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ORIGINAL ARTICLE

Clinical Utility and Accuracy of UTI Calculator for Estimating the Probability of Urinary Tract Infection in Young Febrile Children

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ABSTRACT

Objective: To analyze the prediction of urinary tract infection (UTI) by UTI Calculator (UTI Calc) taking urine culture sensitivity (C/S) results as indices of UTI in children aged >2 month- 24 months.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pediatric Medicine, The Children's Hospital & the Institute of Child Health, Lahore from January 2019 to December 2019.

Material and Methods: A total of 75 admitted children 2 months to <2 years of age with fever >38^{o}C were included. We excluded children who had taken oral or injectable antibiotic. Prediction of UTI was made by using online UTI Calc.

Results: Prevalence of UTI in febrile infants was 9%. The mean age was 9.8 ± 6.8 months with slight male preponderance 40 (53%). In 50 (67%) the clinical UTI probability was high and with urine examination reports the UTI probability was high in only 8 (11%). Urine culture was positive in 7 (9%) and *E. coli* was the predominant organism 4 (5%). Urine culture positivity with clinical prediction alone was low (p=0.132) but was strongly associated with urine probability prediction (p=<0.001). Sensitivity and specificity of UTI Calc in detecting UTI was 100% and 97% respectively.

Conclusion: UTI calc is an excellent online tool in predicting urinary tract infection in young febrile children.

Key Words: *Infection, Urinary tract, Prediction, Probability, Children, UTI calc*

INTRODUCTION

In young children, urinary tract infection (UTI) is a common clinical problem both in the hospital setting as well as in the community.[1] The incidence of UTI among febrile children is 5.3 percent.[2] The presentation of UTI in infancy and childhood is quite diverse and can present with clinical features that are not localized to the urinary tract but may closely resemble other febrile diseases without any focal sign. In addition UTI may co-exist with other common childhood diseases.[3] UTI is more probable without any source of infection in infants with fever of ≥102^{0}F for >48 hours. Urine examination and urine culture

is generally recommended in young infants with no clear cause of infection with fever ≥39°C for >48 hours. Some studies have indicated that UTI must be excluded in girls <24 months of age on the basis of certain characteristics like: age <12 months, fever >39°C, fever for >2 days and absence of another focus of infection.[4] UTI whether symptomatic or asymptomatic is more significant in childhood than in adults as renal scarring mostly occurs within first five years of life after these infections.[5].

UTIs are not commonly identified as a cause of childhood morbidity in developing countries.[6] Urine Culture has the disadvantage of delay of 48 hours to give a result. Therefore rapid diagnostic tests for UTI diagnosis are ideal in children and the rapid tests widely used are dipstick test and urine microscopy. The dipstick includes chemical analysis of nitrite, leukocyte esterase (LE), blood and protein. The benefit of dipstick tests is that they are fast and simple to perform and can provide an immediate result. The microscopic analysis of urine for leukocytes or bacteria also carries vital importance in diagnosing UTI.[4] Clinicians only order urine culture results when they have high UTI concern. Although algorithms have been developed for identification of children with high probability of UTI but they are not commonly followed by the clinicians.

According to a research published in JAMA Pediatrics 2018, a newly developed UTI Calc which can be used to guide further tests and treatment in children with suspected UTI. Compared to the American Academy of Pediatrics algorithm, it has been reported that the clinical and laboratory model of UTI Calc minimizes the testing by 8.1% and reduces the number of missing UTIs from three cases to zero. In addition, the number of treatment delays by the dipstick model in UTI Calc was found to decrease by almost 10.6% relative to the empirical treatment of all children with a leukocyte esterase test result of ≥1.

