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Urinary tract infection in febrile children without any obvious focus of infection and the methods of diagnosis

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ABSTRACT

Background

The purpose of this study was to assess the prevalence of urinary tract infection (UTI) and the validity of routine microscopic urine analysis, enhanced urine analysis, urine dipstick and urine culture in the diagnosis of UTI among febrile children aged 1 month to 5 years who presented without any focus of infection.

Methods

A prospective cross-sectional study was conducted among febrile children aged 1 month to 5 years, who were admitted to the department of Pediatrics at Mahatma Gandhi Medical College and Research institute, Puducherry, India between November 2014 and June 2015. Fifty children were included in the study. Detailed history and examination was recorded. Urine samples underwent routine urine analysis, enhanced urine analysis, urine dipstick and urine culture sensitivity. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 16.0 software.

Results

The prevalence of UTI was 34%. Enhanced urine analysis had 93.3% sensitivity 93.3%, 100% specificity and 100% positive predictive value 100%, and negative predictive value 97.2%. This was comparatively better than the urine dipstick test and urine pus cells.

Conclusion

Enhanced urine analysis was found to have better efficacy in terms of diagnosing the urinary tract infection compared to urine dipstick test and urine pus cells. It was also found to correlate well with culture positivity. Thus, we recommend the use of enhanced urine analysis on a regular basis.

Keywords: Urinary tract infection, Urine analysis, Enhanced urine analysis, Urine dipstick, Culture, Sensitivity

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INTRODUCTION

Fever in children under the age of 5 years accounts for a significant portion of outpatient and emergency department visits.[1-3] Unlike occult (hidden) bacteremia or severe bacterial illness, the identification of urinary tract infection (UTI) in febrile children in the emergency department receives little attention. According to recent data, however, febrile patients have a high prevalence of UTIs and significant associated morbidity.[4]

Antibiotics are frequently given to children with UTIs without a proper diagnosis. In children with undocumented sources of infection, fever with significant bacteriuria and pyuria (bacteria or white blood cells in the urine) must be assumed to be symptoms of pyelonephritis (a kidney infection), requiring prompt treatment. According to recent studies using nuclear scans to determine the presence of pyelonephritis, more than 75% of children under the age of 5 years with a febrile UTI had pyelonephritis. In each year of life, pyelonephritis causes renal scarring in 27–64% of children with UTI.[5,6] This has been shown to be especially true in patients with severe reflux or obstruction, as well as those who had a delay in starting treatment for UTI.

Renal scarring is also common in children under the age of 3 years who have recurrent UTIs. One-third of these children may be asymptomatic.[7] To reduce the risk of life-long morbidity, it is critical to identify UTIs in febrile children and treat them promptly. Renal damage caused by undiagnosed pyelonephritis as a child can lead to hypertension and chronic renal failure later in life. According to one Swedish study, children with focal renal scarring caused by pyelonephritis had 23% risk of hypertension, a 10% risk of end-stage renal disease and a 15% risk of toxaemia during pregnancy.[8] About 13–15% of end-stage renal disease is thought to be linked to a childhood UTI that went undiagnosed and thus was undertreated.[9]

The purpose of this study was to assess the prevalence of UTI and the validity of routine microscopic urine analysis, enhanced urine analysis, urine dipstick and urine culture in the diagnosis of UTI in febrile children aged 1 month to 5 years in order to determine the prevalence of UTI in febrile children in this age group who do not have any obvious focus of infection. A secondary objective was to correlate the results of urine pus cells, enhanced urine analysis and urine dipstick method with urine culture results.

METHODS

A prospective cross-sectional study was conducted among children admitted to the Department of Pediatrics at Mahatma Gandhi Medical College and Research institute, Puducherry, India, between November 2014 and June 2015. Children who had received antibiotics prior to attending outpatient department, children with congenital genitourinary anomalies (on ultrasound) and children with specific focus of infection were excluded from the study. Fifty children were included in the study.

After taking written consent from the parents of study participants, demographic details and detailed medical history were collected and an examination of each child was conducted. A complete history related to the onset, duration of fever and associated symptoms such as nausea, vomitting, diarrhoea, urinary disturbances and other system involvement were obtained. A physical examination with relevant investigation was carried out in all patients.

Routine urine analysis, enhanced urine analysis, urine dipstick and urine culture sensitivity were carried out. An ultrasound examination was carried out in culture positive cases. Detailed data were entered in a proforma.

