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Nitrite and Leukocyte Esterase Activity Test for the Diagnosis of Urinary Tract Infection in Children: A Diagnostic Study

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ABSTRACT

Introduction: Urinary tract infection (UTI) is a common reason for pediatric hospital visits, often leading to misdiagnosis due to nonspecific symptoms. This study aimed to establish the diagnosis of UTI using dipstick tests in children with or without localizing signs and symptoms of UTI. Also comparison between urine culture with a dipstick test for diagnosing UTI was done.

Methods: A diagnostic study included 134 children aged 1 to 60 months presenting with fever or clinical signs of UTI. Urine samples were collected and subjected to culture, routine microscopy, and dipstick testing. The dipstick's leukocyte esterase (LE) test and nitrite test were compared to urine culture to assess their diagnostic accuracy.

Results: Among the 134 cases, 13 were culture positive, with E. coli being the most commonly isolated organism (53.8%). Fever was the most common symptom. Urine microscopy was positive in 21 cases, and 11 were culture positive. Compared to urine culture, the LE test had a sensitivity of 76.92%, specificity of 84.29%, PPV of 34.48%, and NPV of 97.14%. The nitrite test had a sensitivity of 84.61%, specificity of 92.56%, PPV of 55%, and NPV of 98.24%. Comparing either test to urine culture, the sensitivity was 92.30%, specificity was 82.64%, PPV was 36.36%, and NPV was 99.01%.

Conclusions: The combined dipstick test, including the nitrite and LE tests, showed good sensitivity, specificity, and NPV compared to urine culture. It can be reliably used for diagnosing UTI and initiating antibiotic treatment while awaiting urine culture results.

Keywords: *Leukocyte esterase; Nitrite test; Urine culture; UTI.*

INTRODUCTION

Urinary tract infection (UTI) is a common condition characterized by invading pathogens into the urinary tract, affecting the kidneys, bladder or urethra, but research in Nepal is lacking. Diagnosing UTI in neonates and children is challenging due to nonspecific symptoms, causing delayed diagnosis. Children under four years are at risk of complications like renal scarring, septicemia, hypertension, and chronic renal failure.[1,3] If these conditions are not treated on time, it may lead to hypertension and renal failure in later childhood or during adult life.[1,3,4] Timely diagnosis is crucial to prevent these complications. Urine samples are essential for diagnosis, but culture and sensitivity tests are costly and time-consuming. This study aims to evaluate the effectiveness of dipstick tests as a rapid, economical and non-invasive diagnostic tool for UTI in children, regardless of symptoms. By establishing the utility of dipstick tests, this research can improve UTI diagnosis in pediatric populations in Nepal.

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METHODS

This diagnostic analysis was conducted at the Department of Pediatrics in Shree Birendra Hospital over one year, from 2076/01/06 to 2077/01/05 BS. The study focused on children aged one month to 5 years who visited the hospital with clinical signs of urinary tract infection (UTI). Ethical approval was obtained from the Nepalese Army Institute of Health Sciences (NAIHS) ethical committee prior to the study. Non-probability sampling method was employed for sampling purposes.

A total of 155 children with UTI at Shree Birendra Hospital were included in the study, determined based on a prevalence rate of 9.4% from the data over five years. The children enrolled in the study were aged between 1 and 60 months who presented with symptoms such as unexplained fever, vomiting, increased frequency, hesitancy, foul-smelling urine, abdominal pain, incontinence, failure to thrive, poor feeding, jaundice and dysuria. Children with known gross congenital genitourinary anomalies or who had received any antibiotics within 48 hours prior to the study were excluded. Prior to the study, parental informed consent was obtained.

Sample collection techniques:

Resident and medical officers working in the pediatric department were instructed on urine sample collection procedures. The interpretation of dipstick results followed the standard chart provided in the dipstick box. Urine samples were collected in two different containers, under strict aseptic precautions for urinalysis and urine culture. The urine collection methods employed in this study included midstream clean catch sample, catheterization or bag method. To minimize contamination by peri-urethral and preputial organisms, the genitalia were washed with clean water. The dipstick test involved immersing the dipstick in urine for 60 seconds to detect the presence of nitrites and leukocyte esterase.

Statistical Analysis:

Data was entered into Microsoft Excel and analyzed using the statistical package for the social sciences (SPSS) software version 23.0 (SPSS Ltd, Chicago, IL, USA). Continuous data were reported as mean ± SD (if normally distributed) or as median (range) (if non-normally distributed). Results for categorical measurements were presented as numbers and percentages. Sensitivity, specificity, negative predictive value and positive predictive value for leukocyte esterase, pyuria, nitrites and combined nitrite and leukocyte esterase were analyzed by comparing the test results with the gold standard norms (culture-proven UTI cases and sterile culture cases).

