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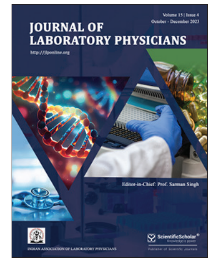

Original Article

Utility of urine dipstick in predicting urinary tract infection in pediatric outpatients

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ABSTRACT

Objectives: Children are most frequently affected by urinary tract infections (UTIs). Urine dipsticks along with use in urine routine testing can help in predicting UTI. In this study we aim to evaluate the utility of individual and combination of urine dipstick parameters, including nitrite and leukocyte esterase (LE), against gold standard urine culture for detection of UTI among pediatric outpatients.

Materials and Methods: Nine hundred and forty-nine pediatric urine samples from January 2021 to December 2021 were cultured on Cysteine Lactose Electrolyte Deficient Agar and incubated at 37°C overnight. Siemens Multistix 10SG strips were used to perform a urine dipstick for urine markers. Results from the urine dipstick and culture were contrasted.

Statistical Analysis: Data obtained in the study was analyzed statistically using stata version 15. Diagnostic performance of urine dipstick parameters was assessed taking urine culture as gold standard. Receiver operating characteristics (ROC) curve was plotted.

Results: About 153 of the 949 urine samples received for culture were positive. Males comprised 102 of the 153 positive patients. The most common organism isolated was *Escherichia coli*, followed by *Klebsiella*, *Pseudomonas*, and *Proteus*. LE, nitrite, red blood cells (RBC), and protein had a sensitivity of 77.1%, 64.7%, 45.1%, and 46.4%, respectively, whereas their specificities were 94.5%, 97.2%, 95.9%, and 93.1%, respectively. When taken together, "LE and Nitrite and RBC and Protein" had a lower area under the curve (AUC) of 0.641, whereas "LE/Nitrite/RBC/Protein" had the highest AUC of 0.914.

Conclusions: The urine dipstick test may be utilized as a screening tool and a positive predictor for UTI. When evaluated simultaneously, nitrite and LE can be used as point-of-care tests preceding the culture examination for decision-making. They can aid in the optimized management of children by minimizing UTI-related complications and inappropriate antibiotic use.

Keywords: Leukocyte esterase, Nitrite, Urine dipstick, Urine culture

INTRODUCTION

Urinary tract infection (UTI) is one of the most common infections, frequently presenting in a clinical setting. High-risk groups for UTI include pregnancy, immunocompromised patients, and children. Among the high-risk groups, children are most commonly affected. Approximately 6–8% of unwell children or febrile infants in general practice, as well as older children with urinary symptoms, are found to have a UTI.[1,2] The prevalence of UTI is higher in the first two years of life and incidence is lower in older children.[3] UTIs can manifest as symptomatic or asymptomatic, with infants and young children often lacking evident symptoms. The major symptoms of UTI in children are fever with chills, poor feeding, poor weight gain, recurrent vomiting, and abdominal pain.[4] Older children and adolescents have complaints of increased frequency, dysuria, urgency, and abdominal or flank pain. Females are more prone to UTI when compared to males because of their anatomical structure.[5,6] Several risk factors, including age, gender, previous antibiotic use, fever, constipation, frequency of urination, bladder dysfunction, and obstructive uropathy are associated with UTI.[5] In developing countries, UTI is associated with unhygienic conditions such as threadworm infection, immunocompromised state, and in children with complicated malnutrition.[7,8] If UTI is not diagnosed timely and is not treated properly then it can complicate to chronic scarring of the kidneys, hypertension, and renal failure thereby leading to high morbidity and mortality in children.[9]

Pyuria and bacteriuria are the key indicators of UTI. Pyuria is defined as the presence of 10 or more white cells per high power field (HPF) in centrifuged urine and >1 per 7 HPF in uncentrifuged urine.[10] Bacteriuria or UTI can be diagnosed through a semi-quantitative culture of urine, with significant bacteriuria defined as the presence of a bacterial colony count of $>10^5$/mL of a single species in a midstream clean-catch sample.[11] However, a culture-based method for the demonstration of bacteriuria is time-consuming and requires technical expertise.

