J Ped Nephrol
Journal of Pediatric Nephrology
2024. Volume 12

Original Article

Reliability of Point-of-care Urine Dipstick Nitrite and Leukocyte Esterase Test in Detecting Pediatric Urinary Tract Infections

Sandeep Garg[1*], Anurag Yenkar[2], Shivanjali Gore[3], Anuradha Joshi[1], Samrat Mehta[1]

1. Department of Pediatrics, Bhaktivedanta Hospital and Research Institute, Thane, India.
2. Department of Pediatrics, Safe Hands Childrens Hospital, Pune, India.
3. Department of Medical Research, Bhaktivedanta Hospital and Research Institute, Thane, India.

Use your device to scan and read the article online

Citation Garg S, Yenkar A, Gore Sh, Joshi A, Mehta S. Reliability of Point-of-care Urine Dipstick Nitrite and Leukocyte Esterase Test in Detecting Pediatric Urinary Tract Infections. Journal of Pediatric Nephrology. 2024; 12:E46018. http://dx.doi.org/10.22037/jpn.v12i1.46018

http://dx.doi.org/10.22037/jpn.v12i1.46018

Article info:
Received: 17 Jan 2024
Accepted: 19 Mar 2024
Publish: 28 Apr 2024

Corresponding Author:
Dr. Sandeep Garg, MD.
Address: Department of Pediatrics, Bhaktivedanta Hospital and Research Institute, Thane, Indi.
E-mail: drsandeep2109@gmail.com

ABSTRACT

Background and Aim: Diagnosing urinary tract infection (UTI) in children is difficult due to its non-specific clinical manifestations, difficulty obtaining a clean urine sample, and risk of renal scarring complications in the future. Urine culture is the gold standard for diagnosing UTI, but it requires 48-72 hours to report, causing delays in treatment. This study aims to evaluate the effectiveness of urine dipstick nitrite and leukocyte esterase tests in detecting UTIs in children.

Methods: This cross-sectional, observational study was conducted on 79 children clinically suspected of UTI. The test results, urine dipstick test (nitrite and leukocyte esterase tests), pyuria in urine microscopy, and urine culture were checked for their sensitivity, specificity, positive predictive value, and negative predictive value.

Results: Among 79 children, fever was the most common clinical manifestation, and Escherichia coli was the most common uropathogen. Compared to urine culture, the sensitivity and specificity of leukocyte esterase and nitrite tests were 83.87%, 45.83%, 9.68%, and 91.67%, respectively. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the combined test were 9.68%, 93.75%, 50.00%, and 61.64%, respectively. Similar sensitivities and specificities were calculated, considering pyuria in urine microscopy as the gold standard in rural areas.

Conclusion: The leukocyte esterase test is reliable for diagnosing UTIs in children, showing good sensitivity. Higher leukocyte esterase grades indicate a higher likelihood of infection. Due to its feasibility and effectiveness, this test can replace urine microscopy for pyuria in rural areas. Nitrite tests, or their combinations, have poor sensitivity but high specificity, making them suitable for proving urinary infections in children.

Keywords: Urinary tract infection, Child, Pyuria, Leukocyte esterase

J Ped Nephrol
Journal of Pediatric Nephrology

Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections affecting children and pose significant morbidity and potential long-term complications if not diagnosed and managed promptly.

The prevalence of UTIs in febrile infants and children older than 1 year of age was 7% and 8%, respectively. It affects approximately 7%-8% of girls and 2% of boys during the first 8 years of life [1, 2]. Classic symptoms, such as frequency, dysuria, urgency, incontinence, vomiting, lethargy, and signs including fever, suprapubic tenderness, and flank tenderness, are often present in older children [3]. These features are often absent in infants, making diagnosis challenging due to their inability to express their symptoms verbally. Hence, current guidelines suggest urine sample collection in young children presenting with unexplained fever for more than 24 h or in older children presenting with the above symptoms [4]. This makes the clinical diagnosis of UTI a contentious topic among pediatricians.

