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Original Research Article

A Study to Evaluate the Test Characteristics of the Urinalysis for Diagnosing UTI in Young Febrile Infants

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Abstract

Aim: The aim of the present study was to evaluate the test characteristics of the urinalysis for diagnosing UTI in young febrile infants.

Material & Methods: A prospective study of febrile infants ≤60 days old at Department of Pediatrics. We evaluated the test characteristics of the urinalysis for diagnosing UTIs, with and without associated bacteremia, by using 2 definitions of UTI: growth of ≥50000 or ≥10000 colony-forming units (CFUs) per mL of a uropathogen. We defined a positive urinalysis by the presence of any leukocyte esterase, nitrite, or pyuria (>5 white blood cells per high-power field).

Results: 205 patients were enrolled in this study out of which 5 patients who met exclusion criteria were excluded. Of the 200 patients enrolled in this study and who met the inclusion criteria, 120 (60%) were male and 80 (40%) were female. 96% of febrile patients (n=192) showed no significant growth on urine culture. 4% (n=8) of the febrile patients had positive cultures. Out of 200 children, 20 (10%) children showed significant pyuria (>5 pus cells/HPF) in centrifuged urine sample of which 12 (60%) were males and 8 (40%) were females. Chi-square analysis was done taking urine culture as gold standard for diagnosis of UTI. Analysis was done for significant pyuria (> 5 pus cells/HPF) and the following were calculated with the standard formulas: Sensitivity=100, Specificity=96.4%, Positive predictive vale=65.5%, Negative predictive value=98.2%, Percentage of false positive=2.5%, Percentage of false negative=0%, Accuracy rates=96.4%.

Conclusion: The urinalysis is highly sensitive and specific for diagnosing UTIs, especially with ≥50000 CFUs/mL, in febrile infants ≤60 days old, and particularly for UTIs with associated bacteremia.

Keywords: Urinary Tract Infection, Urine Analysis, Young Febrile Children.

Introduction

Urinary Tract infections (UTIs) are the most common source of serious bacterial infection in young children. Overall, 3% to 5% of young febrile children have UTIs, including 5% to7% of those "with- out a source of fever." [1,2] Prevalence of UTI between 4.1% and 7.5%. [2,3,4,5] is the commonest bacterial illness among febrile infants and young children. Ranked next to respiratory and gastrointestinal infections, it is the third most common infection in pediatric age group and accounts for 4 to 10% of febrile children admitted to hospital. [6]

Fever has long been considered a finding of clinical importance in children with UTI because it has been accepted as a marker of renal parenchymal involvement (Pyelonephritis). [7] It is only after 5 years of age, the typical triad of abdominal pain, vomiting and fever with chills, rigors or suprapubic pain are common presenting complaints of UTI. The evaluation of febrile infants typically includes the urinalysis, a readily available screening test, to make a preliminary diagnosis of UTI. However, the reported test characteristics of the urinalysis in this age group have varied substantially, with sensitivities ranging from 48% to 99% and specificities ranging from 88% to 98%. [8-11]

Some of the variability in test performance of the urinalysis in this age group can be attributed to differing methods of urine collection (catheterized versus non-catheterized samples)[9] or differing methods of performance of the urinalysis (eg, dipstick with or without microscopy, varying laboratory procedures). [2.8,9,12,13]

Beyond the diagnosis and treatment of UTIs, the identification of a UTI in a young child prompts investigation for vesicoureteral reflux and other urinary tract anomalies that may pre-dispose patients to long-term renal complications. [14-17] Undetected UTI in children is more alarming because of the acute and chronic complications of it

in children which is not seen routinely in adults. The majority of these infections in the first 2 years of life are "occult" and most infection remain undiagnosed if tests are not routinely performed to detect them. The high incidence of undiagnosed and untreated UTI in young children is a cause of concern.

Hence the aim of study was to determine the prevalence of urinary tract infection in febrile children, less than 5 years of age.

Material & Methods

A prospective, cross-sectional study of febrile infants 60 days of age and younger presenting to Department Of Pediatrics, JLNMCH, Bhagalpur, Bihar, India in between the duration of 2 years (Feb 2017 to Jan 2019). Informed consent was obtained from the parent or legal guardian of each enrolled patient. A convenience sample of 200 infants 60 days of age and younger with documented fevers ≥38°C from whom blood cultures were obtained as part of their ED evaluation for serious bacterial infection.