To address these challenges, UTIs can be screened by methods including urine dipstick tests and urine microscopy. While urine microscopic examination requires specialized training in laboratories using clinical laboratory improvement amendments (CLIA)-certified methods, urine dipstick tests offer a cost-effective, rapid, and less labor-intensive alternative that does not require expertise. They can be used as point-of-care testing in peripheral healthcare settings.[12]

Over the years, antimicrobial resistance has been on the rise among adults, and this trend is seen to be significantly affecting pediatric age groups as well. Antimicrobial-resistant microbes are anticipated to kill 10 million people annually by the year 2050,[13] with India being one of the worst affected nations. One of the foremost causes of antimicrobial resistance is the excessive use of antimicrobials in humans and animals.[14]

The diagnosis of UTI may be challenging in infants and young children due to minimal and often non-specific urinary symptoms. In addition, the selection of an appropriate antimicrobial agent for empirical treatment remains a challenge in pediatric patients. Effective treatment for these patients necessitates accurate urine culture and antimicrobial sensitivity testing to prevent future complications.

Therefore, in our study we specifically focus on evaluating the practicality of using urine dipstick parameters, such as nitrite and leukocyte esterase (LE), to predict UTIs in pediatric outpatients.

Our primary objective is to determine whether analysis by urine dipstick, either individually or in combination, can reliably help us in guiding the decision to initiate empirical antibiotics before culture results are available. This approach also aims to reduce the unnecessary consumption of antibiotics in cases where they are not needed, thus potentially mitigating the risk of increased antimicrobial resistance. Ultimately, we aim to provide a more effective and efficient method for diagnosing and managing pediatric UTIs in clinical practice.

MATERIALS AND METHODS

This retrospective cross-sectional study was conducted in Clinical microbiology, Department of Laboratory Medicine of a tertiary healthcare hospital in New Delhi from January 2021 to December 2021.

Inclusion and exclusion criteria

Clean catch midstream urine collected in a wide-mouth sterile container from the pediatric outpatients (0–17 years) received for urine culture sensitivity was included in the study. Adults, pediatric inpatients, and catheterized/percutaneous nephrostomy tube patients were excluded from the study.

Laboratory testing

Well-mixed uncentrifuged urine samples were cultured on Cystine Lactose Electrolyte Deficient agar and were incubated overnight at 37°C. Urine culture showing bacteria growth $\geq 10^5$ Colony forming units (CFU)/mL was taken as "positive" for UTI infection ($\geq 10^5$ CFU/mL significant bacteriuria), whereas bacterial growth $<10^5$ CFU were considered insignificant and culture plates showing no growth were deemed negative.

Routine biochemical parameters in urine were done by dipstick test for the presence of nitrite, leukocyte esterase, protein, and red blood cells (RBC) using Siemens Multistep 10 SG strips. The procedure was performed according to the manufacturer's manual. The reagent strips were read at 30–60 seconds using the principle of reflectance photometry. Results of biochemical parameters such as pH, nitrite, LE, RBC, and proteins by the urine dipstick test were tabulated.

Statistical analysis

Data obtained in the study were analyzed statistically using Stata version 15. Continuous variables were presented as mean ± standard deviation or median (min–max) values according to the distribution of the data. Categorical variables were presented as numbers (n) and percentages (%). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of urine dipstick test were calculated considering urine culture as a gold standard. The dipstick parameters were taken individually as well as in combinations. The kappa coefficient was calculated to look at the agreement between the dipstick and urine culture. The receiver operating characteristics (ROC) curve was used to generate the area under the curve (AUC) value to estimate the diagnostic performance of the dipstick test parameters.

RESULTS

A total of 13,343 urine samples were received during the study period, out of which 949 were pediatric urine samples. About 16% (*n* = 153) of these 949 were urine culture positive and showed significant bacteriuria. They had a mean age of 8.24 ± 5.12 years, males were 67% (*n* = 102) and females were 33% (*n* = 51).

The most frequent organisms isolated were *Escherichia coli* (56.86%, 87/153), *Klebsiella* spp. (18.30%, 28/153) followed by *Pseudomonas* spp. (9.80%, 15/153), *Proteus spp.* (5.88%, 9/153), and least isolated were *Staphylococcus* (3.92%, 6/153) and others, which include *Enterococcus, Acinetobacter,* and *Morganella* (3.27%, 5/153; 1.3%, 2/153; and 0.65%, 1/153), respectively. Gram-negative bacteria were more commonly isolated than Gram-positive bacteria.

The results of sensitivity, specificity, PPV, NPV, and kappa coefficient of individual and combination dipstick parameters against gold standard urine culture are given in Tables 1 and 2. Table 3 shows the urine dipstick results for the most commonly identified organisms.

The sensitivity of LE, nitrite, RBC, and protein was 77.1%, 64.7%, 45.1%, and 46.4%, respectively, with a specificity of 94.5%, 97.2%, 95.9%, and 93.1%.

