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The validity of clinical features and urinalysis in diagnosing urinary tract infection among children

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Abstract
Urinary tract infection is a common disease with a variable clinical presentation during infancy and childhood. It may carry serious consequences unless prompt and accurate diagnosis and treatment are carried out early in the disease. The aim of the present study is to assess the validity of clinical symptoms, signs, and urinalysis in diagnosing UTI among children above two years of age. A sample of 150 children aged 2 – 15 years from both sexes, who were attending Ibn Al-Atheer pediatric hospital in Mosul city at the outpatient department, were enrolled in the study. Children were included if they were suspected to have UTI on clinical bases by a specialist pediatrician. Each one of those children was evaluated for the presence of the classical symptoms and signs of UTI which were recorded using a specially designed questionnaire form. A similar number of healthy children from the same age group attending the same setting (for vaccination or accompanying their relative patients visiting the hospital) were also enrolled in the study as a comparison group. A fresh urine sample was collected from each child and sent to the hospital laboratory where urinalysis and culture were performed on this sample. Results of urine culture were used as a gold standard for the diagnosis of UTI. Sensitivity, specificity, predictive values, and likelihood ratios were estimated for each clinical criterion including the elements of urinalysis. Urinary tract infection was diagnosed by urine culture in 58 (19.3%) patients, 50 (86.2%) were females and 8 (13.8%) were males giving a male to female ratio of [0.16: 1]. The clinical features showed a good sensitivity in diagnosing UTI (93.1%) with a low specificity (60.3%). Urinalysis was found to have a lower sensitivity than the clinical features (77.6%) but a higher specificity (75.2%). Dysuria was the best single predictor of UTI with a sensitivity of (70.7%) and a specificity of (73%). Among the elements of urinalysis, pyuria was found to be the best indicator of UTI with a sensitivity of 77.6% and specificity of 75.2%. The absence of the three criteria: dysuria, frequency, and pyuria had ruled out UTI effectively. The sensitivity of this combination was (96.6%). Presence of fever, cloudy urine, and bacteriuria simultaneously were adequate to rule in the disease. This study suggests that using clinical criteria in combination could improve the performance of physicians in diagnosing UTI among children.

Keywords: children, UTI, infection

Introduction
Urinary tract infection (UTI) in children is a common problem confronting pediatricians and urologists [1]. About 3% of all girls and 1% of all boys are suffering from at least one UTI during their first decade of life [2].

Classification of UTI [3]
1. **Pyelonephritis:** Involvement of renal parenchyma is termed pyelonephritis, whereas if there is no parenchymal involvement the condition termed "Pyelitis". Acute pyelonephritis may result in renal injury which is termed (pyelonephritic scarring).
2. **Cystitis:** Means involvement of the urinary bladder and present as dysuria, urgency, frequency, suprapubic pain, incontinence, and malodorous urine. Cystitis does not result in renal injury.
3. **Asymptomatic Bacteriuria:** This condition is benign and does not cause renal injury, except in pregnant women in whom asymptomatic bacteriuria if left untreated can result in symptomatic UTI.

Routes of infection of urinary tract
- **Ascending Rout:** This is the most common route. The infection is assumed to be ascending from the bowel flora [4, 5].
- **Hematogenous Rout:** It is uncommon pathway of bacterial invasion and it occurs secondary to bacteremia [5].
- **Lymphogenous Route:** Direct extension of bacteria from the adjacent organs via lymphatics may occur in unusual circumstances such as a severe bowel infection or retroperitoneal abscesses [6].
- **Direct Extension:** As in bacterial invasion from a vesico-colic fistula [5].

Clinical features of UTI
The clinical presentation of an infant or child with UTI varies greatly according to age, the younger the child the more non-specific the symptoms [2, 4, 7, 8]. The classic signs and symptoms of UTI are more easily detected when the child becomes toilet trained [8].

