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Original Research Paper

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URINARY TRACT INFECTION IN FEBRILE CHILDREN LESS THAN 5 YEARS OF AGE- A SINGLE CENTRE STUDY INDIA.

Sunil Pawar*	MBBS, DCH DNB (Paed), FIAP In Neonatology, Consultant Paediatrician, Fernandez hospital Hyderabad India; Durgabai Deshmukh Hospital and Research Centre Hyderabad India. *Corresponding Author
Tejopratap Oleti	MD(Ped) DM (Neo), Fernandez hospital Hyderabad India.
Gowthami Muktineni	MD(Ped) IAP Fellow in Neonatology, Fernandez hospital Hyderabad India.

ABSTRACT

Background: UTI is a common paediatric problem with the potential to produce long-term morbidity such as renal scarring. It is essential to identify UTI in febrile children and to institute prompt treatment to reduce the potential for lifelong morbidity.

Objective: The objective is to determine the prevalence of UTI in febrile children less than 5 years of age with demographic difference.

Method: Urine specimen of febrile children aged 1-24 months obtained by transurethral bladder catherization or suprapubic aspiration and for older children midstream methods were analysed using standard laboratory methods of microscopy, culture and sensitivity.

Result: A total of 200 children were enrolled; nearly 59% (118/200) were males. The prevalence of UTI was 5 % and out of 200 febrile children, 61(30.5%) children showed significant pyuria, 8 (13.1%) of significant pyuria cases showed significant bacterial growth. The common clinical features were vomiting, abdominal pain, diarrhoea, urinary frequency and urgency.

Conclusion: UTI is more common in female, the dipstick leucocyte esterase positivity having good correlation with culture positive.

KEYWORDS : urinary tract infection, febrile, children

INTRODUCTION

Urinary tract infection (UTI) is the most common disease in infants and the second most common infectious disease in toddlers. In children, UTI frequency, clinical symptoms and the causative pathogens vary according to sex and age. Moreover because of a wide variety of non-specific and systemic symptoms, it is difficult to perform tests for early diagnosis and the resultant inaccurate diagnosis may lead to antibiotic abuse. Thus in many cases, a severe renal injury occurs even before the UTI is diagnosed. For this reason, an early and accurate diagnosis through careful examination and tests can help in preventing severe renal injuries through adequate treatment and careful follow-up. UTI recurs easily if it is accompanied with anatomical anomalies of the urinary system. If it is not treated adequately or occurs recurrently, UTI may develop into chronic pyelonephritis resulting in hypertension and loss of renal function, a condition normally seen in 15–20% of the cases of chronic renal failure.[1]

UTI accounts for around 5% of febrile illnesses. Over 30 years ago, imaging studies carried out on children with UTI showed that renal scarring was present in 10– 25% and vesicoureteric reflux (VUR) was present in 30%. Renal scarring was worse in children who developed a first infection at a young age, had recurrent UTI, VUR, where there was a delay in diagnosis and treatment.[2] In outpatient department, substantial proportion of the cases is constituted by children with fever.

In children with undocumented sources of infections, fever, significant bacteriuria and pyuria must be presumed to be symptoms of pyelonephritis, an invasive infection of the renal parenchyma requiring prompt treatment. More than 75% of children under 5 years of age with febrile UTI have pyelonephritis as stated by recent studies using renal parenchyma avid nuclear scans to determine the presence of UTI. [3,4,5] Even in the absence of underlying urinary tract abnormalities, pyelonephritis leads to renal scarring in 27% to 64% of children under 5 years of age with UTI.[6,7] In children younger than 4 years of age especially among infants in the first year of life, those with gross reflux or obstruction and those who have a delay in therapy for UTI, most UTI lead to scarring or diminished kidney growth.[4,7] Higher risk for renal scarring is seen in children under 3 years of age with recurrent UTI.[8]

Unrecognised pyelonephritis in childhood results in progressive renal damage which may lead to hypertension and chronic renal failure in later life. Identification of UTI in febrile children and institution of prompt treatment becomes necessary to reduce the potential for lifelong morbidity. The present study is undertaken to estimate the prevalence of UTI in 200 febrile children less than 5 years of age who attended outpatient department or got admitted in Durgabai Deshmukh Hospital & Research Centre, Hyderabad. As well as to assess the validity of routine microscopic urine analysis and urine culture in the diagnosis of UTI and also to assess the validity of dipstick tests and culture in the diagnosis of UTI.