According to the authors "*Accurate diagnosis of UTI is important to reduce the delay in diagnosis and to avoid unnecessary treatment with antimicrobial drugs. The approach advocated here tailors testing and treatment to the risk factors present in the child being assessed, thus offering the potential to improve outcomes for children with UTI*".[7]

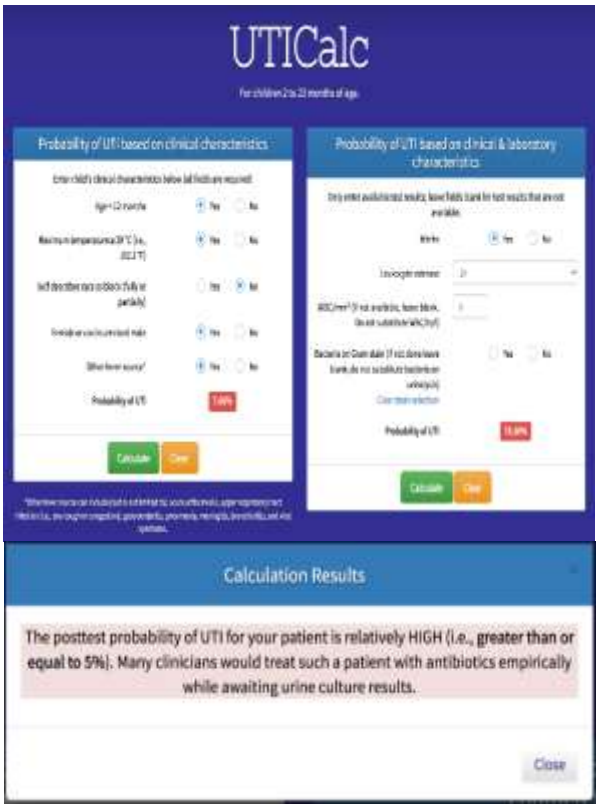
MATERIAL AND METHODS

This was a descriptive study which included a total of 75 patients in 2 months to <2years age range who presented with high grade fever to the Department of Pediatric Emergency of the Children's Hospital & the Institute of Child Health, Lahore, Pakistan between January 2019 to December 2019. Non-probability convenience sampling was done and the data was gathered prospectively. We excluded patients who did not meet study inclusion criteria including: patients who were referred from other hospitals after undergoing treatment with antibiotic, patients who received oral antibiotics, patients presented with seizures and suspected as meningitis or patients who did not sign an informed consent showing their willingness to participate. Febrile children with known renal/bladder malformations or patients with neurogenic bladder were also excluded from the study. Urine was collected by urethral catheterization by doctor/nurse using aseptic technique and no other technique like pediatric bag urine collection sample was taken.

By using Openepi sample size calculator, this sample size of 75 was determined by taking the prevalence of UTI as 5.3%[2] with 95% confidence interval and a 5% error margin. Information on age, gender, circumcision in male children, maximum fever recorded and previous use of antibiotics was documented. The quantitative variable age was expressed as mean ± standard deviation (SD), while the qualitative variables were expressed as frequency and the percentage.

By analyzing clinical and laboratory risk factors, we used a new calculator (UTI Calc) with two models (Clinical Model and Laboratory Model) built to estimate the likelihood of UTI in preverbal children. Five clinical risk factors (age <12 months, body temperature ≥39^0C, brown race, uncircumcised male or female and without any other known cause of pyrexia) were included**.** Five sub-models were included in the Laboratory model; **Dipstick model:** clinical model variables along with nitrite and LE parameters included. **Dipstick plus Gram stain model:** clinical and dipstick model variables used plus the Gram stained urine smear data. **Hemocytometer model:** clinical and dipstick variables plus urine white blood cells (WBC) count (WBC/μL) included.

Enhanced urine analysis model: included variables from clinical and hemocytometer models plus results of Gram stain. **Urine analysis model:** involved bacteria per high-power field (HPF) along with variables of clinical and dipstick models. Pyuria was defined as Pus cells count of ≥5/HPF or ≥10/μLor detection of any LE on strip and yield of a uro-pathogen at a concentration of at least 50 colony forming units per milliliter (CFU/ml). For the clinical model, the risk cutoff was taken as 2% and 5% for the laboratory model referring to the level at or above which children are intent to have fairly high probability of UTI, thus necessitating antibiotic treatment.