Statistical analysis

Collected data were compiled in Microsoft Excel and analysed using Statistical Package for Social Sciences (SPSS) version 16.0 software. Descriptive tables were generated to demonstrate the findings. For descriptive tables mean, standard deviation and percentage analysis were used. Chi-square, ANOVA and Spearman correlation analysis were used to check the hypothesis.The difference was taken as statistically significant if p value was ≤ 0.05.

RESULTS

Of study participants, 26% of cases were aged <1 year, 28% were aged 1–3 years and 46% 3–5 years; 56% were boys and 44% girls; 42% had experienced fever for <3 days and 58% for ≥3 days. (Table 1). Stunting was noted in 14%, malnourishment in 24%. The prevalence of UTI reported was 34%. Out of 10 children showing >5 pus cells in urine, 70% had positive urine culture, which was statistically significant. Culture positivity was seen only in 20% of children with urine pus cells ≤5 pus cells; this was also statistically significant. Urine culture was positive in 80% of children who had a positive dipstick test and negative in all children who had a negative urine dipstick result. This distribution was statistically significant (p<0.0001). In children who showed ≥10 pus cells on enhanced urinalysis, 65.2% had positive urine culture compared to children with <10 pus cells on enhanced urine analysis, in whom only 7.4% were culture positive. This was statistically significant (p<0.0001). (Table 2). On assessing the diagnostic efficacy of urine pus cells, enhanced urine analysis and urine dipstick, enhanced urine analysis had more sensitivity (93.3%) compared to other screening tests: it had 100% specificity and positive predictive value, and 97.2% negative predictive value. Comparison of blood parameters (haemoglobin levels, total leucocytes count, serum urea and creatinine) were performed on positive cases with urine culture, enhanced urine analysis and dispstick test.

The total leucocytes count alone was significant (p=0.0212) compared with the positive cases reported by the above-mentioned tests. The most common organism isolated was *E.coli*, found in 12% of cases, followed by *Klebsiella* in 10% of cases and *Proteus mirabilis* in 4% of cases. *Citrobacter* and *Acinetobacter* were each found in 2% of cases. Urine culture was sterile in 70% of children. *Klebsiella* was commonly isolated in females, whereas *E.coli* was the most common organism in male children. *Proteus, Citrobacter* and *Acinetobacter* were seen in girls only. Table 5 shows the correlation between urine pus cells, endogenous urinary nitrogen, dipstick method and urine culture.

Table 1 Clinical profile of study participants

Variables	Total (n=)	Percentage
Age group		
<1 year	13	26
1-3 years	14	28
3-5 years	23	46
Gender		
Male	28	56
Female	22	44
Socio economic status (SES)		
Class I	01	2
Class II	11	22
Class III	34	68
Class IV	04	8
Duration of fever		
< 3 days	21	42
≥ 3 days	29	58
Temperature		
100-102° F	31	62
>102 ° F	19	38

Table 2 Association between urine culture and three laboratory investigations

Parameter	Urine culture		Total	P Value
	Negative	Positive		
Urine pus cells				
≤ 5cells	32(80)	8(20)	40(100)	< 0.0001*
> 5 cells	3(30)	7(70)	10(100)	
Total	35 (70)	15 (30)	50 (100)	
Dipstick test				
Positive	3(20)	12(80)	15(100)	< 0.0001*
Negative	35(100)	0	35(100)	
Total	38 (76)	12 (24)	50 (100)	
Enhanced urine analysis				
< 10 pus cells	25(92.59)	2(7.40)	27(100)	< 0.0001*
≥ 10 pus cells	8(34.78)	15(65.2)	23(100)	
Total	33 (66)	17 (34)	50 (100)	

Significant

Table 3 Screening efficacy of three laboratory investigations

Parameters	Sensitivity	Specificity	PPV	NPV
Urine pus cells	41%	91%	70%	80%
Enhanced urine analysis	93%	100%	100%	97.2%
Urine dipstick	80%	100%	100%	92%

PPV- Positive predictive value, NPV- Negative predictive value

Table 4 Comparison of blood parameters between positive cases noted in investigations

Variables	Urine culture (n=15)	EU analysis (n=23)	Dipstick test (n=13)	P value
Heamoglobin (gm%)	11±0.6	10±0.9	10±1.0	0.997
Total leucocytes count (cells/cu mm)	16146±6732	13878±2156	14553±5356	0.0212*
Blood urea (mg/dl)	36.6±2.4	36.6±2.6	34±2.1	0.662
Serum creatinine (mg/dl)	0.6±0.1	0.6±0.2	0.6±0.1	0.350

Significant

Table 5 Correlation between urine culture and other three laboratory investigations

Correlations	Urine culture	EU analysis	Dipstick test	Urine culture
Urine pus cells	1	-0.344*	0.22	0.356*
Dipstick test	-0.344*	1	-0.636**	-0.758**
Enhanced urine analysis	0.22	-0.636**	1	0.675**
Urine culture	0.356*	-0.758**	0.675**	1

***** Correlation is significant at the 0.01 level (2-tailed); *Correlation is significant at the 0.05 level (2-tailed)***

A total of 50 children met the study's inclusion criteria: 28 males and 22 females, resulting in a male to female ratio of 1.2:1. The majority of the children with UTI (46%) were between 3 and 5 years of age and most were from lower socioeconomic classes.

