How Sensitive is Urine Dipstick Analysis in Predicting Urinary Tract Infections in Symptomatic Adults in a Primary Care Setting

Mokhtar Shatla (1)
Abdulrahman Almisfer (2)
Shamsuldin Zawawi (2)
Baraah Damanhouri (2)
Fahad Alharthi (2)

(1) Department of Family Medicine, Faculty of Medicine, Menoufia University, Egypt; and Department of Family Medicine, Faculty of Medicine, Umm Alqura University, Saudi Arabia
(2) Student, Faculty of Medicine, Umm Alqura University, Saudi Arabia

Correspondence:
Mokhtar Shatla MD
Department of Family Medicine, Faculty of Medicine, Menoufia University, Egypt
Department of Family Medicine, Faculty of Medicine, Umm Alqura University, Saudi Arabia
Email: mokhtarshatla@gmail.com

Abstract

Background: Urinary tract infection (UTI) is a common clinical problem in the primary care setting. Urine dipstick analysis is a quick, cheap and widely used test to predict UTI in clinically suspected patients.

Objective: To evaluate the sensitivity of urine dipstick analysis as a screening test in predicting UTI in symptomatic adults in the primary care setting.

Methods: A total of 420 culture-positive urine samples from patients with symptomatic UTI, who had dipstick urinalysis in a primary care center were the materials of this study from March to October 2015. The sensitivity of urine dipstick nitrites (NT), leukocyte esterase (LE) and blood was calculated and compared with positive culture samples either individually or in combination.

Results: The sensitivity of dipstick NT alone was the lowest of all tests (20.7%), while LE alone was marginally higher than NT (31.42%), whereas dipstick blood test when considered alone was the highest sensitive (61.9%). In combination, NT and/or LE were marginally higher than either test alone (41.2%), while NT and/or blood were (64.5%). The highest sensitivity of dipstick is obtained when all the three parameters were considered together (NT and/or LE and/or Blood, sensitivity 81.4%).

Conclusion: Dipstick NT, LE, and blood are poor screening tests when used individually. Dipstick sensitivity significantly increases, and it could be considered a good screening test to predict UTI in symptomatic adults in the primary care setting when its three components are considered together. However, negative dipstick analysis should not rule out UTI in symptomatic adults, and urine culture is necessary for accurate diagnosis.

Key words: Urinary tract infection, dipstick analysis, screening, urine culture, nitrites, leukocyte esterase, blood.

Introduction

Overall, urinary tract infections (UTI) are the second most common infectious complaint in outpatient primary care clinics, and the most common outpatient complaint caused by bacteria. [1]It is estimated that, 2-3% of all consultations, and even 6% in the case of women, are due to symptoms suggesting UTI. [2]According to one estimate, 1 out of every 2 women will experience a UTI in her lifetime. [3]Almost 20% of UTIs are found in men especially the elderly due to prostatomegaly and distorted anatomy of the urinary tract. [4]

Symptoms of uncomplicated UTI include frequency, burning, straining, urgency, and pain with voiding. Patients may also experience hematuria, suprapubic pain or tenderness, and a change in the odor of the urine. [5]

Early diagnosis of uncomplicated UTI could significantly improve patient management in addition to providing optimum cost-effectiveness. [6,7] Urine culture is the gold standard for the diagnosis of UTI but is expensive and time consuming, requiring at least 24 hours to produce results. These limitations have made urine analysis including dipstick a preferred first-step investigation among primary care clinicians. [8]

The urine dipstick is a standard diagnostic tool of UTI, but there is much debate about its utility and role. There is doubt that this test is rapid, cheap, quick, and easy to administer. [9] Leukocyte esterase (LE, an enzyme produced by neutrophils) and nitrite (NT, the end product of bacterial nitrate reductase acting on nitrate in the urine), two important parameters of dipstick urinalysis, have been frequently used to predict UTI. Positive results of LE and NT are often used as a reflex to confirm diagnosis by urine culture (both in the presence and absence of clinical symptoms of UTI), or start of empiric antimicrobials. [10] Dipstick detection of blood in urine has been reported to possess a high sensitivity but poor specificity to detect UTI. [11]

There is much debate about the utility and role of Dipstick screening in predicting UTI. [9]Some studies have found negative urine dipstick analysis to be valuable in ruling out UTI. [12]However, other studies have shown a lack of sensitivity and specificity of these tests as indicators of UTI. [13]
So, there is marked heterogenicity in interpretation of results of dipstick analysis. The purpose of this study was to evaluate the sensitivity of dipstick urine analysis with emphasis on NT, LE and blood test, in predicting UTI in symptomatic patients in a primary care setting.