Symptoms in relation to age
1. **Neonates:** UTI may be a part of a general septicemia or may occur by the more usual ascending route. The symptoms are those of any infection at this age, with excessive weight loss, prolonged jaundice, diarrhea or vomiting, lethargy, poor feeding, hypothermia or fever [1, 2, 9].
2. **The first two years:** The presenting symptoms are slow weight gain, poor feeding, fever, vomiting, diarrhea, strong-smelling urine [1, 9].
3. **Between 2-5 years:** Vomiting, diarrhea, abdominal pain, fever, strong-smelling urine, dysuria, urgency, frequency, and occasionally hematuria [1, 4, 9].

4. **School-Aged children:** The expected symptoms of fever, frequency, dysuria, hematuria, abdominal or loin pain, and secondary enuresis (urinary incontinence that occurs during sleep) occur [1, 9].
5. **Adolescents:** Are more likely to have some of the classic adult symptoms of UTI [1, 9].

Physical Signs [1]

- Dribbling, poor stream, or straining to void.
- External genitalia for signs of irritation, pinworms, vaginitis, trauma, or sexual abuse.
- Suprapubic tenderness.
- Costovertebral angle tenderness.
- Palpable bladder.
- Hypertension should raise the suspicion of hydronephrosis or renal parenchyma disease.

Diagnosis of UTI

UTI should be suspected in any infant or child presented with unexplained fever [2, 4], and it is also suspected from clinical signs and symptoms, or findings on urinalysis, or both [3]. Only a positive urine culture of a properly obtained specimen can confirm the diagnosis of UTI [7]. The actual bacterial colony count, the organism cultured, and the intensity of pyuria do not differentiate cystitis from pyelonephritis, nor do they indicate the severity of infection [10]. The site of infection is usually localized as cystitis or pyelonephritis on clinical grounds and imaging studies [10].

Significance of UTI in Children

UTI in infants and children often go undiagnosed because primary care physicians do not recognize the signs which are distinct from those in adults [7]. Early recognition and prompt treatment of UTIs are important to prevent progression of infection to pyelonephritis or urosepsis and to avoid late sequale [1]. Infection of urinary tract is important in 3 aspects:

1. It may be the cause of unpleasant and disabling symptoms [2].
2. In patients with recurrent infections, it may indicate the presence of some congenital abnormality which may lead to loss of kidney function [4].
3. Moreover, it may result in pathological changes with important effects on the function of the urinary tract specially the kidney [1, 7]. For example, UTI and VUR are closely associated with irreversible renal scarring [8], and this type of renal damage is one of the main causes of renal insufficiency needing dialysis and transplantation in childhood and young adults, and is a major cause of hypertension in these age groups [1, 2, 7].

Patients and methods: This is a validity study, which was conducted through the period from the first of November 2014 to the first of May 2015 at Ibn Al-Atheer pediatric hospital in Mosul city. The study population consists of two groups:

1. Group one (cases): this group includes 150 children at age 2-15 years, from both sexes, attending the outpatient department at Ibn-Al-Atheer hospital and had been clinically diagnosed by a specialist pediatrician to have UTI. Children who were taking antibacterial drugs in the preceding 3 days were excluded from the study.
2. Group Two (comparison group): a similar number of healthy children, at the same age range, from both sexes, and recruited from the same setting when they attended to the outpatient department for vaccination, or accompanying their relative patients visiting the hospital. All those children were having no symptoms of UTI and were then sent to the specialist pediatrician for further clinical evaluation to exclude the presence of UTI among them. Any child who was taking antibacterial drugs in the preceding 3 days was excluded from the study. Two questionnaire forms were prepared for this study, one for each group. These forms were checked and modified by several specialist pediatricians. These questionnaire forms were filled in for every child by the investigator, and the necessary information were obtained through direct interview with the patient's parents by asking about the presence or absence of symptoms of UTI. Sometimes, the child was old enough to give the required information. The children were then examined (by the investigator and confirmed by the specialist pediatrician) for body temperature, blood pressure, and for signs of UTI, and again the findings were recorded in the questionnaire paper.

