination of the urine sample for the presence of white blood cells (WBCs), red blood cells (RBCs), and bacteria to determine the presence of pyuria (≥5 WBC/high power field) or bacteriuria (presence of any type of bacteria in a high-power field).[1] Studies have shown that bacteriuria is considered a more accurate predictor of UTI than pyuria. However, the presence of these two predictors strongly suggests the diagnosis of UTI.[5]

Few studies have discussed the effectiveness of urine analysis in comparison to urine culture showed the relationship between the number of leukocytes in microscopic urine analysis and positive urine culture and the association between pyuria and urinary abnormalities.

Hence, the primary objective of this study was to determine the sensitivity and specificity of pyuria as a predictor of culture-proven UTI in paediatric patients at the Department of Paediatrics, King Abdulaziz- University Hospital. (KAUH).

Method

This retrospective study was conducted at King Abdulaziz University Hospital, Jeddah, Saudi Arabia from 2015 to 2020.The study procedures were reviewed and approved by the Research Ethics Committee at KAUH (reference number 533–19). Inclusion criteria were all patients ≤14 years old who had UTI confirmed by culture. Neonates with urogenital abnormalities or neonates who were admitted for surgical reasons were excluded. Asymptomatic patients, for which a urine sample was taken for another purpose, were also excluded. Data were collected from the electronic medical records at the Department of Paediatrics. Sociodemographic variables included age, sex, and nationality.

Microscopic urine analysis was performed on all patients with positive urine culture. For each patient, pyuria (defined as >5 WBC/HPF), ketone bodies, glucose, protein concentration, pH, and the method of urine sampling were determined. Complete blood count values (CBC) performed on the same day of urine analysis were also retrieved.

In addition, the medical histories of the patients were assessed to determine the presence of chronic diseases, congenital anomalies, acute renal condition, or a history of antibiotic use before admission to the hospital.

The values were presented as mean +/- standard deviation (SD), minimum and maximum for parametric data, or number (per cent), as appropriate. Data were analysed using SPSS version 23 (IBM SPSS, IBM Corp., Armonk, N.Y., USA). Shapiro – Wilk test was used to evaluate the normality of data distribution. Comparison between samples containing *E. coli* and non-*E. coli* organisms was made using Mann-Whitney U test for nonparametric data and Pearson chi-squared test or Fisher's exact test for categorized data, as appropriate. Diagnostic comparisons were made using 2×2 tables to estimate sensitivity, specificity and accuracy of laboratory data.

Results

Background data

The total sample size was 315 paediatric patients. Among these patients, 140 were female, and 175 were male. Age ranged between two months and 17 years with a mean of 5.60±4.28 years. A positive culture was detected in 36.9 per cent and 36.3 per cent of those aged ≤2 years and >2 years, respectively. UTI was diagnosed in 115 patients (36.8 per

cent) based on a positive urine culture. Demographic data of culture positive patients are shown in Table 1.

Urine analysis variables

Along with urine culture, pyuria and other urinalysis parameters were analysed, as shown in Table 2; of these, pyuria was found to be the most significant. Of the total sample, 134 (42.5 per cent) were positive. 80 of them were confirmed UTI, with sensitivity of 70 per cent and specificity of 73 per cent. Pyuria was associated with a positive urine culture (P=0.001). There were no significant differences between sex and pyuria.

Positive urine cultures showed 20 different types of organisms. The most common organism isolated was *Escherichia coli* (n=30, 26 per cent), followed by *Klebsiella pneumoniae* (n=20, 17 per cent), *Enterococcus faecalis* (n=12, 10 per cent), and ESBL *Escherichia coli* (n=8, 7 per cent). Other organisms were found at relatively similar frequencies, as shown in Table 3.

Vesicoureteral reflux was found in 13 per cent of the patients diagnosed with UTI compared with 2 per cent without UTI (*P*<0.001). Furthermore, gram-negative *Escherichia coli* was the most common organism isolated. Of the cases with *E. coli*, 66.7 per cent were females and 33.3 per cent were males.

Pyuria has a high sensitivity in detecting UTI caused by *E. coli* (83 per cent). The nitrite test yielded the highest specificity for both *E. coli* (86 per cent) and non-*E. coli* (83 per cent) pathogens. Other variables were studied, as shown in Table 4.

Results of the logistic regression analysis are presented in Table 5. This indicates that pyuria (WBC>5) may be a good independent predictor of UTI in children. Blood WBC count, female gender, antibiotic use, and vesicoureteral reflex also significantly predict UTI. Otherwise, age, chronic illness, and method of sample collection appear not to provide any significant correlation with UTI.