Materials and Methods

This study evaluated the urine dipstick analysis of 420 culture-positive urine samples of patients who attended the family medicine and internal medicine outpatient clinics of Umm Alqura University Medical Center, Makkah, Saudi Arabia, from March to October 2015. The center provides primary health care to the university employees and their families.

Urine samples from patients of both sexes and complaining of symptoms suggestive of UTI were included. Samples of patients less than 16 years of age, and pregnant women were excluded. The study was approved by the Research and Ethics Committee of Umm Alqura Faculty of Medicine.

Samples were collected by the patients themselves where they were asked to provide a midstream clean catch urine sample in the same day of the test. Dipstick urine analysis was done using multistix 10 SG (Siemens) and clinitek advantus analyzer. The reagent strip contains test pads for NT, LE, blood, glucose, protein, ketone, pH, specific gravity, bilirubin and urobilinogen. In this study, urine parameters considered in dipstick analysis were NT, LE, and blood. Reading time for NT and blood was one minute, and two minutes for LE. Cut-off values for a positive result was trace or more of LE, nitrite (+) and blood (+).

The presence of infection in this study was determined by quantitative urine culture. This is the gold standard criterion against which the three dipstick tests were compared. The cultures were done using blood agar and MacConkey agar plates. The cultures were read after 24 hours of incubation at 37°C. A colony count of more than 104 organisms/ml (for one organism) was defined as a positive urine culture for clean catch specimens. Full bacterial identification and antimicrobial susceptibility testing were performed for all positive specimens.[14] Specimens that contained more than two isolates (with any quantitation) were considered contaminated and were not included in the analysis. Dipstick urinalysis data as regards NT, LE, and blood were compared with positive culture results. The comparison was made for every individual test alone, then in combinations.

Results

In this study, the urine dipstick analyses of 420 culture-positive urine samples of symptomatic adults were studied. Age of included patients ranged from 21 to 64 years. The mean age of the patients was 39 years. Among 420 patients, 77.6% were females (n=326), and 22.4% were males (n=94).

Of the 420 culture positives samples, E. coli (62.1%) was the predominant isolate followed by Enterococcus species, Klebsiella, Proteus, Pseudomonas, Streptococcus species, Candida, and staphylococcus aureus, and others [Table 1].

Table 1: Number and percentage of the isolated organisms on the culture positive specimens

Organism	Number of Isolates	Percentage (%)
Escherichia Coli	261	62.14%
Enterococcus aeruginosa	52	12.4%
Klebsiella pneumoniae	30	7.14%
Proteus mirabilis	22	5.23%
Pseudomonas aeruginosa	15	3.6%
Streptococcus pyogenes	13	3%
Candida species	9	2.14%
Staphylococcus aureus	7	1.66%
Streptococcus saprophyticus	5	1.2%
Streptococcus agalactiae	3	0.72%
Miscellaneous	3	0.72
Total	420	100%

The sensitivity of dipstick NT alone was the lowest of all tests (20.7%), while LE alone was a little higher than NT (31.42%), whereas dipstick blood test when considered alone was the highest sensitive (61.9%). In combination, NT and/or LE were marginally higher than either test alone (41.2%), while NT and/or blood were (64.5%). The sensitivity increases when LE and/or blood were considered (69.7%). The highest sensitivity of dipstick screening is obtained when all the three test parameters are considered together (81.4%) [Table 2].

Table 2: Sensitivity of the urine Dipstick analysis used for screening UTI

Parameter	Sensitivity
Nitrite test	20.7% (n=87)
Leukocyte esterase test	31.42% 132
Blood test	61.9% 260
Nitrite and/or leukocyte esterase	41.2% 173
Leukocyte esterase and/or blood	69.7% 293
Nitrite and/or blood	64.5 271
Nitrite and/or blood and/or leukocyte esterase	81.4% (342)

UTI: urinary tract infections

Discussion

Urinary tract infection is the second common bacterial infection in the primary care setting. It is more common in females especially during their reproductive age. In this study, most patients diagnosed with UTI were females. This coincides with many studies which reported higher prevalence of UTI in adult women compared to men mainly due to the anatomy of the female genito-urinary tract.[3]

Diagnosis of UTI is based on clinical symptoms, together with positive urine culture.[15] However, the concerns of cost-effectiveness and lengthy processing time in urine culture have stimulated the use of other rapid diagnostic tools to predict UTI.[16] Dipstick analysis is a common rapid laboratory screening tool used by many primary care clinicians to predict UTI in symptomatic patients. It assesses presence of bacteriuria, pyuria, and hematuria associated with UTI. Notably, several studies have demonstrated significant heterogenicity in interpretation of dipstick results.[17]