When any of LE or nitrite was considered, the sensitivity was 84.3% (77.6–89.7) and specificity was 94.5% (91.6–96.6). When both LE and nitrite were considered together, the sensitivity decreased to 57.5%, but specificity increased to 97.5%, and the PPV increased from 86.6% to 89.8%.

When LE, nitrite, and RBC all three were positive, sensitivity decreased to 32%. However, specificity increased to 98.1%. Adding proteins to LE and nitrite with or without RBC could not further increase specificity.

When the four parameters "LE/nitrite/RBC/proteins" were considered, NPV was 96% (93.3–97.8%), AUC was a maximum of 0.914 and the kappa agreement coefficient was also the highest, 0.806. When all four parameters "LE AND nitrite AND RBC AND proteins" were positive the specificity was highest at 98.6% (96.8–99.6%) with a PPV of 90% (78.2–96.7%), however, the kappa coefficient was low at 0.350.

On ROC analysis is shown in Figure 1, AUC for "LE AND nitrite" taken together was 0.77; with "LE or nitrite" was 0.89, the highest ROC was for "LE/nitrite/RBC/proteins" 0.91, and lower AUC was for "LE AND nitrite AND RBC AND proteins" that is 0.64.

Table 1: Diagnostic performance of individual urine dipstick parameters LE, Nitrite, RBC, and Proteins in comparison to urine culture.

	LE	Nitrite	RBC	Protein
Sensitivity (%)	77.1 (69.5–83.5)	64.7 (56.6–72.3)	45.1 (37.1–53.3)	46.4 (38.34–54.6)
Specificity (%)	94.5 (91.6–96.6)	97.2 (95–98.7)	95.9 (93.3–97.7)	93.1 (90–95.5)
Positive predictive value (%)	85.5 (78.5–90.9)	90.8 (83.8–95.5)	82.1 (72.3–89.6)	74 (64–82.4)
Negative predictive value (%)	90.7 (87.3–93.4)	86.7 (83–89.8)	80.5 (76.5–84.1)	80.4 (76.3–84.1)
Area under curve	0.857	0.808	0.703	0.697
Kappa coefficient	0.737	0.676	0.471	0.443

Results are depicted as 95% confidence interval. LE: Leukocyte esterase, RBC: Red blood cells

Table 2: Diagnostic performance of the combination of urine dipstick parameters LE, Nit, RBC, and Prot in comparison to urine culture.

	LE/nitrite	LE and Nit	LE/Nit/RBC	LE and Nit and RBC	LE/Nit/Prot	LE and Nit and Prot	LE/Nit/Prot/RBC	LE and Nit and Prot and RBC
Sensitivity (%)	84.3 (77.6–89.7)	57.5 (49.3–65.5)	87.6 (81.3–92.4)	32 (24.7–40)	90.2 (84.3–94.4)	32.7 (25.3–40.7)	90.8 (85.1–94.9)	29.6 (22.5–37.5)
Specificity (%)	94.5 (91.6–96.6)	97.2 (95–98.7)	92.8 (89.7–95.3)	98.1 (96–99.2)	91.7 (88.4–94.3)	97.2 (95–98.7)	92 (88.7–94.6)	98.6 (96.8–99.6)
Positive predictive value (%)	86.6 (80–91.6)	89.8 (82–95)	83.8 (77.1–89.1)	87.5 (75.9–94.8)	82.1 (75.5–87.6)	83.3 (71.5–91.7)	82.7 (76.2–88.1)	90 (78.2–96.7)
Negative predictive value (%)	93.4 (90.4–95.8)	84.4 (80.6–87.8)	94.6 (91.8–96.7)	77.3 (73.2–81.1)	95.7 (93–97.6)	77.4 (73.2–81.1)	96 (93.3–97.8)	76.9 (72.8–80.7)
Area under curve	0.893	0.772	0.903	0.648	0.910	0.647	0.914	0.641
Kappa coefficient	0.793	0.606	0.794	0.368	0.797	0.363	0.806	0.350

Results are depicted as 95% confidence interval. LE: Leukocyte esterase, RBC: Red blood cells, Nit: Nitrite, Prot: Proteins