MATERIALS AND METHODS

The study was a hospital based cross-sectional descriptive study conducted between January 2012 and May 2013 in the department of Paediatrics, Durgabai Deshmukh Hospital and Research Centre, Hyderabad over a period of 18 months. Ethical approval was obtained from the Institution's Health Research and Ethics Committee before the commencement of the study. Children aged 1 month to 60 months presenting with fever (axillary temperature ≥ 37.6°C) with or without localizing sign (s) were recruited consecutively. Exclusion criteria included children below 1 month and above 5 years. Any child who had received antibiotics 48 hours prior was not included in the study, children with known congenital genitourinary anomalies, Parents/Guardians not willing to enrol the child in the study. Relevant information such as age, sex, place of domicile, symptoms, was obtained. Physical examination was carried out on each subject to identify possible focus of infection and other features that could facilitate the establishment of a clinical diagnosis. A clinical diagnosis of UTI was made in subjects with any of the following: Pain or crying on micturition, urinary frequency, urgency, loin pain, suprapubic tenderness.

Children were interviewed using structured questionnaire for urinary tract infection. A complete history related to the onset, duration of fever, associated symptoms such as nausea, vomiting, diarrhoea, urinary disturbances and other system involvement was obtained. A thorough physical examination with relevant investigations was carried out in all patients. Routine blood counts, dipstick tests, urine analysis, urine culture and sensitivity was done in them, USG examination and DMSA renal scan was done in culture positive cases and the detailed data was entered in the proforma.

AIMS AND OBJECTIVES

1. To determine the prevalence of UTI in febrile children less than 5 years of age.
2. To assess the validity of microscopic urine analysis and urine culture in the diagnosis of UTI.
3. To assess the validity of dipstick tests and urine culture in the diagnosis of UTI.

COLLECTION OF URINE SAMPLE

From all 200 cases a sample of urine was collected. In children below 2 years of age, urine sample was collected under aseptic precautions by transurethral bladder catheterisation or suprapubic aspiration. Urine was collected around 10 ml into sterile bottle and sent for dipstick tests, urine analysis, culture and sensitivity. In children above 2 years of age, a clean-catch mid-stream specimen was used to minimise contamination by periurethral flora. Contamination was minimised by washing the genitalia with soap and water. Child was allowed to pass urine; mid-stream sample was collected in sterile bottle and was sent for dipstick tests, urine analysis, culture and sensitivity.

DIPSTICK TESTS: The urine dipstick test was performed immediately on all samples of fresh urine. Results of the dipstick test (Multistix 10SG 228) were interpreted visually according to standard colour charts. The leukocyte esterase (LE) measurement was read after 2 minutes and recorded as negative, trace, small (+1), moderate (+2), or large (+3). The nitrite measurement was read at 60 seconds and recorded as negative or positive.

URINE ANALYSIS: The fresh urine samples obtained from the above techniques were subjected for urinalysis. The urine specimens were centrifuged in a standard manner, 10ml of urine was spun at the rate of 2500 rpm for 20-30 minutes, supernatant decanted off and sediment resuspended in the remaining 0.2ml. The urine was examined under microscope for hematuria and leukocyturia. In the present study more than 5 pus cells/HPF in a centrifuged urine sample was taken as significant pyuria.

URINE CULTURE: Urine received in sterile containers was inoculated into blood and Mac-Conkey agar plates with a 0.01ml calibrated loop. All plates were incubated at 35-37^{0}C for 24 hours under aerobic condition to obtain accurate colony count. On culture of urine, a colony count of more than $>10^5$ /ml organisms of a single species was considered significant. Samples showing insignificant growth, mixed growth of two or more pathogens or growth of non-pathogens were not considered as culture positive. The following definitions were employed in the present study.