Discussion

UTI can vary according to sex, age, prevalence, and isolated organism. In our study, the prevalence of UTI was found to be 36.8 per cent. Several studies have analysed the prevalence of UTI. In 2020, Amin et al. reported a significant difference between males and females, with a prevalence of 54.8 per cent and 45.2 per cent in females and males, respectively.[6] Moreover, a study conducted in a tertiary care center in Riyadh, Saudi Arabia found that 162 patients (80.2 per cent) were female, while 40 (19.8 per cent) were male.[7] These results were similar to our findings in that females had a higher prevalence than males [59 (42.1 per cent) and 56 (32 per cent), respectively.

Similar to previous research, our results showed that the most commonly isolated organisms were *Escherichia coli* (26 per cent), *Klebsiella pneumoniae* (17 per cent), *Enterococcus faecalis* (10 per cent), and *ESBL Escherichia coli* (3 per cent). A Turkish study of 1373 children diagnosed with UTI showed the most commonly isolated organisms were *E. coli* (68.5 per cent), Proteus spp., coagulase-negative *Staphylococci*, Enterococcus spp., Klebsiella spp., and *Pseudomonas aeruginosa*.[5] In addition, Hameed et al. reported that the most common pathogens were *E. coli* (75.7 per cent), followed by *K. pneumoniae* (9.4 per cent), *P. aeruginosa* (5.9 per cent), and Enterococcus species (3.5 per cent).[7]

Urinalysis is the primary diagnostic tool for UTI.[8] According to the 2011 APA Guidelines; the findings of pyuria along with ≥50.000cfu/mL growth for a single organism are the diagnostic criteria. However, a lack of pyuria cannot exclude UTI in symptomatic patients.[9] Concerning sex-pyuria association, our results were consistent with previous findings. A retrospective study involving 1181 children showed no significant association between pyuria among males and females diagnosed with UTI.[10] Moreover, the study investigated the diagnostic accuracy of pyuria, with a sensitivity of 70 per cent and specificity of 73 per cent. Similarly, the American Academy of Paediatrics reported a sensitivity of 73 per cent and specificity of 81 per cent .[9] The ability of nitrite to detect UTI has been widely studied. It was shown that false positive results were rare with a sensitivity of about 50 per cent and high specificity of 98 per cent.[11-13] Furthermore, according to an Egyptian study, nitrite has a sensitivity of 73.3 per cent and specificity of 83.2 per cent.[14] Empirical treatment can be started with children who have a clinical suspicion of UTI caused by Enterobacteriaceae family (*E. coli*, Klebsiella spp., and Proteus spp.) and *E. coli* pathogens as their urinalysis have been shown the presence of nitrite and the absence of pyuria.[10] In our study, nitrite was highly specific for both *E. coli* and non-*E. coli* pathogens.

Leukocyte esterase is another urinalysis parameter to be considered. Mohammed et al. reported a sensitivity of 25

per cent and specificity of 92 per cent, which is different from previous studies that showed higher sensitivity (84 per cent) and lower specificity (78 per cent).[11-14] Our study showed a sensitivity of 14 per cent and specificity of 82 per cent.

Different species of pathogens have been shown in pyuria positive individuals. A study reported 89.3 per cent in *E. coli*, 54.3 per cent in Enterococcus spp., 73.9 per cent in Klebsiella spp., and 61.5 per cent in *P. aeruginosa*.[7] Moreover, a recent meta-analysis found that children diagnosed with non-*E. coli* associated UTIs were more susceptible to acquiring renal scarring; this may be explained by a delay in treatment due to high probability of pyuria absence.[13] Our results also showed that pyuria was more sensitive to detect *E. coli* UTI compared to non-*E. coli* (83 per cent *vs.* 65 per cent, P value =0.044). The difference in response of the immune system according to various organisms is thought to be related to their biofilm formation and intracellular bacterial colonies. Genetic and anatomic factors that can be related to the host's immune response have also been investigated.[10,15] Nitrite appears also to be significantly more sensitive in detecting *E. coli* UTI than non-*E. coli* UTI (20 per cent *vs.* 7 per cent, P value =0.046).

Multiple studies have investigated the value of a combined test (leukocyte esterase and nitrite) in detecting paediatric UTIs. A systematic review revealed good sensitivity and specificity in older children, while it is of less value in infants.[16] In our study, we report a sensitivity of 69 per cent and specificity of 67 per cent.

Renal anomalies were closely correlated with UTI in children.[17] Both the American Academy of Paediatrics and the National Institute of Clinical Excellence (NICE) recommended an ultrasound study as initial screening.[8,18] Additionally, to identify vesicoureteral reflux defects, voiding cystourethrogram (VCUG) is advised.[8,17-18] Since consanguinity is familial in Saudi culture, renal anomalies are frequently detected.[19] In this study, 6 per cent of patients reported vesicoureteral reflux. Non-*E.coli* case were more likely to have vesicoureteral reflux compared to *E. coli* (P=0.0406).

The current study found that pyuria independently predicts UTI in the paediatric age group, which is consistent with other studies.[9,20] Another important finding was that the use of antibiotics[8], vesicoureteral reflex,[21] and the presence of WBCs count in blood were positively correlated with UTI.