In children, it can be difficult, if not impossible, to identify UTI based solely on signs and symptoms, which can cause delays in diagnosis and treatment. A missed diagnosis of UTI can lead to serious complications, such as urosepsis or renal scarring, with low yet potentially harmful long-term consequences, such as renal hypertension or reduced kidney function [5]. Congenital anomalies, such as vesicoureteral reflux or bowel bladder dysfunction observed in children, increase the risk of recurrent UTIs [6]. A meta-analysis showed that the risk of renal scarring increases substantially after a second episode of febrile UTI in children [7]. Hence, proper diagnosis and prompt UTI treatment are paramount in the pediatric population.

The gold standard for diagnosis is urine culture; however, various rapid diagnostic tests and imaging techniques can assist in the swift identification of UTIs [3]. However, a urine culture will take at least 48-72 h, causing a delay in starting antibiotics. This highlights the need to identify rapid, feasible, and reliable alternatives for diagnosing UTIs in children. The existing dipstick tests for nitrite, leukocyte esterase, and pyuria urine microscopy are prime contenders for early interpretation of UTIs.

This cross-sectional study aims to assess the diagnostic accuracy of dipstick tests (nitrite and leukocyte esterase tests) for pediatric UTIs. By understanding the strengths and limitations of different diagnostic approaches, healthcare providers can enhance their diagnostic strategies, ultimately improving patient outcomes and reducing the burden of this common infection.

Materials and Methods

This cross-sectional, observational, single-center study was conducted in the outpatient and inpatient departments of pediatrics at a tertiary care center over 7 months from September 2019 to March 2021 after obtaining approval from the Institutional Ethics Committee. Children up to 15, including both sexes, were enrolled. A total of 79 clinically suspected UTI cases were enrolled in this study. Informed written consent was obtained. The demographic data and relevant history of the children were recorded. Clean-catch midstream urine samples were collected in a sterile container in a hospital setting, with aseptic precautions. A sterile urinary catheterized sample was collected from infants.

Children who were admitted for a different primary diagnosis other than UTI, children who had received any antibiotics within 48 h before urine sampling, children with any local inflammation of the urinary area and those whose parents or guardians were not willing to enroll their child in the study were excluded.

Three tests were performed: The urine dipstick test (nitrite and leukocyte esterase test), urine microscopy (for pyuria), and urine culture. For the urine dipstick test, Orinasys B10 reagent strips were used, which were dipped into the urine sample, removed immediately, and interpreted after the recommended waiting time (60 s for the nitrite test and 120 s for the leukocyte esterase test). Some of the gram-negative bacteria species that most commonly cause UTI (Escherichia coli, Enterobacter, Klebsiella, Citrobacter and Proteus) have enzymes that reduce the nitrate present in urine to nitrite, and the urine reactive strips detect nitrite by using the Greiss reaction to produce a pink azo dye. The urine strip test for white blood cells detects leukocyte esterase, which is present in azurophilic granules of neutrophils to produce a violet-colored azole dye and is reported as the number of leukocytes per microliter of urine.

The numerical data were summarized using descriptive statistics, such as n, Mean±SD, median, minimum and maximum. Frequency count and percentage summarized categorical data, and significance was analyzed using the chi-square and ANOVA tests. The sensitivity, specificity, positive predictive value and negative predictive value were calculated. All statistical data were analyzed using IBM SPSS software Version 23. $P<0.05$ was considered statistically significant.

Results

Demography: The study included 79 children with clinical suspicion of UTI, with their age, sex and symptoms distribution (Table 1).

Dipstick test parameters: A positive leukocyte esterase test was observed in 65.82% (n=52) of the patients, and a positive nitrite test was observed in 8.86% (n=7) of the patients, 7.6% (n=6) of patients had positive results in both the above tests.

Urine microscopy (for pyuria): 93.67% (n=74) of patients had positive urine microscopy for pyuria (they had significant pus cells: >10 white blood cells (WBCs)/mm^3 in urine microscopy).

Urine culture: 39.24% (n=31) of patients had positive urine cultures.