Our study found a 34% prevalence of UTI, which is significantly higher than studies by Bauchner et al[10] and Hobermann et al,[11] which found a prevalence of only 1.7% and 5.3%, respectively. This could be due to our selection criteria, which included only children with fever and no localizing signs or symptoms.

A smaller number of children have studied as a result of our stricter criteria for selection of cases than was used for these other studies, but our method should provide a definitive picture of the prevalence of UTI in young febrile children under the age of 5 years who had no localizing signs or symptoms.

The prevalence of UTI in our study was 8% in 1 year old children and 3% in children aged 1–3 years, which was higher than in the study by Hobermann et al.[11] The prevalence of UTI in children aged 3-5 years was 19%, which is higher than in a study conducted by Dilip et al,[12] which recorded 10% prevalence.

A urine test revealed pyuria in 20% of the children. In 23 (46%), increased urinalysis was indicative of a UTI: 13 (26%) of the children tested positive for UTI using the dipstick method. 15 (30%) of the children showed a positive culture. This is similar to the numbers recorded in studies by Hobermann et al,[11] Jenkins et al[13] and Gorelick MH et al.[4]

Children with pyuria (n=10) made up 20% of the study participants. Pyuria was the most common finding reported among the children aged 3–5 years and, notably, pyuria was more commonly reported in female children (60%) compared to male children (40%). Higher rates of culture positivity were found in children with pus cells >5 per high power field compared to children with fewer pus cells in urine, which was statistically significant. Linn et al[14] and Hobermann et al[11] have made similar observations.

Children with endogenous urinary nitrogen (EUN) (n=23) made up 46% of the study group. It was most common in children aged 1–3 years old, and in female children (56% compared with 43% in males). When compared to children with less than 10 white blood cells/cumm^3, children with 10 or more leucocytes had higher rates of culture positivity, consistent with the findings observed by Gorelick MH et al[4]

Children who tested positive for UTI on a dipstick (n=13) made up 26% of the study group. It was most common in children aged 3–5 years, and it was more common in female children (69%) than males (30%).

Higher rates of culture positivity were observed in children who had a positive dipstick result. These findings were consistent with the findings of Hobermann et al[11] and Gorelick MH et al[4].

Male infants had a higher number of culture positive cases than female infants, with a M:F ratio of 3:1. This is similar to the findings by Chang et al.[15] In the 1–5 years age group, culture positive cases were less common in boys than girls, with a M:F ratio of 1:4.5

E.coli was isolated in 40% of children, followed by *Klebsiella* (33%). Other organisms including *Proteus*, *Citrobacter* and *Acinetobacter* were isolated in the remaining cases (27%). Our findings are consistent with those of other studies. *E.coli* was found to be the most common urinary pathogen in 85% of cases in a study by Bryan et al.[16] According to Bagga et al,[17] *E.coli* was responsible for 90% of the first symptomatic UTI and 70% of recurrent infections. *E.coli* was the most common bacterium isolated in the study by Hoberman et al.[11]

DISCUSSION

Enhanced urine analysis (EUN) was found to be the most sensitive tool for diagnosing UTI, with 93.3% sensitivity, 100% specificity, 100% positive predictive value and 97.2% negative predictive value. This correlates well with a study by Lin et al[13] which reported that EUN was the most sensitive tool in diagnosing UTI and a significant predictor for diagnosing UTI in children.

In comparison to previous studies, the sample size in our study was extremely small. This is because we only included children who were hospitalized and had a fever without focus. Children who were treated as outpatients were excluded from the study. Other studies, on the other hand, did not use such stringent selection criteria and included both outpatient and inpatient children. It would be a valuable exercise to repeat this study with a much larger sample size.

CONCLUSION

UTI is common in febrile children under the age of 5 years who require hospitalization. In children with a suspected UTI, an enhanced urine analysis was found to have better efficacy in terms of diagnosing the UTI compared to urine dipstick test and urine pus cells and was found to correlate well with culture positivity. Thus, we recommend the use of enhanced urine analysis on a regular basis.

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