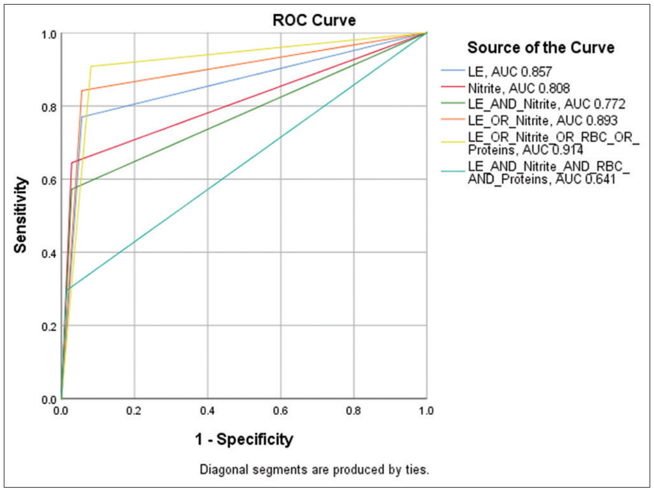

Figure 1: Receiver operating characteristics (ROC) curve and area under curve (AUC) for urine dipstick parameters against urine culture; LE: Leukocyte esterase, RBC: Red blood cells.

DISCUSSION

We tried to evaluate the utility of dipsticks in predicting UTI in pediatric outpatients.

The gold standard to diagnose UTI is urine culture; however, it is time-consuming and might take more than 48 h to report results. Antibiotic treatment should be started within 48 h of fever onset because delayed treatment increases the risk of renal scarring and other complications.[15] To avoid complications leading to increased morbidity in patients, the urine samples can be screened by use of urine dipsticks or microscopic examination of urine. However, we need to balance early detection with growing concern of false positives, which can contribute to indiscriminate use and thus proliferation of antibiotic-resistant pathogens.

Microscopic examination of urine, not included in our study, though somewhat accurate, involves monotonous, time-consuming screening and is reliant on expert person interpretation. Conversely, the urine dipstick test offers a user-friendly, point-of-care alternative that does not require any expertise. Our study aimed to assess the diagnostic efficacy of urine dipstick parameters such as nitrite, LE, RBC, and protein compared against the gold standard of urine culture.

Urine dipstick can test for various parameters such as specific gravity, pH, urobilinogen, ketones, glucose, proteins, blood, bilirubin, LE, nitrite, microalbumin, and creatinine. Strips with all or a few of these parameters may be available. The dipsticks are simple and cost-effective and are analyzed by comparison of color development against the standard strip provided by the manufacturer. Semi-automated analyzers have the capability of reading the strips through reflectance photometry, making them accessible to health-care providers with minimal level of expertise. Care has to be taken so that results are read at the appropriate time without delay to get adequate results.

In our study, out of all the samples received from pediatric patients, 16% (n = 153) were culture-positive, 92.8% were gram-negative, and 7.2% were gram-positive organisms. The most important analytes that point toward UTI are LE and nitrite. LE detects the white blood cells (WBC) produced in response to UTI. It is an enzyme found in neutrophil granules that hydrolyzes amino acid ester to liberate a pyrrole compound that, in turn, reacts with diazonium salt present on the dipstick to produce a purple color in 1–2 min. The LE dipstick test can detect both intact and lysed WBC and is indicative of various conditions, including bacterial UTI, fungal infections, urethritis, or pyelonephritis. However, false positive LE results can occur in the absence of UTI in conditions such as contamination with vaginal discharge, eosinophils, trichomonas, and contamination with oxidizing agents such as bleach.[16] False-negative results can be attributed to glycosuria, a few drugs such as cephalothin or tetracycline, urobilinogen, and high specific gravity. Since there is low sensitivity and interferences producing negative results, a negative result does not exclude infection and needs to undergo further workup if the patient is symptomatic. In our study LE when used alone had a sensitivity of 77.1% (69.5–83.5%) and specificity of 94.5% (91.6–96.6%), results consistent with previous studies.[17-19]

Nitrite positivity is associated with infections caused by these nitrate-reducing bacteria, particularly, *Enterobacteriaceae*, which are the predominant cause of UTIs. Nitrite reacts with p-arsanilic acid in the dipstick, generating a diazonium compound that couples with quinoline reagent on the dipstick to produce a pink color in 60 s. A study done by Papava *et al.*[20] in uncomplicated UTI patients showed that the presence of nitrites is highly specific for bacteriuria (94–100%) with a low sensitivity of 25%. Other studies[21,22] have also given a higher specificity but a relatively lower sensitivity of the nitrite test for bacteriuria similar to our study that showed nitrites had a specificity of 97.2% (95–98.7%) and sensitivity of 64.7% (56.6–72.3%) for detection of UTI. Other studies showed a somewhat lower sensitivity of <40%.[23-25]

