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Original Research Article

Urinary tract infection in children: clinical aspects and utility of urine dipstick test

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ABSTRACT

Background: Urinary tract infection (UTI) is a common genitourinary disease in children and accounts for significant morbidity. To prevent the potentially dangerous sequel, early detection of UTI in childhood is essential. This depends entirely on strong clinical suspicion and urine culture report. Recently, advances in investigations are taking place to diagnose UTI rapidly. Urine dipstick is one such bedside method to diagnose UTI. This study aims at studying the clinical features of UTI and evaluating sensitivity and specificity of urine dipstick in diagnosing UTI.
Methods: This study was conducted at a tertiary care hospital in Vadodara from January 2013 to June 2014, on 60 children admitted with clinical suspicion of urinary tract infection. Along with study of clinical features, results of urine dipstick tests (Nitrite and Leukocyte esterase), urine microscopy and urine culture were compared. Accuracy of urine dipstick tests was assessed statistically by evaluating sensitivity, specificity, positive and negative predictive values considering urine culture as a gold standard.
Results: Fever was found to be the most common presenting features (53%) in all the patients studied. The sensitivity of urine microscopy, Nitrite test and Leucocyte esterase test was 63.5%, 50% and 61% and specificity was 25%, 31% and 25% respectively. Combination of Nitrite and Leucocyte Esterase test had an improved sensitivity (68%).
Conclusions: Urinary tract infection can present with variety of non-specific signs and symptoms especially in younger age. Dipstick test using Leucocyte Esterase and Nitrite together is better than urine microscopic examination alone. Urine culture as a confirmatory test still remains gold standard.

Keywords: Leukocyte esterase test, Nitrite test, Urine culture, Urine microscopy

INTRODUCTION

Urinary tract infection (UTI) represents the most common genitourinary disease in children and accounts for a significant morbidity in pediatric patients. The incidence of UTI in term neonates is approximately 1% and in preterms is 3%, both with male preponderance (male: female - 5:1). During infancy, the risk of developing UTI is equal in boys and girls, and thereafter higher in girls.[1]

The risk of developing symptomatic UTI before the age of 14 years is 1-2% in boys and 3-8% in girls.[1] Risk of UTI is higher in children with malnutrition and chronic diarrhea. These infections may present in children without any obvious presenting symptoms, or may present atypically.

The specific symptoms of urinary tract infection may go unnoticed specifically in infants and young children and significant finding may only be failure to thrive. These

children later in childhood may develop obvious infection and end stage renal disease during adolescent period.

Essential to the diagnosis of urinary tract infection, is a culture of urine, with colony count, showing a significant number of bacteria or fungi. To prevent the potentially dangerous sequel like renal scarring, early detection of UTI in childhood is essential, which depends entirely on the physician's degree of suspicion, urine routine microscopy and culture.[2] Urine culture though is considered a gold standard test to diagnose UTI, is time consuming, costly and requires good microbiology laboratory facilities. Also, the timing and method of collection of urine sample plays a major role in isolation of organisms from urine culture.

To diagnose UTI rapidly, advances in investigations are taking place. Urine dipstick is a rapid bedside method to diagnose urinary tract infection. Leukocyte esterase (LE) is a semi quantitative test that detects neutrophil specific esterase released from degraded white blood cells present in urine. Nitrite reduction test detects nitrite produced by urinary tract pathogens. Nitrite is usually not found in urine but present when urinary bacteria reduces nitrate to nitrite. Many gram negative and gram positive organisms are capable of doing so. A positive dipstick nitrite test indicates that those bacteria are present in significant number (>100,000/ml).

METHODS

This study was carried out with the following aims and objectives in mind: 1) to study clinical profile of UTI in children 2) to correlate results of urine dipstick, microscopy and culture 3) to determine utility of urine dipstick in the diagnosis of UTI.