Inclusion Criteria

- If Infants had urinalyses (evaluating both LE and nitrite at a minimum) performed and urine cultures obtained via urethral catheterization or suprapubic aspiration.

Exclusion Criteria

- Infants were excluded if they had clinical sepsis, a history of prematurity, significant comorbid conditions, or recent systemic antibiotic use. [13]
- If infants had bacteremia without associated UTI, if they had bacteremia and concurrent UTI caused by different pathogens, if the bacteremia status was unclear (such as having a Gram-stain with positive results but no bacterial growth or growth of multiple organisms), or if the urine culture was obtained via a bag specimen or an unknown method.

Methodology

The urinalyses were completed as per standard procedures at the participating hospitals' clinical laboratories. We evaluated both the individual components of the urinalysis and the urinalysis in aggregate. The 3 individual components of the urinalysis assessed included LE, nitrite, and pyuria. For our analysis of the aggregate urinalysis, we defined a urinalysis as positive if LE, nitrite, or pyuria was present. The aggregate urinalysis to be negative if the LE, nitrite, and pyuria components all revealed negative results. The aggregate urinalysis to be negative if the LE and nitrite components revealed negative results and pyuria was not assessed. The test characteristics for the aggregate urinalysis for the entire cohort as well as stratifying by age group (≤28 or 29–60 days old) was analysed. [2] A different definitions of UTI, given varied definitions of UTI in the literature for this age group based on colony counts was applied. [9,15-18] For analysis, a defined UTI as the growth of ≥50000 CFUs/Ml of a known urinary pathogen from a culture obtained via catheterization or ≥1000 CFUs/Ml from a culture obtained via suprapubic aspiration. For secondary analysis, a defined UTI as the growth of ≥10000 CFUs/Ml of a known urinary pathogen from a culture obtained via catheterization or ≥1000 CFUs/Ml from a culture obtained via suprapubic aspiration. In instances in which the reporting of the CFUs per Ml was provided as a range that crossed a definition threshold, excluded the infant from that analysis. For example, if the urine culture was reported as 25000 to 75000 CFUs/Ml, we excluded that particular infant from the primary analysis because our primary definition of UTI (growth of ≥50000 CFUs/Ml) fell within the range reported, but we included the infant in the secondary analysis using the ≥10000 CFUs/Ml definition. A negative urine culture as one with no growth, growth of a contaminant in the absence of a pathogen, or growth of a urinary pathogen that did not reach the CFUs per Ml threshold was analysed. Contaminants were defined as bacteria known to be skin or genitourinary flora, such as coagulase-negative Staphylococcus, Lactobacillus, and Corynebacterium species. Additionally, a urine culture to be contaminated and negative if it revealed growth of more was considered than 2 organisms of any type. On the basis of the presence or absence of the same pathogen growing in the blood culture, UTIs were categorized as with or without bacteremia for further analysis.

Statistical Analysis

Bivariable analyses to compare the demographic and clinical characteristics between infants with and without UTIs and between infants with UTIs with and without associated bacteremia. We analysed categorical variables by using the $\chi 2$ test and continuous variables by using Wilcoxon rank tests. We calculated the sensitivity, specificity, positive and negative predictive values, and positive and negative likelihood ratios of the urinalysis results (with 95% confidence intervals [Cis]) for all infants and then calculated these values separately for infants with and without bacteremia. All analyses were performed in SAS version 9.4 (SAS Institute, Inc, Cary, NC).

Results

Table 1: Demographic data and pathogens in urine culture

Gender	**N%**	
Male	120 (60)	
Female	80 (40)	
Pathogens in urine culture	**Male**	**Female**
Acinetobacter	1	1
E. Coli	1	1
No growth	116	76
Proteus	1	1
Serratia	1	1
Total	120	80

205 patients were enrolled in this study out of which 5 patients who met exclusion criteria were excluded. Of the 200 patients enrolled in this study and who met the inclusion criteria, 120 (60%) were male and 80 (40%) were female. 96% of febrile patients (n=192) showed no significant growth on urine culture. 4% (n=8) of the febrile patients had positive cultures.