This study had several limitations. First, the retrospective nature of the study. Second, our results may not be generalizable as the study was conducted in a single centre. Third, information concerning types and doses of antibiotics were not readily available for all cases.

Conclusion

In conclusion, pyuria is a strong predictor with high sensitivity and specificity for detecting urinary tract infection in the paediatric age group and would be of great value as an initial test. In contrast, nitrite has high specificity but low sensitivity. Leukocyte esterase and nitrite were detected more frequently in positive urine cultures with non-*E. coli* uropathogens. On the other hand, *E. coli* was more associated with pyuria-positive UTIs and was less associated with urogenital anomalies.

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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Table 1: Demographic characteristics of the culture positive patients (n= 115)

Variable	*E. coli* (n =30)	Non-*E. coli* (n =85)	P-value
Age at time of admission (years)	5.48±3.65 (0.33-14.00)	5.77±4.38 (0.08-17.00)	0.746
Sex			**0.031**
Male	10 (33.3%)	46 (54.1%)	
Female	20 (66.7%)	39 (45.9%)	
Nationality			0.093
Saudi	11 (36.7%)	45 (52.9%)	
Non-Saudi	19 (63.3%)	40 (47.1%)	
Methods of urine sampling			0.673
Mid-stream	19 (63.3%)	49 (57.6%)	
Trans-Urethral	11 (36.7%)	32 (37.6%)	
Nephrostomy tube	-	3 (3.5%)	
Suprapubic aspiration	-	1 (1.2%)	
Vesicourethral reflux			**0.0406**
No	29 (96.7%)	69 (81.2%)	
Yes	1 (3.3%)	16 (18.8%)	

Table 2: Specificity and Sensitivity of urine analysis values

	No. of positive from the total sample	No. of positive with UTI (n=115)	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Pyuria	134	80	70%	73%	60%	81%
Leukocyte esterase	52	16	14%	82%	31%	62%
High pH	86	25	22%	70%	29%	61%
Protein	121	50	43%	65%	41%	67%
Ketones	48	21	18%	87%	44%	65%
Glucose	45	20	17%	88%	44%	65%
Nitrite	46	24	21%	66%	26%	59%

Table 3: Organisms in urine culture of patients

Organism	**Frequency**	**Percent**
Escherichia coli	30	26%
Klebsiella pneumoniae	20	17%
Pseudomonas aeruginosa	15	13%
Enterococcus faecalis	12	10%
ESBL Escherichia coli	8	7%
ESBL klebsiella pneumoniae	5	4%
Coagulase negative staphylococcus	3	3%
Streptococcus agalactiae	3	3%

Enterobacter cloacae	3	3%
Morganella morganii	3	3%
Acinetobacter baumannii	2	2%
Enterococcus faecium	2	2%
MRSA	2	2%
Staphylococcus	1	1%
Aeromonas sobria	1	1%
Proteus mirabilis	1	1%
Diphtheroid species	1	1%
Klebsiella oxytoca	1	1%
Acinetobacter junii	1	1%
Lactobacillus species	1	1%

Table 4: Comparison of the sensitivity and specificity of pyuria and nitrite for *E. coli vs.* Non-*E.coli*

Urine analysis	***E. coli***		**Non-*E. coli***		**P-value**
	Positive for *E. coli* (n=30)	**Not positive for *E. coli* (n=285)**	**Positive for Non-*E. coli* (n=85)**	**Not positive for Non-*E. coli* (n=230)**	
Pyuria					
Positive	25 (sensitivity=83%)	109	54 (sensitivity=64%)	79	0.044
Negative	5	176 (specificity=62%)	31	151 (specificity=66%)	-
Nitrite					
Positive	6 (sensitivity=20%)	40	6 (sensitivity=7%)	40	0.046
Negative	24	245 (specificity=86%)	79	190 (specificity=83%)	-

Table 5: Logistic regression of the predictors of UTI culture positive cases

Variables	**Odds ratio**	**95% C.I.**	**P-value**
Pyuria (>5 WBC/HPF) *No* *Yes*	Ref. 4.233	2.123–8.437	<0.0001
Age	0.997	0.909–1.095	0.957
WBC count	0.934	0.890–0.982	0.007
Gender *Male* *Female*	Ref. 2.226	1.150–4.308	0.018
Antibiotic/s use *No* *Yes*	Ref. 0.440	0.228–0.850	0.015
Chronic illness *No* *Yes*	Ref. 1.933	0.931–4.012	0.077

Vesicoureteral reflux *No* *Yes*	Ref. 5.570	1.327–23.375	0.019
Method of sample collection *Suprapubic* *Nephrostomy tube* *Midstream* *Transurethral*	Ref 0.084 0.000 0.000	0.000–. 0.000–. 0.000–.	1.000 1.000 1.000