Laboratory Examination:

Mid-stream urine samples were collected from all children in both groups by following the proper method of obtaining a clean catch urine sample: preliminary cleaning of the perineum, spreading the labia in females, retracting the prepuce in uncircumcised males, and a mid-stream urine sample collected in a sterile container. The urine samples were transported to the laboratory department immediately where each specimen is divided into two parts: one for urinalysis and the other part for urine culture. In the laboratory, it has been arranged that the analysis of all the urine samples is going to be performed by the same laboratory worker in order to avoid inter-observer variability of the results. The same arrangement was done for the urine culture. Observational bias was avoided by blinding the laboratory workers about the source of urine samples. Cultures revealing multiple pathogens were considered contaminated samples and were excluded from the study. A urinalysis considered to be positive for UTI when it shows significant pyuria (i.e. more than 5 WBCs per HPF in a centrifuged urine sample). A urine culture was considered positive for UTI when it shows heavy growth (≥ 100,000 CFU per ml of urine) of a single pathogen. The results of urinalysis and urine culture were then taken to a specialist pediatrician for further discussion and evaluation.

Analysis of Data [11, 12]

The validity of each clinical criterion and for all the clinical criteria together was estimated using the urine culture results as the gold standard. In another analysis, the validity of the urinalysis elements (alone and in combination) was estimated using the results of urine culture as the gold standard.

The following measures of data analysis were used

1. Sensitivity: It is the probability of a positive test result among all persons with the disease [11].
2. Specificity: It is the probability of a negative test result among all persons without the disease [11].
3. Positive predictive value (PPV): It is the probability that a person is actually has the disease, given that he or she tests positive [11].

4. Negative predictive value (NPV): It is the probability that an individual is truly not diseased, given a negative screening test [11].
5. Positive Likelihood Ratio (LR+): It is the probability of a positive test result for a person with the disease of interest divided by the probability of a positive test result for a person without the disease. It is calculated by: Sensitivity / (1- Specificity) [12].
6. Negative Likelihood Ratio (LR-): It is the probability of a negative test result for a person with the disease of interest divided by the probability of a negative test result for a person without the disease. It is calculated by: (1- Sensitivity) / Specificity [12].

Results

A total of 150 children with signs and symptoms of UTI and 150 healthy children were enrolled in the study. Their ages ranged from2 – 15 years. Generally; all the studied symptoms had low sensitivity and high specificity in detecting UTI among children as shown in Table (1).

Table 1: Sensitivity, specificity, predictive values, and likelihood ratios of the studied symptoms in diagnosing UTI.

symptom	sensitivity %	specificity %	PPV %	NPV %	LR+	LR-
dysuria	70.7	73.1	83.7	91.2	2.63	0.33
frequency	63.8	69	33	88.8	2.06	0.53
fever	56.9	80.6	41.3	88.6	2.93	0.54
abdominal pain	44.8	74.8	29.9	85	1.78	0.74
flank pain	34.5	88	40.8	84.9	2.88	0.74
cloudy urine	34.5	93.8	57.1	85.7	5.56	0.7
Foul smell urine	32.8	81.8	30.2	83.5	1.8	0.82
enuresis	22.4	86.4	28.3	82.3	1.65	0.9
hematuria	19	93.8	42.3	82.9	3.1	0.86
urgency	17.2	90.5	30.3	82	1.81	0.92
incontinence	17.2	93.4	38.5	82.5	2.61	0.89
rigor	15.5	95.5	45	82.5	3.4	0.89

Physical signs were found to have very low sensitivity and high specificity in detecting UTI as seen in Table (2).

Table 2: Sensitivity, specificity, predictive values, and likelihood ratios of the studied signs in diagnosing UTI.

Sign	sensitivity %	specificity %	PPV %	NPV %	LR+	LR-
temperature>38˚c	37.9	83.5	35.5	84.9	2.3	0.74
straining	22.4	90.5	36.1	83	2.36	0.86
poor stream	20.7	96.7	60	83.6	6.3	0.82
dribbling	17.2	93.8	40	82.6	2.77	0.88
external genitalia irritation	17.2	92.6	35.7	82.4	2.32	0.89
palpable bladder	17.2	97.9	66.7	83.2	8.19	0.85
suprapubic tenderness	17.2	88	25.6	81.6	1.43	0.94
costovertebral angle tenderness	12.1	97.9	58.3	82.3	5.76	0.9

Table (3) show the association between the elements of urinalysis that suggest infection and UTI proved by urine culture.