Ethical consideration

Ethical approval was obtained from the ethical committee prior to study. Informed consent was taken from parents before enrolling their babies into the study. If any complications occur, it was managed according to the standard protocol of the hospital. Patients were allowed to withdraw from the study if they wished to do so any time.

RESULTS

A total of 155 cases were initially considered for the study, but only 134 were included after excluding 21 cases. Among the excluded cases, 12 parents did not provide consent, and nine children did not meet the inclusion criteria. Therefore, a total of 134 cases were enrolled in the study.

Of the 134 cases, 23 cases (17.16%) were in the age group of 1 month to 1 year, 29 cases (23.4%) were in the age group of 1.1 to 2 years, 36 cases (26.87%) were in the age group of 2.1 to 3 years, 31 cases (23.13%) were in the age group of 3.1 to 4 years and 15 cases (11.19%) were in the age group of 4.1 to 5 years. The study population was evenly distributed between genders. However, six males and seven females tested positive for culture, indicating that female participants had 1.18 times higher odds of urinary tract infection than male participants. The most common symptoms reported were fever (74.63%), followed by vomiting (54.48%) and abdominal pain (42.54%), with a statistically significant p-value of 0.038.

Among the total cases, only 13 were positive in urine culture, while 121 showed no growth, resulting in a prevalence rate of UTI of 9.7%. The leukocyte esterase test was negative in 105 cases (78.36%) and positive in 29 cases (21.64%). The sensitivity, specificity, positive predictive value and negative predictive value of leukocyte esterase compared to urine culture were 76.92%, 84.29%, 34.48%, and 97.14% respectively, with a statistically significant p-value of <0.001.

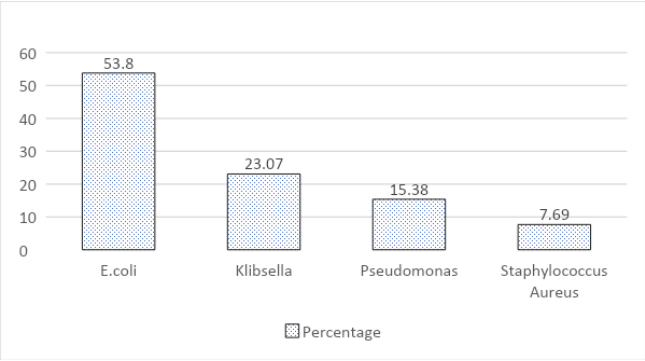
Additionally, the nitrite test was negative in 114 cases (85.07%) and positive in 20 cases (14.93%). The sensitivity, specificity, positive predictive value and negative predictive value of the nitrite test compared to urine culture were 84.61%, 92.56%, 55%, and 98.24%, respectively, with a statistically significant p-value of <0.001.

Table 1. Dipstick test and pyuria sensitivity, specificity, NPV and PPV

	Sensitivity	Specificity	PPV	NPV
Leucocyte and/or nitrate	92.30% (82.83-98.21)	82.64% (78.23-87.05)	36.36% (25.63-47.09)	99.01% (97.74-99.98)
Leucocyte and/or nitrate and/or pus cells	-	80.16% (75.52-84.81)	35.13% (25.07-45.19)	-

When considering the sensitivity, specificity, positive predictive value, and negative predictive value of the nitrite test and leukocyte esterase alone or in combination compared to urine culture, they were found to be 92.30%, 82.64%, 36.36% and 99.01% respectively. Similarly, the specificity and positive predictive value of the nitrite test, leukocyte esterase, and pus cells alone or in combination compared to urine culture were 80.16% and 35.13% respectively. The p-value calculated using the chi-square test was <0.001, indicating statistical significance. Among all the culture-positive cases, seven were positive for E.coli, three for Klebsiella, two for Pseudomonas aeruginosa and one for Staphylococcus aureus (Figure 1).

Figure 1. Culture Positive organism percentage



DISCUSSION

In our study, among the 134 patients analyzed, 9.7% tested positive for UTI, while 90.3% tested negative. Similar to other studies conducted by Sumit et al. in North India and Fernandes et al. regarding urinary tract infections in the pediatric population, our study also found a higher prevalence of UTI in females compared to males. [5,6] Baral et al. conducted a study in the Department of Microbiology at BPKIHS, where out of 202 suspected cases, 20.8% were culture positive with 72% being female and 28% male. [7]

The frequency of UTI in our study was higher in children under five years of age, which is consistent with studies conducted by Ojha et al., who enrolled 110 children and found that 29% of cases were culture positive, with 56% being female and 44% male. [8] Among the positive cases in females, the most common age group affected was 1-5 years. In males, the most common age group affected was over five years. Shrestha et al. enrolled 575 cases, of which 110 (19.1%) were culture positive.[9] Girls were more affected than boys (69.1% vs. 30.9%); the most common age group affected was 1-5 years. Amatya et al. conducted a study in Patan Hospital, Kathmandu, which found that the most common age group affected by UTI was 2-12 months, followed by less than two months of age, 1-5 years of age, and then over five years of age. [10]