The likelihood of UTI risk was determined by this free online UTI Calc based on clinical characteristics and graded into high risk or low risk. Complete urine examination was performed for nitrites, LE, WBC/mm^3 and bacteria and the dipstick model in UTI Calc measured the risk of UTI. Urine samples were sent for culture and sensitivity testing and the outcomes were correlated with UTI Calc risk prediction. The sensitivity, specificity, positive predictive value and negative predictive value of UTI Calc was determined using urine culture as gold standard.

RESULTS

Prevalence of UTI in febrile infants was 9%. Mean age of the children was 9.8 ± 6.8 months and majority were 2-6 months age 32 (42%). Slight male preponderance 40 (53%) was observed including 13 (17%) uncircumcised boys (table 1). Nutritional status was at or above median weight for age in 33 (44%), 15 (20%) were moderate or severely malnourished. In 50 (67%) cases, the clinical UTI probability was high and with urine dipstick and microscopy report the UTI probability was high in 9 (12%). Urine culture was positive in 7 (9%) and *E. coli* was the predominant organism 4 (5%), Details of urine dipstick report and urine Culture reports shown in (table 2). In two patients in which there was high UTI probability, the urine culture report showed a mixed growth and was discarded and considered contamination by the microbiologist. Urine culture was positive in significantly more children having temperature >39^{o}C as compared to temperature between 38-39^{o}C (p=0.049). No association of gender, uncircumcised males or other focus of infection was found with positive urine cultures (p=>0.05). Urine culture positivity with clinical prediction alone was low (p=0.132) but was strongly associated with urine probability prediction (p=<0.0001). Sensitivity and specificity of UTI Calc in detecting UTI as shown in table 3.

TABLE 1: Clinical model characteristics of the study participants

Characteristics	Number (%)
Age	
Mean age	9.8 ± 6.8
2-6 months	32 (42.0)
6.1-12 months	23 (31.0)
12.1-23 months	20 (27.0)
Gender	
Females	35 (47.0)
Male	40 (53.0)
Uncircumcised males	13 (17.0)
Focus of infection	
Present	42 (56.0)
Temperature	
38-39^{o}C	50 (67.0)
>39^{o}C	23 (33.0)
Clinical Probability of UTI	
High	50 (67.0)
Low	23 (33.0)

TABLE 2: Laboratory model characteristics of the study participants

Results	Characteristics				
	Nitrites	**Leucocyte esterase**	**WBC**	**Bacteria**	**Culture**
Positive	08 (11%)	08 (11%)	10 (13%)	09(12%)	07 (9%)
Negative	67 (89%)	67 (89%)	65 (87%)	66 (88%)	68 (91%)
Microorganism isolated on Urine Culture					
E-faecalis 2 (2.7%)		*E. coli*4 (5.3%)		*Klebsiellaspp*1 (1.3%)	
Lab UTI Probability					
High 9 (12%)			Low 66 (88%)		

TABLE 3: Sensitivity and specificity of clinical and laboratory model of UTI Calc

Models	Sensitivity	Specificity	p- value
Clinical Model	57%	32%	0.680
Laboratory Model	100%	97%	<0.0001

The positive predictive value of clinical model was 08% as compared to laboratory model 88%. The negative predictive value of clinical model was 77.8% as compared to Laboratory model 100% (p value <0.001).

DISCUSSION

A urinalysis and urine culture should be performed of children <3 years of age with high grade fever with no obvious source, as recommended by the international guidelines. Many of the guidelines for children >3 years of age are focused solely on expert opinion due to lack of research.[8] In infants and young children with unexplained fever (>38 ^{o}C), UTI must be considered as a cause of fever.[9]

In our study, the frequency of UTI was 9% comparable to the UTI prevalence of 9.2% in a research on UTI in febrile children.[10] In a study published by Gonzalez, the prevalence of UTI was found to be 15.5% in febrile children under the age of two years.[11] This difference is due to their large sample size and a multi centric study. A much higher percentage was documented in a research from Japan by a diaper screening test using LE.[12] The plausible explanation in the difference in the prevalence of UTI is due to the sampling method and sample size.