SIGNIFICANT PYURIA: Presence of more than 5 pus cells /HPF in a centrifuged urine sample. POSITIVE URINE CULTURE: A positive urine culture was defined as growth of $>10^5$ colonies of a single urinary tract pathogen/ml of urine specimen. IMAGING: All children diagnosed to have UTI would undergo USG Abdomen, DMSA and MCUG scans as indicated by UTI management guidelines. USG: All the UTI culture positive cases were subjected to USG Abdomen. DMSA: All the UTI culture positive cases were subjected to DMSA renal scan. Technetium-99m–labelled dimercaptosuccinic acid scans were considered normal if homogeneous uptake of the radioisotope was evident throughout the kidneys and the renal contour were preserved. Acute pyelonephritis was defined by the presence of focal or diffuse areas of decreased uptake of labelled dimercaptosuccinic acid without evidence of cortical loss or by the presence of diffusely decreased uptake in an enlarged kidney. Renal scarring was defined by the presence of decreased uptake of labelled dimercaptosuccinic acid associated with loss of the contours of the kidney or by the presence of cortical thinning with decreased volume. The degree of scarring was assessed quantitatively by outlining the scarred area and calculating its ratio to the total area of the kidney.

ANALYSIS OF DATA:

The term validity refers to what extent the test accurately measures which it purports to measure. The term "valid" implies that there is some sort of external standard or "gold standard" against which the current measurement is being compared. The data was analysed by SPSS version 17 software along with below mentioned appropriate statistical tests at 5% level of significance.

OBSERVATIONS AND RESULTS

General characteristics of the study population: Out of 200 patients in study, 118 (59%) were males and 82 (41%) were females. Male to female ratio was 1.3:1, <1 year were 20%, 1-2 years : 27%, 2- 3 years : 11 %, 3-4 years : 13% and 4-5 years were 29% respectively. Out of 200 children, 61(30.5%) children showed significant pyuria in centrifuged urine sample of which 35(57.4%) were males and 26(42.6%) were females. Majority were <2 years, 39 (64%). Out of 61(30.5%) children showing significant pyuria in centrifuged urine sample, 70.5% of children showed 5-10 pus cells/HPF and 29.5% showed >10 pus cells/HPF.

Table 1: Age and Sex Distribution of 200 Febrile Children.

Age Group (months)	% of Febrile Patients with urine culture positive	Prevalence (%)	Prevalence %	
			Females	Male
0-1	92	6.9	5.1	8.5
1-3	80	5.5	5.9	5.3
3-6	33	3.6	5.1	2.5
6-9	24	2.1	3.7	0.8
9-12	23	1.4	2.3	0.7
12-18	19	0.8	1.4	0.4
18-24	17	0.8	1.4	0.3
All Groups	30	2.1	2.9	1.5

Table 2: Age and Sex Distribution of 200 Febrile Children with Urine Showing >5 Pus Cells/HPF.

AGE	SEX				TOTAL (n=61)
	MALE		FEMALE		
	5-10	>10	5-10	>10	
<1YR	10(35.71%)	1(14.28%)	7(46.60%)	2(18.18%)	20(32.70%)
1-2YR	10(35.71%)	4(57.14%)	3(20%)	2(18.18%)	19(31.14%)
2-3YR	04(14.28%)	1(14.28%)	2(13.30%)	3(27.27%)	10(16.39%)
3-4YR	04(14.28%)	1(14.28%)	3(20%)	1(09.09%)	9(14.75%)
4-5YR	00(00)	00(00)	00(00)	3(27.27%)	3(4.91%)
TOTAL	28(100%)	07(100%)	15(100%)	11(100%)	61(100%)

Table 3: Distribution of Urine Culture.