In our study, the most common organism isolated among the culture-positive cases (13 out of 134) was E. coli, followed by Klebsiella, Pseudomonas, and Staphylococcus aureus. Similar findings have been reported in other studies.[5-10] Three different studies conducted by Sumit et al, Fernandes et al and Shrestha et al showed the most common organism causing UTI was E. Coli followed by klebsiella, Proteus and Pseudomonas. [10,31,36] Similarly Ojha et al in his study found that E. coli was the most common organism followed by Klebsiella than staphylococcus and Pseudomonas having equal prevalence. [34] Amatya et al and Baral et al also in their studies showed that E. coli was the most common organism which was followed by Klebsiella and the least prevalent being Enterobacter. [11,40]

Regarding the symptoms observed in UTI, fever was the most common symptom. In the study done by Sumit Gupta et al, most common symptom was fever followed by dysuria, burning micturition, abdominal pain, malodorous urine, poor feeding, vomiting respectively in this order.[5] In a study conducted by Ojha et al, the most common symptom was fever (62.5%) followed by burning micturition (34.4%), vomiting (19%), malodorous urine (19%), pain abdomen (15.6%), increased frequency (15.6%), straining (12.5%) and diarrhea (6%).[8] Amatya et al in his study also found fever was the most common presenting symptom.[10]

In our study, the leukocyte esterase test showed high sensitivity and specificity compared to other studies. The positive predictive value was lower but within the range of most studies, and the negative predictive value was high and consistent with other studies. This indicates that leukocyte esterase can be used as a reliable screening test for UTI.[11,12,13,14] Similarly, the nitrite test in our study showed slightly higher sensitivity than other studies. It also exhibited high specificity and negative predictive value for diagnosing UTI, with positive predictive value within the range of other studies. Based on these results, nitrite can be considered a reliable test for diagnosing UTI. [6-8,12,15,16]

Our study demonstrated very good sensitivity, moderate specificity, and negative predictive value in combined dipstick testing. The positive predictive values were slightly lower compared to other studies. The sensitivity and specificity observed in our study were comparable to other studies, which ranged from 70-90% and 80-95%, respectively.[6,8,11,12,17,18]

The use of dipstick tests can reduce testing time and costs. Applying these screening tests to exclude UTI can save resources and time. An effective screening test for UTI should have good sensitivity to avoid missing any cases and good specificity to prevent false positive results. The predictive values should be high to rule in or rule out UTI reliably. In our study, the leukocyte esterase test had a low positive predictive value (34.48%) but a high negative predictive value (97.14%), indicating its

reliability for excluding UTI. The nitrite test showed high sensitivity, specificity and negative predictive value, making it a good screening test for diagnosing UTI and initiating antibiotics in suspected cases while waiting for urine culture reports, especially in resource-limited settings.

This study limits the use of dipstick in babies less than 1 month of age. Also, sensitivity of the antibiotics for the organism has not been included in this study. Follow up study such as USG abdomen and pelvis, renal function test, MCG and DMSA has not been done in culture positive cases. This study is also limited to a single center, thus data from multiple centers could have given a better result.

CONCLUSIONS

E. coli is the most common organism causing UTI in children, followed by Klebsiella. The positive and negative predictive value of urine microscopic analysis is significantly less. Hence it cannot be reliably used in screening for UTI. Leukocyte esterase has good sensitivity and moderate specificity; hence it is a good screening test for UTI. The sensitivity and specificity of the nitrite test are good and lies within the norm of AAP; thus, it can be reliably used as a test to diagnose UTI. A combined dipstick test that is LE and Nitrite test has good sensitivity, specificity, and NPV compared to urine culture; thus, it can be reliably used for diagnosing UTI and starting antibiotics while waiting for urine culture. The most common organism causing UTI in children are gram-negative organisms; thus, prophylactic antibiotics can be started if there is a strong clinical suspicion after the urine samples are sent for investigation. Urine microscopy is not the best screening test for the confirmation of UTI. LE test has a high sensitivity; thus, it can be used as a good screening test for UTI, but urine samples must be sent for nitrite test and culture to confirm diagnosis. The Nitrite test has good specificity compared to urine microscopy and LE test. So, it can be used to diagnose UTI if other resources are unavailable. The combined LE and nitrite test has better sensitivity, specificity and NPV than either of the test alone. Thus, it can be used as a diagnostic tool for UTI. If the nitrite test is positive, it is highly suggestive of gram-negative organisms, as these organisms can only reduce nitrate to nitrite. Dipstick can be used as a good diagnostic tool for UTI where there is a lack of culture facility, rural health centers, or in conditions where the reports of culture and microscopy are delayed.

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CONFLICT OF INTEREST

None

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