Mean age of the children included in a large study was10 ± 5.5 months comparable to the mean age of 9.8 ± 6.8 in our study participants 9.8 ± 6.8.[11] A much younger age of 3.6 ± 1.4 months was described in a study by Yoon et al.[13] Age is one of the best known risk factors for concurrent bacteremia in UTI. The prevalence of concomitant UTI bacteremia decreased with age in pediatric studies.

The urine dipstick incudes nitrites and LE and our study also used a method having two models; clinical and laboratory method using dipstick and urine microscopy for identification of UTI in children. In our study, LE and nitrites were highly sensitive and specific in UTI diagnosis by taking urine culture as gold standard. A review article also supported our finding narrating that nitrites alone have a relatively high probability ratio. Moreover LE alone tends to be a weak test for ruling in and ruling out disease. A combination of LE and nitrites can provide the best value for both diagnosis and ruling out disease. It can be summarized that the highest probability ratio is a dipstick positive for both LE and nitrites and a negative dipstick test has the highest negative likelihood ratio suggesting that this test combination may be used to rule out disease.[14]

Screening methods as microscopic analysis for WBCs and bacteria as well as dipstick analysis for LE and nitrites are widely used but with poor sensitivity. Although the combination of positive test results is very sensitive, even with high possibility, the utility of dipstick alone to control infection remains method of choice. Therefore, for clinicians, accurate prediction of culture results are important to shorten the diagnosis time and for patients to receive treatment as soon as possible.[15] Sensitivity and specificity of various dipstick test is variable in detecting UTI in children. An article published in *Pediatrics and Child Health* showed that nitrites were 98% specific and combination of LE, nitrites or

microscopy had 99.8% sensitivity in diagnosing UTI.[8]

Negative results of dipstick for both LE and nitrites or microscopic examination for pyuria or bacteria in clean void urine, bag or nappy/pad test can fairly be used to rule out UTI. These children, without the need of confirmatory urine culture, may then confidently be exempted from further examination. Similarly, combination of positive test may be used for decision making and need for further investigation.[16]

In our research, the clinical model had low sensitivity and specificity as compared to Laboratory model using dipstick and microscopy. A study conducted on parent-reported symptoms, signs elicited by clinician, clinician made diagnosis of UTI and urine dipstick results, reported that a symptom based and sign based clinician diagnosis works well for recognizing young children with UTI and dipstick provide additional diagnostic value for empiric antibiotic therapy.[17] A similar research also narrated that children when using clinical judgment predict almost more than half of children who had a confirmed UTI.[18]

Among the positive cultures reported in our research, *E. coli* was the most common microorganism isolated followed by *Enterococcus-faecalis* and *Klebsiella spp* comparable with a study conducted in Nepal.[19] *E coli* as a predominant uro-pathogen was identified in a research by Liang[10] and a local study by Hussain.[20] Similar *E. coli* predominance was reported in many studies on UTI in children.[10,17,21]

Limitations: The key limitation of this report is the small sample size which restricts the generalization of our findings. It can be helpful if we replicate the same study with a larger sample size to give an accurate picture.

CONCLUSION

UTI calc is an excellent online tool in predicting urinary tract infection in young preverbal febrile children. Clinical model based diagnosis of UTI has low sensitivity and specificity for diagnosing UTI in preverbal febrile children but urine dipstick and microscopy provides an additional diagnostic value for empiric antibiotic therapy.

Recommendations: It is recommended that laboratory method with urine dipstick and microscopy results can be used as a rapid diagnostic test for diagnosing UTI in young febrile children and for starting antibiotics empirically to avoid delay in specific management.

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