In a recent study on febrile infants, the most specific individual dipstick test for UTI was the presence of nitrites. A specificity of 0.91% (95% confidence interval [CI] = 0.86–0.94) and a sensitivity of 0.42% (95% CI = 0.26–0.59) was obtained with nitrites.[26] On the other hand, the most sensitive dipstick test for UTI was LE having a sensitivity of 0.87% (95% CI = 0.69–0.94) and a specificity of 0.73% (95% CI = 0.67–0.79).[26]

The variability in diagnostic performance across different studies may be attributed to variations in pediatric age groups considered.[27,28] A meta-analysis revealed that urine dipstick testing performed less effectively in younger children compared to older children. Infants, in particular, exhibited lower reliability, with a positive likelihood ratio

(LR) of 7.62 (95% CI = 0.95–51.85) for nitrite and LE, and a negative LR of 0.34 (95% CI = 0.66–0.15), which was less favorable than in older age groups.[29]

Sample collection and sample processing also play pivotal roles, especially in the pediatric population where the sample collection can be challenging, leading to false negative results if proper collection procedures are not followed. Nitrite concentration can increase with the duration of urine retention in the bladder before collection. Therefore, the first early morning samples have a higher chance of giving positive results. Conversely, false-negative results may be obtained due to factors such as short bladder incubation time, lack of dietary nitrate, dilution of the nitrite in the urine (such as with diuretics),[30-32] or infection with non-nitrate-reducing bacteria, including *Staphylococcus*, *Enterococcus*, or *Pseudomonas*. LE and nitrite, when both positive or both negative, help to rule in or rule out UTI, but if one of them is positive, and other negative, creates confusion or diagnostic uncertainty.

In some studies[33] like ours, combining LE and nitrite improved the diagnostic accuracy. Our study showed that this combination increased the specificity to 97.2% (95–98.7%) with a sensitivity of 57.5% (49.3–65.5%). It also resulted in a higher PPV of 89.8% (82–95%), making it effective in identifying true positive cases fit for empirical treatment.

The sensitivity of "LE OR nitrite" 84.3% was higher than that of "LE and nitrite" 57.5%, showing better performance in cases where both the tests were considered to identify the true culture-positive cases and thereby recognizing candidates for empirical treatment. These findings align with that of the previous study by Dadzie *et al*.[23] They showed that a combination of nitrite OR LE positivity achieved the highest sensitivity of 72.3% (95% CI = 59.8–89.7) and NPV value of 93.6% (95% CI = 90.1–96.2). In contrast, the combination of both nitrite and LE while giving a high specificity of 99.7% (95% CI = 98.5–100), demonstrated a low sensitivity of 16.9% (95% CI = 8.8–28.3) but a PPV of 91.7% (95% CI = 61.5–99.8).[23]

Although a few studies such as Başer *et al*. have recommended the start of antimicrobial therapy based on both nitrite and LE positivity,[34] this finding can be doubted given the non-consideration of clinical details. Moreover, in settings where there is a low prevalence of UTI, the sensitivity of these tests can be even lower. Therefore, emphasizing patient symptoms and clinical context alongside positive screening results is advisable.[35] If both parameters are positive and the patient is symptomatic, especially in populations with relatively high prevalence, the likelihood of UTI is increased. On the other hand, if both parameters are negative, the probability of UTI decreases. Out of the two, nitrites or LE, nitrite is a direct and more useful indicator of UTI.

The presence of blood or protein in urine identified by dipstick examination is a poor indicator of UTI. While dipsticks can detect the presence of RBC (erythrocytes) in urine, often associated with UTIs, these cells can also be present in various other conditions, including glomerular diseases, non-glomerular issues such as calculi, tumors, tuberculosis, post-trauma, strenuous exercise, prostate diseases, hydronephrosis, or pyelonephritis. In addition, dipsticks cannot distinguish between myoglobin and hemoglobin, necessitating the revaluation of hematuria by microscopy. Similarly, the presence of proteins in urine may be due to numerous causes, including glomerular diseases, tubular, overflow proteinuria, hemodynamic proteinuria due to high fever, hypertension, heavy exercise, congestive cardiac failure, seizures, or post-renal proteinuria. Considered alone, they are not useful to predict UTI. In isolation, the use of individual dipstick parameters is insufficient for predicting UTIs, even in the samples with high pre-test probability. When considered together, the "LE AND nitrites AND protein;" "LE AND nitrites AND RBC;" and "LE AND nitrites AND protein AND RBC" had sensitivity and specificity of 32.7% and 97.2%; 32% and 98.1%; and 29.6% and 98.6%, respectively.) Although blood and proteins may be associated with other pathology, in the presence of symptoms or positive nitrite and LE testing, its presence may increase the probability of UTI.