This prospective and cross sectional study was conducted at a tertiary care hospital in Vadodara from 1st January 2013 to 30th June 2014. The study was approved by institutional scientific and ethical committee. The study included children between 1 year and 12 years presenting with signs and symptoms of UTI, fever without focus or with known congenital anomaly of urinary tract. Children with an obvious focus of fever except urinary tract and those who were already on antibiotics were excluded.

Once UTI was suspected on clinical grounds, detailed history was taken and complete clinical examination was done. Urine samples were taken for urine routine and microscopic examination, urine culture and sensitivity testing and urine dipstick test. Other routine blood investigations were sent as required. Ultrasonography of abdomen was done in all patients.[2,3] Other special investigations like MCUG and Renal Scan were done as per Indian Pediatric Nephrology Group (IPNG) protocol and Indian Society of Pediatric Nephrology (ISPN) revised statement.[4,5]

Urine samples were collected either by mid-stream-clean-catch method or by catheterization with all proper aseptic precautions. Samples were preserved at 2-8 ^{0}C in case of delay in processing. Urine sample was examined for color, appearance, presence of sugar and protein. The sediment of centrifuged specimen was examined for presence of white blood cells (pus cells), red blood cells, epithelial cells, bacteria, casts and crystals. Urine routine microscopy was considered positive for UTI if there were 6-8 pus cells/hpf (high power field) in male patients or 8-10 pus cells/hpf in female patients.

Urine culture was done within 1 hour of collection by streak plate culture method. Isolation and identification of the organisms were done by their characteristic colony, motility, relevant biochemical reactions as well as gram staining. Bacterial count was done and count of more than 1 lakh colony forming units/ml was considered significant.

Urine dipstick test was done bedside with Combur 10 Test M reagent strips. These strips for urine analysis are plastic strips to which are affixed several separate reagent areas, amongst which Nitrite and Leukocyte Esterase which are specific for UTI are included in the study. Urine specimen was collected in a clean, dry container and was mixed well immediately before testing. One strip was removed from bottle and cap was replaced. Reagent areas of strip were completely immersed in urine and were removed immediately. While removing, entire length of the strip was run against the rim of the urine container to remove excess urine. The strip was held in a horizontal position to prevent possible mixing of chemical from adjacent reagent areas and contamination of hand with urine.

Reagent areas were compared to corresponding colour chart on the bottle label. Laying the strip directly on the colour chart was avoided, as this could result in the urine soiling the colour chart. Nitrite reading was taken at 60 seconds. Any degree of development of uniform pink colour was interpreted as a positive result suggesting presence of more than 1 lakh organisms per ml. Leukocyte esterase reading was taken at 2 minutes and development of purple colour was interpreted as positive result.

All the data were taken on a Microsoft excel sheet and analysed. Accuracy of urine dipstick tests was assessed statistically by evaluating sensitivity, specificity, positive and negative predictive values considering urine culture as a gold standard.

RESULTS

The present study included 60 patients of urinary tract infection and was conducted over a period of 1.5 years from 1st Jan 2013 to 30th June 2014 in a tertiary care hospital near Vadodara. The study included 36 males and 24 females. Out of 60 patients, 12 (20.3%) patients were

between 1 to 2 years of age, 20 (33.3%) between 2 and 5 years and 28 (46.4%) were between 5 to 12 years of age.

Fever was the commonest symptom (53%), followed by puffiness of face (28%), abdominal distension (27%) and pedal edema (25%) (primarily in Nephrotic syndrome). Other symptoms were burning micturition (26%), oliguria (21.6%), vomiting (21.6%), frequency (15%) and abdominal pain (10%) (Figure 1). Typical urinary symptoms were found in 37 (61.7%) and atypical urinary symptoms were noted in 23 (38.3%).