Dipstick nitrite test (NT) is used to detect bacteriuria. Normally, nitrites are not found in urine but result when bacteria reduce urinary nitrates to nitrites. Many gram-negative bacteria including E. Coli, and some gram-positive bacteria are capable of this conversion, and a positive dipstick nitrite test indicates that these bacteria are present in significant numbers (i.e., more than 10,000 per mL). [18] However, non-nitrate-reducing organisms

e.g. Candida and Streptococci including Enterococci do not reduce nitrates, and may cause false-negative results. Although E. coli was the predominantly isolated organism in this study (62.1%), similar to other studies,[19-21] almost 20% of the isolates were Enterococci, Candida, and Streptococcus species, which do not produce nitrites.

Also, for bacteria to be able to reduce nitrates and produce nitrites, urine should contain sufficient dietary nitrates and have been retained in the bladder for more than 4 hours before voiding.[22,23] Performing this test on dilute urine may contribute to false-negative findings.[24] In patients who urinate frequently, dilution of NT may result in negative results. The first voided urine morning specimen has been proven to be accurate for nitrate, but such sample collection was not possible in all patients in this study. [25]Also, NT may be affected by common antibiotics e.g. nitrofurantoin, cephalexin, doxycycline, as well as vitamin C and phenazoperidine leading to suboptimal detection of bacteria. [26] Hence, an absence of urinary nitrite cannot rule out UTI.

All mentioned above may be the likely explanations for the low sensitivity of nitrite test in this study when done alone. This has been supported by findings from other similar studies. [27, 28] However, the sensitivity of nitrites in other studies varied between 39% and 81%. [19, 25, 29]

The leukocyte esterase (LE) test detects esterase, an enzyme released by neutrophils and may indicate white cells in urine (pyuria) associated with UTI. [22] Normally, urine is negative for LE. Positive value of the test correlates with the number of WBC/hpf urine sediment, and can vary from trace to many. [30] However, there are many conditions other than UTI causing pyuria and subsequent positive LE test results e.g. chlamydial urethritis, analgesic nephropathy and bladder tumors. False positives are seen in conditions when the urine is contaminated with bacteria, eosinophils or trichomonas. These reasons cause the positive predictive value of the LE test to vary from 19% to 88%. [31, 32]

False negative results may occur in the presence of significant levels of protein or glucose and in urines with high specific gravity which can crenate the white blood cells, leaving them unable to release esterases. [26, 33]

Similar to NT, LE results may be affected by common antibiotics mentioned above, as well as vitamin C, phenazoperidine, glycosuria, and urobilinogen. Also, high proteinuria has been shown to inhibit LE test. [26,34,35]

Hence, LE when considered alone as a parameter for diagnosing UTI is not as sensitive as when it is combined with nitrites in urine. A similar finding by Bhavsar et al., [36] found only substantial improvement of sensitivity when NT and LE are combined together to predict UTI in urine culture positive patients. This finding was different from other studies where the sensitivity of LE alone was high and varied between 61.7% and 77%. [29, 37, 38]

The explanation for low sensitivity of LE in this study may be attributed to some patients' self-initiation of common antibiotics to treat their condition. These medications are given over-the-counter in Saudi Arabia. Moreover, false negative LE test may be attributed to glycosuria and proteinuria, a common association of a prevalent medical problems in Saudi Arabia, diabetes mellitus.

The dipstick test for blood detects the peroxidase activity of erythrocytes in case of hematuria with UTI. However, myoglobin and hemoglobin also will catalyze this reaction, so a false positive test result may occur with conditions other than UTI including hematuria and myoglobinuria e.g. ureteric calculus, glomerular diseases, menstrual blood, malignancy, medications, concentrated urine, and strenuous exercise. [34] False negative results occur if pH of urine is less than 5.1, high specific gravity, and ascorbic acid (vitamin C) is present in the urine. [22] Blood test was the highest sensitive single test in this study. It has been reported that dipstick sensitivity for blood ranges from 91-100%.[22,39,40]

In this study, the sensitivity of dipstick was highest (81.4%) when its three parameters (NT/LE/blood) were all considered together, where any positive dipstick test results for detection of bacteruria by NT and/or detection of pyuria by LE and/or detection of blood improves sensitivity significantly, a finding comparable with that of Mambatta et al. with sensitivity 74%,[40] and Memişoğullari et al. with a sensitivity of 80%, [41]. However, in almost one fifth of the patients, there will be no positive dipstick test results and the patient's diagnosis might be missed. Hence, correlation of the dipstick test results with the patient's clinical condition is essential for accurate diagnosis.