Comparison of urine dipstick test with urine culture: When compared with urine culture as the gold standard test for diagnosing UTI, the leukocyte esterase test has a significant correlation (P=0.01). It resulted in a sensitivity of 83.87%, specificity of 45.83%, positive predictive value (PPV) of 50.00%, and negative predictive value (NPV) of 81.48%. The nitrite test resulted in a sensitivity of 9.68%, a specificity of 91.67%, a positive predictive value of 42.86% and a negative predictive value of 61.11%. The sensitivity, specificity, PPV, and NPV of both leukocyte esterase and nitrite combined test were 9.68%, 93.75%, 50.00% and 61.64%, respectively, in diagnosing UTI (Table 2).

Compared with pyuria by urine microscopy (pus cells: >10 WBCs/mm^3 in urine microscopy), the leukocyte esterase test resulted in a sensitivity of 68.92%, a specificity of 80%, a positive predictive value of 98.08% and a negative predictive value of 14.81%. The nitrite test resulted in a sensitivity of 9.46%, a specificity of 100%, a PPV of 100%, and a NPV of 6.94% in diagnosing UTI. The sensitivity, specificity, positive predictive value and negative predictive value of both leukocyte esterase and nitrite combined test was 25%, 100%, 100%, and 16%, respectively (Table 3).

Leukocyte esterase results were further graded from 1 to 3. A total of 34.18% (n=27) of cases had negative results, 24.05% (n=19) had grade 1+, 21.52% (n=17) had grade 2+ and 20.25% (n=16) had grade 3+ leukocyte esterase positivity. Increasing leukocyte esterase grading positively correlated with the mean number of pus cells (observed on microscopy); the correlation was significant (P=0.009). Also, the correlation between leukocyte esterase activity grading and urine culture positivity was significant (P=0.001) (Table 4).

Discussion

In the present study, female predominance was observed among the clinically suspected cases of UTI. There is always female preponderance for acquiring UTI, as observed in existing literature [2]. Fever was the most common symptom in this study, as suggested in the current guidelines [4]. Boon et al. also suggested that signs and symptoms may help diagnose UTIs when paired with clinical prediction rules, such as diagnosis of tract infection in young children (DUTY) or the UTI-

Table 1. Demographic details and clinical presentation of the patients (n=79)

Variables	Classification	No. (%)
Age group	<1 month	7(8.86)
	1 month to 2 years	22(27.85)
	2 years to 5 years	21(26.58)
	>5 years	29(36.71)
Gender	Male	32(40.51)
	Female	47(59.49)
Symptoms	Fever	72(91.14)
	Dysuria	25(31.65)
	Pain in abdomen	6(7.59)

J Ped Nephrol
Journal of Pediatric Nephrology

Table 2. Comparison of leukocyte esterase, nitrite, and combined tests considering urine culture as a gold standard test for diagnosing UTI

Test	Test Result	Urine Culture, No. (%)			%			
		Positive	Negative	Total	Sensitivity	Specificity	PPV	NPV
Leukocyte esterase test	Positive	26(50)	26(50)	52(65.82)	83.87	45.83	50.00	81.48
	Negative	5(18.51)	22(81.48)	27(34.17)				
	Total	31(39.24)	48(60.75)	79(100)				
Nitrite test	Positive	3(42.85)	4(57.14)	7(8.86)	09.68	91.67	42.86	61.11
	Negative	28(38.88)	44(61.11)	72(91.13)				
	Total	31(39.24)	48(60.75)	79(100)				
Combined nitrite and leukocyte esterase test	Positive	3(50)	3(50)	6(7.59)	09.68	93.75	50.00	61.64
	Negative	28(38.35)	45(61.64)	73(92.40)				
	Total	31(39.24)	48(60.75)	79(100)				

Abbreviations: UTI: Urinary tract infection; PPV: Positive predictive value; NPV: Negative predictive value.

calc score; however, external validation is required [8]. Of the 31 culture-positive cases in this study, 90.33% had grown Escherichia coli, suggesting that E. coli is the most common uropathogen responsible for UTI in children, as observed in a previous study [3].