URINE CULTURE	SEX		TOTAL (n=200)
	MALE	FEMALE	
NO GROWTH	113(95.76%)	76 (92.68%)	189 (94.5%)
E.COLI	05(4.24%)	02(2.48%)	07(3.5%)
ACINETOBACTER	00(0 0)	01(1.21%)	01(0.5%)
PSEUDOMONAS	00(0 0)	01(1.21%)	01(0.5%)
SERRATIA	00(0 0)	01(1.21%)	01(0.5%)
PROTEUS	00(0 0)	01(1.21%)	01(0.5%)
Total	118(100%)	82(100%)	200(100%)

Out of 200 children, 94.5 % of febrile children showed no significant growth on Urine culture. Among 11 (5.5%) positive cultures, 63.6% showed E.coli, 9.1% showed Acinetobacter, Pseudomonas, Proteus and Serratia species each .

Table 4: Distribution of Leucocyte Esterase Dipstick Test Based on Sex

LEUCOCYTE ESTERASE	SEX		TOTAL (n=200)
	MALE	FEMALE	
POSITIVE	21(17.8 0%)	19(23.17%)	40(20%)
NEGATIVE	97(82.2 0%)	63(76.83%)	160(80%)
TOTAL	118(100%)	82(100%)	200(100%)

Among 200 febrile children, 40(20%) were leucocyte esterase positive, of which 53 % were males and 47% were females. Among 200 febrile children, 17(8.5%) nitrite were positive, of which 6(35%) were males and 11(65%) were females. Among 200 febrile children, 13(6.5%) were leucocyte esterase and nitrite positive, of which 6(46%) were males and 7(54%) were females. Majority (59%) of nitrite positive cases were found in febrile children < 2years.

Prevalence of UTI in febrile children in infants was 5%, < 2 years of age was 4.25 % and <5 years was 5.5%. In the present study, Sensitivity and Specificity of dipstick leucocyte esterase was 81.81% and 83.59%. PPV and NPV was 22.5% and 98.75%. Percentage of false positive and false negative was 16.4% and 18% respectively. Accuracy rate was 83.5%. In the present study, Sensitivity and Specificity of dipstick nitrite was 45.45% and 93.65% respectively. PPV and NPV was 29.41% and 96.7%. Percentage of false positive and false negative was 6.34% and 54.54% respectively. Accuracy rate was 91%.

Table 5: Validity Of Leucocyte Esterase And Nitrite Dipstick.

Validity	Sensitivity	Specificity	PPV	NPV	% of False Positive	% of False Negative	Accuracy Rate
LEUCOCYTE ESTERSAE	81.81	83.59	22.50	98.75	16.40	18.18	83.50

In the present study, Sensitivity and Specificity of dipstick leucocyte esterase and nitrite was 45.45% and 95.76% respectively. PPV and NPV was 38.46% and 96.79% respectively. Percentage of false positive and false negative was 4.23% and 54.54% respectively. Accuracy rate was 93%. In the present study, Sensitivity and Specificity of urine analysis was 72.72% and 71.95% respectively. PPV and NPV was 13.11% and 95%. Percentage of false positive and false negative was 28% and 27% respectively. Accuracy rate was 72%.

DISCUSSION

This study was a hospital based Cross sectional study carried out in the Department of Paediatrics, Durgabai Deshmukh Hospital and Research Centre, Hyderabad, over a period of 12 months to determine the prevalence of urinary tract infection in febrile children aged between 1 month to 5 years. As well as to assess the validity of routine microscopic urine analysis and culture in the diagnosis of urinary tract infection and also to assess the validity of dipstick tests and culture in the diagnosis of urinary tract infection.