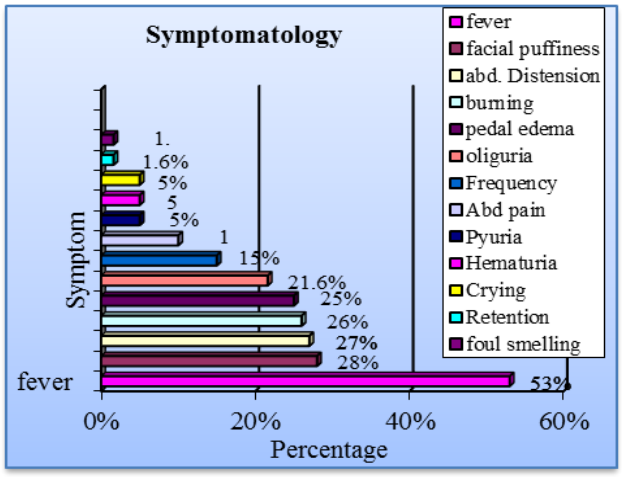

Figure 1: Symptomatology of urinary tract infection.

Out of 60 patients, 40 (66.67%) patients had positive urine microscopy. 33 (55%) had Nitrite test positive, 39 (65%) had Leucocyte esterase (LE) test positive, 30 (50%) had both Nitrite and LE test positive and 42 (70%) had either or both the tests positive. Out of 60 urine samples sent for culture, 44 samples were culture positive. Thus, 73.33% of patients with suspected urinary tract infection turned out to be culture positive (Table 1).

Table 1: Results of dipstick tests, urine microscopy and urine culture.

Results	No. of cases (out of 60)
Nitrite positive	33 (55%)
Leucocyte esterase positive	39 (65%)
Both Nitrite and LE positive	30 (50%)
Either or both positive	42 (70%)
Urine Routine and Microscopy	40 (66.67%)
Urine Culture	44 (73.33%)

Out of 44 patients in whom organism was isolated from the urine, *E. coli* was the most common. *E. coli* was isolated in 26 (59%), *Klebsiella* in 16 (36.6%), while *Proteus* and *Pseudomonas* were isolated in 1 (2.2%) each. In patients less than 2 years, *Klebsiella* was the commonest organism (54.5%). In 2-5 years and 5-12 years age group *E. coli* was the commonest (64% and 62% respectively) (Table 2).

Table 2: Causative organisms isolated from urine culture.

Age group/Sex→ Organism↓	1-2 yrs M N=8	1-2yrs F N=4	2-5 yrs M N=11	2-5yrs F N=9	5-12yrs M N=17	5-12yrs F N=11	Total N=60	Culture positive N=44
E. coli	3	2	8	3	6	4	26	59%
Klebsiella	4	2	2	2	3	3	16	36.6%
Proteus	0	0	1	0	0	0	1	2.2%
Pseudomonas	0	0	0	1	0	0	1	2.2%
Total	**7**	**4**	**11**	**6**	**9**	**7**	**44**	**100%**

Table 3: Predictive parameters of the tests.

Screening test	U-culture+ve	U-culture–ve	Total
NITRITE+VE	22(True +ve)	11(False +ve)	33
NITRITE–VE	22 (False –ve)	5(True–ve)	27
LE+VE	27(True +ve)	12(False +ve)	39
LE–VE	17 (False –ve)	4(True–ve)	21
LE and /or N+VE	30(True +ve)	12(False+ve)	42
LE and/or N–VE	14 (False –ve)	4(True–ve)	18
Urine R/M+VE	28(True +ve)	12(False+ve)	40
Urine R/M–VE	16 (False–ve)	4(True–ve)	20
Total	**44**	**16**	**60**

U=Urine, LE=Leucocyte esterase, N=Nitrite, R/M=Routine and microscopy, +ve=positive, -ve=negative