The sensitivity of the leukocyte esterase test compared to urine culture in our study was 83.87% (Table 2). Similarly, compared to various studies conducted in India, 61%, 73.5%, 92%, and 95% sensitivity for the leukocyte esterase test was observed by Mod et al. [9], Taneja et al. [10], Gupta et al. [11], Suresh et al. [12]. Goldsmith and Campos [13] reported a sensitivity of 76%, while Williams et al. reported a sensitivity of 86% [14]. The specificity of the leukocyte esterase test in our study was 45.83%, similar to the findings of Mod et al. [9] and Taneja et al. [10]. In contrast, 75.76%, 87%, and 94.3% of specificity were reported by Fernandes et al. [15], Gupta et al. [11], Suresh et al. [12]. The positive predictive value (PPV) for the leukocyte esterase test in our

Table 3. Comparison of leukocyte esterase and nitrite tests considering urine microscopy (for pyuria) as standard

Test	Test Result	Urine Microscopy			%			
		Positive	Negative	Total	Sensitivity	Specificity	PPV	NPV
Leukocyte esterase test	Positive	51	1	52	68.92	80.00	98.08	14.81
	Negative	23	4	27				
	Total	74	5	79				
Nitrite test	Positive	7	0	7	09.46	100.00	100.00	06.94
	Negative	67	5	72				
	Total	74	5	79				
Combined leukocyte esterase and nitrite test	Positive	7	0	7	25.00	100.00	100.00	16.00
	Negative	21	4	25				
	Total	28	4	32				

PPV: Positive predictive value; NPV: Negative predictive value.

Table 4. Comparing leukocyte esterase activity with urine microscopy (for pyuria) and urine culture results

Leukocyte esterase activity	No. (%)	Mean±SD	P	Urine Culture, No. (%)		P
		Urine Microscopy (for Pyuria) Pus Cell Number/hpf		Positive	Negative	
Negative	27(34.18)	13.89±9.32	0.009 (ANOVA test)	5(18.5)	22(81.5)	0.001 (chi-square test)
+1	19(24.05)	21.79±10.9		5(31.6)	13(68.4)	
2+	17(21.52)	28.18±22.1		7(41.2)	10(58.8)	
3+	16(20.52)	32.25±28.5		13(81.2)	3(18.8)	
Total	79(100)	22.58±19.1		31(39.2)	48(60.8)	

ANOVA: Analysis of variance; HPF: High power field.

study was 50%, similar to Mod et al. [9] and Fernandes et al. [15] and NPV for the leukocyte esterase test in our study was 81.48% as compared to 88.8% by Taneja et al. [10]. We can interpret with the given data that the leukocyte esterase test has good sensitivity (83.87%) and NPV (81.48%) to correctly identify UTI cases as proven by urine culture with low false negative cases, but specificity (45.83%) and PPV (50%) were poor, suggestive of high false positivity (nearly 50% cases as false positive). These data prove that the leukocyte esterase test is a reliable screening test to detect UTI in children (Table 2).

Similarly, the sensitivity of the nitrite test, considering urine culture as the gold standard, was 9.68%. In contrast to our findings, Mod et al. [9], Taneja et al. [10], Gupta et al. [11], Suresh et al. [12] reported sensitivities of 50%, 57.1%, 48%, and 81.9%, respectively. The specificity of the nitrite test in this study was 91.67%. Gupta et al. [11], Suresh et al. [12], and Fernandes et al. [15] reported specificities of 97%, 98.9% and 93.94%, respectively. The PPV for the nitrite test in our study was 42.86% (42.7%) according to Taneja et al. [10], and the NPV for the nitrite test in our study was 61.11% compared to 86.8% according to Taneja et al. [10]. The nitrite test has poor sensitivity (9.68%) and PPV (42.86%), which suggest very high false negativity in detecting UTI; hence, it is a poor screening test for UTI. However, high specificity (91.67%) and NPV (61.11%) suggest that patients with positive results are highly likely to have UTIs (Table 2).