A total of 200 febrile children were included in the study, out of which, 118 (59%) were males and 82 (41%) were females. Among 200 febrile children, <1year were 20%, 1-2years : 27%, 2-3years : 11%, 3-4years : 13% and 4-5years : 29% respectively. 18% belonged to class II, 44% belonged to class III and 38% belonged to class IV Socio economic status according to Modified B.G.Prasad Classification. 44% belonged to normal nutritional status, 21% belonged to grade I PEM, 17.5% belonged to grade II PEM, 15% belonged to grade III PEM and 2.5% belonged to grade IV PEM according to IAP Classification. In our study, prevalence of UTI in febrile children in infants was 5%, < 2 years of age was 4.25% and <5 years was 5.5%. Out of 200 febrile children, 61(30.5%) children showed significant pyuria, 8 (13.1%) of significant pyuria cases showed significant bacterial growth. 40(20%) out of 200 children showed dipstick leucocyte esterase positivity while 9 (22.5%) of dipstick leucocyte esterase positive cases showed significant bacterial growth. 17(8.5%) children showed dipstick nitrite positivity while 5(29.4%) of dipstick nitrite positive cases showed significant bacterial growth. 13(6.5%) children showed dipstick leucocyte esterase and nitrite positivity while 5(38.5%) of dipstick leucocyte esterase and nitrite positive cases showed significant bacterial growth. 39% of children showing >10 pus cells were culture positive whereas only 2.3% of children showing >5 pus cells were culture positive. 81.81% of children showing dipstick leucocyte esterase positivity were culture positive and 45.45% of children showing dipstick nitrite positivity were culture positive, whereas 45.45% of children showing dipstick leucocyte esterase and nitrite positivity were culture positive.

In the present study prevalence of UTI in febrile children <5 years was 5.5% which is similar to Quigley R[9] study were prevalence of 7% was noted, Nethersole PY *et al*[10] showed prevalence of 4.1% to 7.5%, Ferrara P *et al*[11] 2.1% to 8.7% and Kaushal RK *et al*[12] 8.4% which is almost similar to the present study. In contrast to the present study, two different studies (Bauchner *et al*[13] and Schlager TA[14]) reported similar low prevalence of 1.7%, whereas Rabasa AI and Gofama MM[15] reported high prevalence of 13.7%. In the present study prevalence of UTI in febrile children <1year was 5% and is almost similar to studies by Hoberman *et al* [16] 5.3%, Dharni Dharaka *et al* [17] 5.4%, Schlager TA[14] 5.3%, Kanellopoulos TA *et al* [18] 5.3% respectively. Shaw KN and Gorelick MH and Saleh SI *et al*[19] stated prevalence of 3-5% and 4.1-7.5% respectively which co-relates with the present study. In contrast to present study Shaikh N *et al* [20] and Kaushal RK *et al* [12] reported prevalence of 7% and 12.3% respectively. In present study prevalence of UTI in febrile children <2years was 4.25% which was similar to studies by Roberts k *et al*[21] 4.1% and Schlager TA[14] 4.1% respectively. In contrast to present study P.R Srivasths *et al*[17] reported a prevalence of 2.48% in children <2years which was lowest prevalence reported from a developing country. Bachur R and Harper MB[22] reported prevalence of 2.1%. In the present study prevalence of UTI in febrile preschool children was 5.2% which is almost similar to the study by Fallahzadeh MH *et al*[23] who reported prevalence of 4.4%. In contrast to present study, Musa-Aisien AS *et al*[24] reported prevalence of 9%.

Out of 200 febrile children, 11(5.5%) were culture positive of which Male: Female ratio of culture positive cases in the age group of <1year was 1:1, in children >1year was 0.8:1 with female preponderance. In this study, among 11 culture positive cases, 7(63.6%) grew E.coli and 1(9.1%) each of Pseudomonas, Acinetobacter, Serratia, Proteus sp. As reported by Byran CS *et al*[25] E.coli was the most common urinary pathogen accounting for 85% of community acquired UTI. According to Bagga A *et al*[26] about 90% of first symptomatic UTI and 70% of recurrent infections are due to E.coli. Waisman Y *et al*[27] stated in their studies that of the 35 cultures, 27 were positive for E.coli (76%), 2 for Klebsiella (6%), 2 for Enterococcus (6%), 2 for Pseudomonas (6%), 1 for group B streptococcus (3%), and 1 for Staphylococcus coagulase negative (3%). According to Chris H *et al* the most commonly isolated urinary pathogens are enteric, gram-negative bacteria especially E.coli. Others include Enterobacter, Klebsiella, and Proteus sp. Zamir G *et al*[28] studied children with UTI and found the main causative agents were Escherichia coli 229 (85%), Klebsiella sp. 13 (5.1%), Proteus sp. 12 (4.7%), Pseudomonas aeruginosa, Enterococcus fecalis and Morganella morgana (1%) each.