Table 2: Distribution of pus cells in urine

PUS Cells	**Sex**		
	Male	**Female**	**Total**
5-10	10	6	16 (80%)
>10	2	2	4 (20%)
Total	12	8	20 (100%)
X^2 =0.832, p=0.314 not significant.			

Out of 200 children, 20 (10%) children showed significant pyuria (>5 pus cells/HPF) in centrifuged urine sample of which 12 (60%) were males and 8 (40%) were females.

Table 3: Chi Square Analysis (urine analysis*urine culture)

Sensitivity	100%
Specificity	96.4%
Positive predictive vale	65.5%
Negative predictive value	98.2%
Percentage of false positive	2.5%
Percentage of false negative	0
Accuracy rates	96.4%

Chi-square analysis was done taking urine culture as gold standard for diagnosis of UTI. Analysis was done for significant pyuria (> 5 pus cells/HPF) and the following were calculated with the standard formulas: Sensitivity=100, Specificity=96.4%, Positive predictive vale=65.5%, Negative predictive value=98.2%, Percentage of false positive=2.5%, Percentage of false negative=0%, Accuracy rates=96.4%.

Discussion

UTI was first described by Roger in 1839 and since then considerable clinical experience and research have been done on this entity. It has been established by various workers, both in India and other countries that UTI is one of the commonest infection in children. Infants and young children are of particular concern because UTI in this age group may cause few recognizable signs or symptoms other than fever and has a higher potential for renal damage than in older children. [19-21] High incidence of suspicion is needed for diagnosing UTI as it may bring to attention a child with an obstructive anomaly or severe VUR. Second, because these children with UTI may have a febrile illness and no localizing findings, there may be a delay in diagnosis and treatment of the UTI. Third, first attack of UTI in infancy and early childhood is usually not a single attack but beginning of a continuous process with the risk of recurrences. The risk of renal damage increases as the number of recurrences increase. Proper diagnosis and prompt treatment of UTI in children is therefore vital

205 patients were enrolled in this study out of which 5 patients who met exclusion criteria were excluded. Of the 200 patients enrolled in this study and who met the inclusion criteria, 120 (60%) were male and 80 (40%) were female. In the present study prevalence of UTI in febrile children <5 years was 5.0% which is similar to Quigley R[22] study were prevalence of 7% was noted. Out of 200 children, 20 (10%) children showed significant pyuria (>5 pus cells/HPF) in centrifuged urine sample of which 12 (60%) were males and 8 (40%) were females. 96% of febrile patients (n=192) showed no significant growth on urine culture. 4% (n=8) of the febrile patients had positive cultures. As reported by Byran CS et al [22] E.coli was the most common urinary pathogen accounting for

66.6% of community acquired UTI. According to Bagga A et al [23] about 90% of first symptomatic UTI and 70% of recurrent infections are due to E.coli. Waisman Y et al [24] 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 [25] 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 [26] 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. Saadeh SA and Mattoo TK [27] reported E.coli (60–92%) as the most common pathogen and other organisms were Klebsiella, Proteus, Enterococcus and Enterobacter sp.

Chi-square analysis was done taking urine culture as gold standard for diagnosis of UTI. Analysis was done for significant pyuria (> 5 pus cells/HPF) and the following were calculated with the standard formulas: Sensitivity=100, Specificity=96.4%, Positive predictive vale=65.5%, Negative predictive value=98.2%, Percentage of false positive=2.5%, Percentage of false negative=0%, Accuracy rates=96.4%. Waisman Y et al [28] reported sensitivity and specificity of 88.6% and 88.4% respectively, almost similar to present study. Waisman Y[28] reported PPV and NPV of 75.6% and 95% respectively which is similar to our study. In contrast to our study, Zorc JJ et al [29] reported sensitivity and specificity of urine analysis as 67% and 79%. ShawKN28 et al stated sensitivity and specificity of 57- 87% and 53-79% respectively.

Conclusion

Urine culture is the gold standard test in diagnosing UTI. Urine culture positivity was more in urine analysis showing >10 pus cells/HPF as compared to >5 pus cells/HPF. In diagnosing UTI, pyuria >10 pus cells/HPF was more specific (100%) with higher positive predictive value than the conventional >5 pus cells/HPF. Many of the patients who had a different provisional diagnosis turned out to be UTI hence a high index of suspicion is needed to diagnose UTI and prevent complications.

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