Upon reviewing the literature, substantial differences were found in nitrite test sensitivities in symptomatic UTIs, according to Powell et al. [16]. This variability was attributed to the different incubation times for E. coli in their study, in which they found that the longer the incubation time, the greater the possibility of the nitrite test becoming positive. A similar explanation was given for asymptomatic patients who had anatomical uropathies and tested positive for the urine nitrite test, as it was attributed to increased bladder holding time. Children aged up to 15 years were included in this study. Children tend to void urine frequently and have smaller bladder capacities; therefore, it is difficult to hold urine for a long time.

Moreover, bladder control occurs beyond 2 years of age, increasing bladder holding time. These factors can be attributed to the lower sensitivity of this study and the variable sensitivities observed in other studies. Different causes of UTI can also explain the variability in the sensitivity of nitrite tests in literature. Anatomical causes of UTI tend to have more bladder holding time due to urinary stasis; hence, nitrite test sensitivity is higher. Factors, such as varying the testing kits can also affect the results. Furthermore, as the etiology of UTI studied in different studies would be variable, the microorganisms responsible could be different, affecting nitrite test positivity.

The combined nitrite test and leukocyte esterase test positivity were particular in our study (93.75%) but poorly sensitive (9.68%). Fernandes et al. [15] found that combined nitrite and leukocyte esterase had a specificity as high as 96.97%. Similar results were reported by Gupta et al. [11], where the combined specificity of nitrite and leukocyte esterase tests was 99.5%. The combined test (nitrite test + leukocyte esterase test) has similar accuracy to the nitrite test; hence, it can also be considered a poor test to screen UTI in children, as was the nitrite test.

A urine culture facility is privileged in resource-limited setups, particularly in rural India. In such conditions, clinicians mostly resort to urine microscopy to detect the presence of a significant number of pus cells (pyuria:

pus cells >10 WBCs/mm^3 in urine microscopy) and accordingly determine infectivity. Therefore, a comparison was made between the nitrite test, leukocyte esterase test, and urine microscopy for pyuria, considering urine microscopy (for pyuria) as a routine standard in rural setups. Leukocyte esterase was fairly sensitive, with a PPV of 98.08%, using the standard of urine microscopy (pyuria). Most studies have compared urine microscopy (for pyuria) with urine culture [9, 10, 13, 15]; hence, our results comparing dipstick tests with urine microscopy (for pyuria) in rural areas are unique.

Our study showed that the grades of the leukocyte esterase test increase proportionally with the number of pus cells/high power field (hpf) in urine samples, which further confirms the reliability of this test. On comparing the grades of the leukocyte esterase test with the culture positivity of the urine samples, it was found that as the grades of the leukocyte esterase test increased, culture positivity increased. This suggests that as the grade of the leukocyte test increases, the culture is more likely to be positive. Hence, these point-of-care dipstick tests can be used as screening tools for diagnosing UTIs in children.

Conclusion

The leukocyte esterase test is reliable to diagnose UTI in children with good sensitivity. Higher leukocyte esterase grades and UTIs are likely present. Nitrite or combination tests have poor sensitivity and high specificity; therefore, they cannot be used to rule out UTIs in children. In rural setups where urine microscopy (for pyuria) is considered a standard, the leukocyte esterase test can replace it due to its feasibility and effectiveness.

The main limitation of this study was the small sample size used to ascertain the reliability of nitrite and leukocyte esterase tests in various age groups.

Ethical Considerations

Compliance with ethical guidelines

No ethical considerations were considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualization, Methodology, and Investigation: Sandeep Garg, Anurag Yenkar, Anuradha Joshi, and Samrat Mehta; Software, Validation, Formal analysis, and Data curation: Sandeep Garg, Anurag Yenkar, and Shivanjali Gore; Writing—final manuscript: Sandeep Garg and Shivanjali Gore; Resources and Project administration: Sandeep Garg, Anurag Yenkar, Anuradha Joshi, and Samrat Mehta.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

We thank Ms. Ria Vijay, Ms. Vrutti Mistry for assisting with data analysis and manuscript writing, and Vedanti Patil, Medical Research Department, for assisting with publication.