Table 3: Sensitivity, specificity, predictive values, and likelihood ratios of the studied urinalysis elements.

Element	sensitivity %	specificity %	PPV %	NPV %	LR+	LR-
pyuria	77.6	75.2	42.9	93.3	3.13	0.3
hematuria	48.3	84.3	42.2	87.2	3.1	0.61
turbidity	46.6	90.9	55.1	87.7	5.31	0.57
bacteriuria	36.2	92.2	52.5	85.8	4.6	0.69
high(alkaline)PH	17.2	97.9	66.7	83.2	8.19	0.85
WBC casts	5.2	99.2	60	81.4	6.5	0.96

Table (4) shows the association between the clinical features and UTI proved on the basis of urine culture. According to sex; females had a slightly higher sensitivity, specificity, PPV and LR+ than males.

Table 4: The association between the clinical features and UTI proved by urine culture according to sex.

sex	sensitivity %	specificity %	PPV %	NPV %	LR+	LR-
male	87.5	58.5	15.2	98.2	2.11	0.21
female	94	61.5	45.2	96.8	2.44	0.1
total	93.1	60.3	36	97.3	2.35	0.11

Table (5) shows the association between urinalysis elements and UTI proved by urine culture. Females appeared to have a better sensitivity and PPV than males, but the specificity and the likelihood ratios appeared higher in males

Table 5: The association between urinalysis and UTI proved by urine culture according to sex.

sex	sensitivity %	specificity %	PPV %	NPV %	LR+	LR-
male	50	83	20	95.1	2.94	0.6
female	82	70.3	48.2	92	2.76	0.26
total	77.6	75.2	42.9	93.3	3.13	0.3

Table (6) demonstrates the performance of two chosen models of combinations of symptoms, signs, and urinalysis according to the degree of their association after analysis of the results.

Table 6: The performance of two chosen combinations in diagnosing UTI among children.

validity		dysuria, frequency and pyuria	fever, cloudy urine and bacteriuria
UTI	present (n = 58)	56	7
	absent (n = 242)	114	2
Sensitivity	%	96.6	12.1
Specificity	%	52.9	99.2
PPV	%	32.9	77.8
NPV	%	98.5	82.5
LR+		2.05	15.6
LR-		0.06	0.9

Discussion

The present study could be helpful for pediatricians and primary care physicians to make a fast and easy diagnosis of

UTI in children with a high degree of certainty at the out-patient clinic depending on the clinical presentation of the child and a simple urinalysis test. Children enrolled in this study were older than two years of age. This was done to avoid the uncertainty associated with the clinical presentation of UTI at younger age group. The classical signs and symptoms of UTI are difficult to detect at such an age group. Beside, infants and the majority of very young children are not toilet-trained.