The predictive parameters of the Nitrite tests, Leucocyte esterase test and urine routine microscopy considering urine culture as gold standard is given in (Table 3). Comparison of validity and reliability parameters of all these tests which includes sensitivity, specificity, positive predictive value and negative predictive value is given in (Table 4). In the present study, ultrasonography was performed in all 60 patients. Amongst them 22 (36%)

were detected to have some abnormality. Hydronephrosis was detected in 13 (21.6%), cystitis in 5 (23%), calculus in 2 (3.3%) and medical renal disease in 2 (3.3%). Ultrasound positivity rate in different age groups is 1 out of every 2 in <2 years, 1 out of every 3 in 2-5 years and 1 out of every 4 in 5-12 years. MCUG (micturiting cystourethrogram) was done in 9 patients amongst whom 2 were abnormal. DTPA (diethylenetriaminepentaacetic acid) renal scan was performed in 4 patients and DMSA (dimercaptosuccinic acid) scan in 1 patient. Surgical interventions were required in 6 patients (Figure 2).

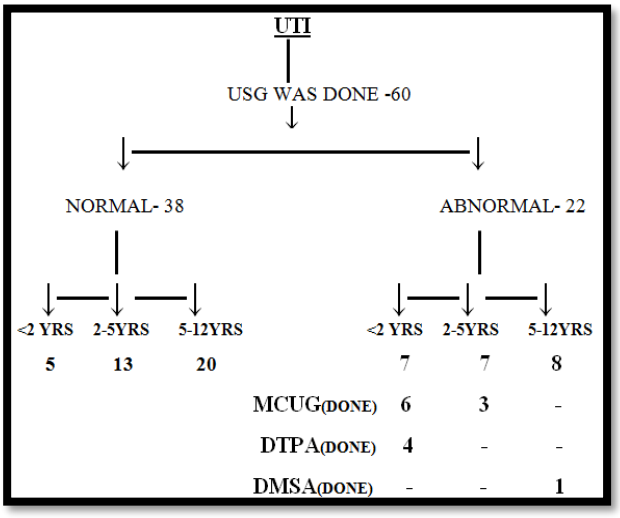

Figure 2: Imaging studies in urinary tract infection.

DISCUSSION

In the present study, the M: F ratio was 2:1, 1.2:1 and 1.5:1 in age group of 1-2 years, 2-5 years and 5-12 years respectively. The IPNG group consensus statement states that male to female ratio during first 2 years of life is 3-5:1 unlike a female preponderance of 1:10 in the age group of 2-12 years.[4] Sanath et al studied that during preschool and school age, females tend to suffer more episodes of UTI than males.[6] The risk of developing symptomatic UTI before the age of 14 years is 1-2% in boys and 3-8% in girls.[1] However, in this study, female preponderance was not found probably indicating a gender bias in seeking medical treatment. Validity and reliability parameters of urine microscopy found in this study are as follows: sensitivity 63%, specificity 25%, positive predictive value 70% and negative predictive value 20%. Urine microscopy alone thus remains poorly sensitive to diagnose UTI (Table 4).

Table 4: Comparison of validity and reliability parameters of nitrite test, leukocyte esterase test and urine microscopy.

Screening test	Sensitivity (True+ve) %	Specificity (True-ve) %	PPV %	NPV %
Urine R/M	63.5	25	70	20
LE	61	25	69	19
Nitrite	50	31	66	18.5
LE and /or N	68	25	71.4	22

Table 5: Comparison of validity and reliability parameters of nitrite test.

Screening test (nitrite)	Present study	Al-Daghistani et al	Hida et al	Rehmani R et al	Antwi S et al	Williams GJ et al	Huysal K et al
Sensitivity (True +ve)	22/44x100 =50%	59%	86.6%	81%	96.7%	49%	22%
Specificity (True –ve)	5/16x100 =31%	78%		87%	58.8%	98%	99.3%
Positive predictive value	22/33x100 =66%	60%			26.1%		88.2%
Negative predictive value	5/27x100 =18.5%	86.2%	89.9%		99.2%		85.5%

In the present study, sensitivity of LE and/or Nitrite (either of two positive or both positive) is 68%, which is more than Nitrite (50%) or LE (61%) alone. Specificity of both tests (either of two positive or both positive) is 25%, which is same as LE but lower than Nitrite (31%). Positive predictive value is 71.4%, which is comparable to LE (69%) but more than Nitrite. Negative Predictive Value of LE and/or Nitrite, Nitrite and LE are 22%, 18.5% and 19% respectively. Thus, dipstick test using Leucocyte Esterase and Nitrite together is better than urine microscopic examination alone in early diagnosis of UTI (Table 4).