According to Zorc JJ *et al*[29] the most common pathogen that

caused UTI was E.coli (80%), Klebsiella pneumonia (9%), Enterobacter species (5%), Citrobacter species (4%) and Pseudomonas species (1%). Nowell L *et al*[30] stated the organisms most commonly isolated in children with UTI were Coagulase negative Staphylococcus (28%), E.coli (17%), Enterococcus sp. (12%), and Klebsiella sp. (11%). Saadeh SA and Mattoo TK reported E.coli (60–92%) as the most common pathogen and other organisms were Klebsiella, Proteus, Enterococcus and Enterobacter sp. In the present study, Sensitivity and Specificity of urine analysis was 72.72% and 71.95%. PPV and NPV was 13.11% and 95%. Percentage of false positive and false negative was 28% and 27% respectively. Accuracy rate was 72%. CHON CH *et al*[31] stated sensitivity and specificity of 73% and 81%, almost similar to present study. In study by Zorc JJ *et al*[29] reported sensitivity and specificity of urine analysis as 67% and 79% which matches with the present study. In correlation to present study Shaw KN *et al* stated sensitivity and specificity of 57-87% and 53-79% respectively. In contrast to present study Bachur R and Harper MB[22]stated sensitivity and specificity of 82% and 92% respectively. Waisman Y *et al* reported sensitivity and specificity of 88.6% and 88.4% respectively. And in contrast to the present study Waisman Y reported PPV and NPV of 75.6% and 95% respectively.

In the present study, Sensitivity and Specificity of dipstick leucocyte esterase was 81.81% and 83.59%. PPV and NPV was 22.5% and 98.75%. Percentage of false positive and false negative was 16.4% and 18% respectively. Accuracy rate was 83.5%.Yuen SF *et al* reported sensitivity and specificity of 72% and 85.8%, almost similar to present study. Yuen SF *et al*stated PPV and NPV of 55.4% and 92.6% which matches with the present study. Zorc JJ *et al*[29] reported sensitivity and specificity of 83% and 84% respectively. CHON CH *et al*[31] coated sensitivity and specificity of 83% and 78% respectively. Almost similar results to our study were reported by Saadeh SA and Mattoo TK. which showed sensitivity and specificity of 79% and 87% respectively. Another study by Williams GJ *et al* sensitivity and specificity of 47–95% and 23–100% was stated.

In the present study, Sensitivity and Specificity of dipstick nitrite was 45.45% and 93.65% respectively. PPV and NPV was 29.41% and 96.7%. Percentage of false positive and false negative was 6.34% and 54.54% respectively. Accuracy rate was 91%. Saadeh SA and Mattoo TK reported sensitivity and specificity of 49% and 98% respectively, almost similar to present study. Study by Zorc JJ *et al* stated sensitivity and specificity of 50% and 98% respectively which matches with the present study. CHON CH *et al* coated sensitivity and specificity of 53% and 98% respectively. Williams GJ *et al* reported sensitivity and specificity of 83–95.2% and 49.9–100%. In the present study, Sensitivity and Specificity of dipstick leucocyte esterase and nitrite was 45.45% and 95.76%. PPV and NPV was 38.46% and 96.79%. Percentage of false positive and false negative was 4.23% and 54.54% respectively. Accuracy rate was 93%. Saadeh SA and Mattoo TK reported sensitivity and specificity of 45% and 98%, almost similar to present study. In a study by Shaw KN *et al* sensitivity and specificity of 79% and 97% and PPV of 46% which matches with the present study. In contrast to present study, Waisman Y *et al* reported sensitivity and specificity of 97.1% and 82.5% and PPV and NPV of 69.4% and 98.6% respectively. Zorc JJ *et al* stated sensitivity and specificity of 88% and 93%. CHON CH *et al* reported sensitivity and specificity of 93% and 72%.

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