Other studies have also tried to evaluate the combination of dipstick parameters for the prediction of UTI. Few have evaluated the findings of urine cultures in comparison with dipstick and the wet mount of uncentrifuged urine

Table 3: Urine dipstick test results for most commonly isolated organisms.

Organism	Nitrite positive *n* (%)	Leukocyte esterase positive *n* (%)	Total *n* (% of 153)
Escherichia coli	67 (67)	74 (63.2)	87 (56.8)
Klebsiella pneumoniae	17 (17)	16 (13.6)	28 (18.3)
Pseudomonas spp.	8 (8)	9 (7.69)	15 (9.8)
Proteus spp.	5 (5)	7 (5.98)	9 (5.88)
Staphylococcus spp.	1 (1)	5 (4.27)	6 (3.92)
Enterococcus spp.	1 (1)	3 (2.56)	5 (3.26)
Acinetobacter spp.	1 (1)	2 (1.70)	2 (1.30)
Morganella spp.	0 (0)	1 (0.85)	1 (0.65)

Results are depicted as number (percentage): *n* (%)

to diagnose UTI. In a particular research, when the results of microscopy and dipstick LE and nitrites (when either of them was positive) were combined, a very high sensitivity of 95.9%, NPV of 97.9%, and diagnostic odds ratio of 25.7 were obtained. This approach which incorporates urine wet mount microscopy and dipstick tests into the routine laboratory practices, could potentially reduce costs by 79% and thus aid in faster and cheaper diagnosis of UTI.[21]

In a study involving 262 children aged 0–16 years, the presence of any of the three dipstick parameters LE, nitrite, or RBC exhibited a high sensitivity of 0.97% (95% CI = 0.95–0.99). Furthermore, the sensitivity of pyuria (≥100 cells/mm^3) was 0.92% (95% CI = 0.89–0.95).[22]

In a study on women presenting to the emergency department, overtreatment and undertreatment rates were identified based on urine dipstick tests and urinalysis.[36] Out of 331 patients, 46% (152/331) patients had positive urine culture results. When considering urine dipstick positive for LE or nitrite or blood with results more than a trace, an overtreatment rate of 47% (156/331) and an undertreatment rate of 13% (43/331) were identified. A combined analysis of nitrite and LE exhibited greater sensitivity than LE alone (85% and 79%, respectively) despite having a similar specificity (84%). The 96% NPV for combined positive nitrite or LE tests suggested that urine culture requests can be ruled out in 96% of cases with both parameters testing negative,[25] potentially saving both time and cost for the patients.

Overall, our study revealed that nitrite and LE were the most reliable indicators of UTI, with significant specificity and sensitivity. Combining these two parameters improved diagnostic accuracy. The sensitivity of "nitrite OR LE" (84.3%) was higher than that of "LE and nitrite" (57.5%), making it particularly effective in identifying true culture-positive cases for empirical treatment. The presence of blood or protein in urine, while detectable by dipstick examination, proved to be poor indicators of UTI, as they can be associated with various other conditions. Our study's strengths lie in its focus on pediatric outpatients, where early diagnosis and treatment are crucial to prevent complications. However, our limitation was that while we analyzed the diagnostic performance of dipstick parameters, clinical context, and patient symptoms were not considered, which could influence treatment decisions. Despite this, our study underscores the potential of dipstick parameters, particularly nitrite and LE when used in combination, as valuable tools in the initial screening and management of pediatric UTIs, contributing to improved patient care and prudent antibiotic use. Further research in diverse settings is warranted to validate and extend our findings.

CONCLUSIONS

Utilization of urine dipstick tests as a screening tool and a positive predictive indicator for UTI can significantly enhance the management of pediatric outpatients. When evaluated concurrently, nitrite and LE are reliable indicators of positive urine cultures with a PPV of 89.8% and specificity of 97.2%. These dipstick parameters can be effectively employed as point-of-care tests preceding the culture examinations helping to minimize UTI complications and inappropriate antibiotic use, thus optimizing the healthcare provided to children.

Ethical approval

The research/study complied with the Helsinki Declaration of 1964.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Nil.

Conflicts of interest

Dr. Suneeta Meena is on the Editorial Board of the Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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