All the laboratory examinations of urine were performed on fresh mid-stream urine samples. Although urine collection by suprapubic puncture or urinary catheter is considered to be superior to mid-stream urine [13], but these are impractical methods to be conducted in the outpatient clinic. Most of the symptoms evaluated in this study showed statistically significant associations with the presence of UTI. Furthermore, many of these symptoms had appropriate likelihood ratios to rule in or rule out UTI.The symptoms of UTI when considered individually were found to have a sensitivity ranging from fair to poor, with inadequate positive predictive values. But, their specificities and negative predictive values were good. Among these symptoms, dysuria was probably the most useful single symptom in this study as an indicator of UTI according to its sensitivity and specificity. A child who had UTI had a positive likelihood ratio of 2.63 times more likely to have dysuria as compared to a child without UTI. Furthermore, dysuria showed good positive and negative predictive values. Most of the signs in the present study showed significant associations with UTI with adequate likelihood ratios when assessed individually. All of these signs were not sensitive indicators of UTI with low positive predictive values, but they were highly specific with high negative predictive values. The sensitivity of the clinical features in diagnosing UTI had much improved when the signs and symptoms were assessed simultaneously. The clinical picture became a more sensitive indicator of UTI with adequate likelihood ratio and negative predictive value but less specific with low positive predictive value. According to sex, there was no obvious difference in the association between males and females. The results of urinalysis have shown statistically significant associations between the elements of urinalysis and UTI with appropriate positive and negative likelihood ratios. Among the urinalysis elements pyuria was found to be the best indicator of UTI with adequate sensitivity, specificity and likelihood ratios. A child who had UTI was about 3.13 times more likely to have pyuria compared with a child without UTI. Bacteriuria and other elements of urinalysis were found to have poor sensitivity and high specificity in diagnosing UTI. Simultaneous evaluation of the elements of urinalysis showed an improvement in the sensitivity, while a small decrease was observed in the specificity. Urinalysis in females was found to be more sensitive in detecting UTI than in males but less specific. This might probably resulted from the contamination of the urine samples with vaginal secretions in females. To reach an accurate diagnosis of UTI, the physicians in their daily practice try to assess the presence or absence of many clinical findings in their patients. The use of multiple indicators at the same time in parallel (i.e considering the presence of any single criterion as a positive diagnosis) increases the sensitivity and reduces the false negative diagnosis. Conversely, the use of multiple indicators in serial way (considering the absence of any indicator as a negative diagnosis) maximizes the specificity and minimizes the false positive diagnosis. To achieve this, two models of combinations of clinical criteria have been tested. These combinations were limited to criteria which yielded a significant association with UTI. The first model combined criteria with high sensitivity (dysuria, frequency, and pyuria). This combination was found to be very sensitive (96.6%) but not specific (52.9%). The presence of any of these three criteria as positive finding had missed the identification of only two of the 58 patients with UTI. On the other hand, absence of these three criteria at the same time might rule out UTI more effectively than any other single clinical indicator assessed in this study. To increase the specificity of the clinical criteria in detecting UTI in children, the second model had been used. This combination was restricted to criteria with high specificity (fever, cloudy urine, and bacteriuria). Absence of any of these three criteria had a high specificity (99.2%). This will be on the expense of the sensitivity which was about 12%. Children with UTI are 15.6 times likely to have these three criteria simultaneously as children without UTI. The advantages of these two models are being simple and less time consuming. Doctors are familiar with these easily recognized criteria in their daily practice. Moreover, assessment of children for the presence or absence of these criteria requires no further training or additional equipments other than that of routine inquiry by physicians and simple urinalysis testing.

Clinicians can use the first model when they need a highly sensitive method to predict UTI in children without missing any patient. When the child has fever, cloudy urine and bacteriuria simultaneously, UTI can be predicted with high certainty and treatment can be started.

Screening program for UTI among children can use the first model as a first step. This is more likely to detect the children with UTI because it rarely misses a case. The second model used in the next step to exclude children who are actually free from the disease because this model rarely misclassifies children without UTI as diseased because it gives few false positive results.

Conclusions and recommendations

This study found that none of the clinical features or urinalysis elements was having the best validity in diagnosing UTI simultaneously. The patients or the care-givers of children should be inquired about the presence of symptoms that have high sensitivity to reduce the possibility of missing the diagnosis in children with UTI. The clinical criteria, which yielded a significant association with UTI, when used in combinations this will improve their validity in diagnosing UTI among children. This study recommends the use of clinical criteria in combination to improve the performance of physicians in diagnosing UTI. The presence of any of the three criteria (dysuria, frequency, and pyuria) had better sensitivity than any individual criterion. Absence of all these three criteria had better negative predictive value and negative likelihood ratio than any individual criterion. The absence of any of the three criteria (fever, cloudy urine, and bacteriuria) yielded higher specificity and positive likelihood ratio than any single indicator.

The suggested two models are recommended for use in screening UTI among children. The first model used primarily to detect all the children with UTI because it

rarely misses a case. The next step is to apply the second model on the detected children to exclude those who are really not diseased.

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