References

[1] Montini G, Tullus K, Hewitt I. Febrile urinary tract infections in children. N Engl J Med. 2011; 365(3):239-50. [DOI:10.1056/nejmra1007755] [PMID]

[2] Roberts I. Nelson's textbook of pediatrics (20th edn.), by R. Kliegman, B. Stanton, J. St. Geme, N. Schor (eds). Pediatr Radiol. 2017; 47(10):1364-5. [DOI:10.1007/s00247-017-3907-9]

[3] Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: An overview of diagnosis and management. BMJ Paediatr Open. 2019; 3(1):e000487. [DOI:10.1136/bmjpo-2019-000487] [PMID]

[4] NICE. Urinary tract infection in under 16s: Diagnosis and management. London: National Institute for Health and Care Excellence; 2022. [Link]

[5] Hannula A, Perhomaa M, Venhola M, Pokka T, Renko M, Uhari M. Long-term follow-up of patients after childhood urinary tract infection. Arch Pediatr Adolesc Med. 2012; 166(12):1117-22. [DOI:10.1001/archpediatrics.2012.1383] [PMID]

[6] Kosmeri C, Kalaitzidis R, Siomou E. An update on renal scarring after urinary tract infection in children: What are the risk factors? J Pediatr Urol. 2019; 15(6):598-603. [DOI:10.1016/j.jpurol.2019.09.010] [PMID]

[7] Shaikh N, Haralam MA, Kurs-Lasky M, Hoberman A. Association of renal scarring with number of febrile urinary tract infections in children. JAMA Pediatr. 2019; 173(10):949-52. [DOI:10.1001/jamapediatrics.2019.2504] [PMID]

[8] Boon HA, Van den Bruel A, Struyf T, Gillemot A, Bullens D, Verbakel JY. Clinical features for the diagnosis of pediatric urinary tract infections: Systematic review and meta-analysis. Ann Fam Med. 2021; 19(5):437-46. [DOI:10.1370/afm.2684] [PMID]

[9] Mod HK, Jeeyani HN, Shah BM. Urinary tract infection in children: Clinical aspects and utility of urine dipstick test. Int J Contemp Pediatr. 2017; 4(3):790-5. [DOI:10.18203/2349-3291.ijcp20171491]

[10] Taneja N, Chatterjee SS, Singh M, Sivapriya S, Sharma M, Sharma SK. Validity of quantitative unspun urine microscopy, dipstick test leucocyte esterase and nitrite tests in rapidly diagnosing urinary tract infections. J Assoc Physicians India. 2010; 58:485-7. [PMID]

[11] Gupta V, Adhikari KM, Kumar M. Utility of simple dipstick test in diagnosing urinary tract infection in children presenting with fever: A prospective observational study. Med Res Chron. 2022; 9(1):69-77. [Link]

[12] Suresh J, Krishnamurthy S, Mandal J, Mondal N, Sivamurukan P. Diagnostic accuracy of point-of-care nitrite and leukocyte esterase dipstick test for the screening of pediatric urinary tract infections. Saudi J Kidney Dis Transpl. 2021; 32(3):703-10. [DOI:10.4103/1319-2442.336765] [PMID]

[13] Goldsmith BM, Campos JM. Comparison of urine dipstick, microscopy, and culture for the detection of bacteriuria in children. Clin Pediatr. 1990; 29(4):214-8. [DOI:10.1177/000992289002900402] [PMID]

[14] Williams GJ, Macaskill P, Chan SF, Turner RM, Hodson E, Craig JC. Absolute and relative accuracy of rapid urine tests for urinary tract infection in children: A meta-analysis. Lancet Infect Dis. 2010; 10(4):240-50. [DOI:10.1016/s1473-3099(10)70031-1] [PMID]

[15] Fernandes DJ, MD J, Castelino DN. Utility of dipstick test (nitrite and leukocyte esterase) and microscopic analysis of urine when compared to culture in the diagnosis of urinary tract infection in children. Int J Contemp Pediatr. 2017; 5(1):156-60. [DOI:10.18203/2349-3291.ijcp20175578]

[16] Powell HR, McCredie DA, Ritchie MA. Urinary nitrite in symptomatic and asymptomatic urinary infection. Arch Dis Child. 1987; 62(2):138-40. [DOI:10.1136/adc.62.2.138] [PMID]