In this study, the sensitivity of nitrite test is 50%, which is comparable to Williams et al (49%).[7] On contrary to this, Huysal et al found only 22% sensitivity.[8] Rest of the studies observed sensitivity above 50% with nitrite test.[9,11-13] In this study, the specificity is 31%, which is lowest as compared to other studies.[7-9,12,13] Huysal et al attained a specificity of 99.3%.[8] Positive predictive value for nitrite test is 66% in the present study, which is comparable to that of Daghistani et al and Wammanda et al.[9,10] However, the negative predictive value is only 18.5% in the present study, unlike in Daghistani et al, Wammanda et al and Hida et al who showed a negative predictive value of 86.2%, 80.8% and 89.9%

respectively.[9-11] Low specificity and low negative predictive value in our study is due to a low figure for "True negative" dipstick (Table 5).

In the present study, LE sensitivity is 61%, which is comparable to study of Daghistani et al (68.5%).[9] Antwi et al found the highest sensitivity of 96.7%, whereas Huysal et al observed sensitivity of 33.8%.[8,12] Specificity for LE was only 25%, which is relatively lower than the observations made by others.[7-9,12,13]

Positive predictive value is 69%, which is more as compared to that of Daghistani et al (44%).[9] Negative predictive value is 19% which is much lower as compared to other studies (Table 6).[8,9,12]

E. coli was the commonest organism found in our study followed by *Klebsiella*, *Proteus* and *Pseudomonas* which is comparable to other studies.[17,18] Rate of isolation of *E. coli* was found to be 59% which is comparable to other studies (47%-89%).[14-18]

Rate of isolation of *Klebsiella* was high (36.6%) as compared to other studies (3.7-10%).[14-18] Rate of isolation of *Proteus* and *Pseudomonas* was almost comparable to other studies (Table 7).[14-18]

Table 6: Comparison of validity and reliability parameters of leukocyte esterase test.

Screening test (LE)	Present study	Al-Daghistani et al[9]	Rehmani R et al[13]	Antwi S et al[12]	Williams GJ et al[7]	Huysal K et al[8]
Sensitivity (True +ve)	27/44x100 =61%	68.5%	77%	96.7%	88%	33.8%
Specificity (True –ve)	4/16x100 =25%	73.%	54%	58.8%	79%	93.6%
Positive predictive value	27/39x100 =69%	44%		26.1%		53.4%
Negative predictive value	4/21x100 =19%	88.5%		99.2%		86.8%

Table 7: Comparison of urine culture results with other studies.

Studies	Present study	Pahl et al	Pape L et al	Sakran et al	Qureshi et al	McLoughlin et al
E. coli	59%	75%	47%	87%	71%	89%
Klebsiella	36.6%	10%	4%	4%	13%	3.7%
Proteus	2.2%	15%	8%	4%	11%	1.2%
Pseudomonas	2.2%		5%		1%	
E. fecalis			23%			3.7%
Citro-bacter						1.2%

Limitation

Limitation of this study was infants were not included in the study as collection of urine samples with proper aseptic precaution was difficult. Further studies on large scale with inclusion of infants are required for better results and comparison.

CONCLUSION

Urinary tract infection can present with variety of atypical signs and symptoms, especially in young children. High clinical suspicion and thorough investigations are needed in young children specially less than 2 years of age, who present with fever without focus.

Urine dipstick can be used as a rapid bedside investigation. If one test has to be chosen, dipstick test using Leucocyte esterase and Nitrite together is better than urine microscopic examination alone for early diagnosis. Above all, urine culture remains gold standard for the diagnosis of UTI.

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