Conclusion

Dipstick NT, LE, and blood are poor screening tests when used individually. However, Dipstick sensitivity significantly increases, and it could be considered a good screening test to predict UTI in symptomatic adults in the setting of primary care when its three components are considered together. However, negative dipstick analysis should not rule out UTI in adult patients with symptoms suggestive of UTI, and urine culture is recommended for these patients for proper diagnosis and management.

Recommendations

Primary care and family physicians are encouraged to utilize the quick, cheap, sensitive dipstick screening to predict UTI in symptomatic adults in primary care centers, and to delegate the expensive, time consuming urine culture for highly suggestive conditions of UTI with negative dipstick screening. Larger studies are recommended for larger samples from multiple primary care centers for more data generalizability.

References

1. Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. Am J Med. 2002;113(Suppl 1A):5S-13S.
2. Brooks D: The management of suspected urinary tract infection in general practice. Br J Gen Pract 1990, 40:399-402.
3. Kunin CM. Urinary tract infections in females. Clin Infect Dis. 1994;18:1-12
4. Griebling TL. Urinary tract infection in men. In: Litwin MS, Saigal CS, Editors. Urologic Diseases in America. DHHS, PHS, NIH, NIDDK. Washington, DC: GPO; NIH publication 075512; 2007. p. 62145.
5. Medina-Bombardo D, Segui-Diaz M Roca-Fusalba C, Llobera J. What is the predictive value of urinary symptoms for diagnosing urinary tract infection in women? Fam Pract. 2003;20:103-107.
6. Gupta K, Hooton TM, Naber KG, et al. Infectious Diseases Society of America, European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;Mar;52(5):e103-20.
7. Little P, Turner S, Rumsby K, et al. Developing clinical rules to predict urinary tract infection in primary care settings: sensitivity and specificity of near patient tests (dipsticks) and clinical scores. Br J Gen Pract. 2006 Aug;56(529):606-612.
8. Lohr JA: Use of routine urinalysis in making a presumptive diagnosis of urinary tract infection in children. Pediatr Infect Dis J 1991, 10:646-50
9. Deville WLJM, Yzermans JC, van Duijn NP, Bezemer PD, van der Windt DAWM, Bouter LM. The urine dipstick test useful to rule out infections: a meta-analysis of the accuracy. BMC Urol. 2004;4:1-14.
10. Lohr JA, Portilla MG, Geuder TG, Dunn ML, Dudley SM. Making a presumptive diagnosis of urinary tract infection by using a urinalysis performed in an on-site laboratory. The Journal of Pediatrics. 1993;122:22-25.
11. Anderson J, Fawcett D, Goldber L, et al. Joint consensus statement on the initial assessment of haematuria. Prepared on behalf of the Renal Association and British Association of Urological Surgeons. 2008. Available from: www.baus.org.uk (Accessed Jan, 2016).
12. Ohly N, Teece S. Accuracy of negative dipstick urine analysis in ruling out urinary tract infection in adults. Emerg Med J 2003;20:362-3.
13. Van Nostrand JD, Junkins AD, Bartholdi RK: Poor predictive ability of urinalysis and microscopic examination to detect urinary tract infection. American Journal of Clinical Pathology. 2000;113:709-713.
14. McCarter YS, Hall GS, Zervos M. Laboratory diagnosis of urinary tract infections. Cumitech. Edited by Coordinating ed. SSE. Washington, DC: ASM Press, 2009.
15. Brendler, CB. Evaluation of the urologic patient: history, physical examination and urinalysis. In: Campbell MF, Walsh PC. Campbell's Urology. 7th ed. Philadelphia: Saunders, 1998:144-56.
16. Lifshitz E, Kramer L: Outpatient urine culture: does collection technique matter? Archives of Internal Medicine. 2000;160:2537-2540.
17. Gorelick MH, Shaw KN. Screening tests for urinary tract infection in children: A meta-analysis. Pediatrics.1999;04: e54.
18. Pels RJ, Bor DH, Woolhandler S, Himmelstein DU, Lawrence RS. Dipstick urinalysis screening of asymptomatic adults for urinary tract disorders. II. Bacteriuria. JAMA. 1989;262:1221-4.
19. 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.
20. Marques LP, Flores JT, Barros Junior Ode O, Rodrigues GB, Mouraccde M, Moreira RM. Epidemiological and clinical aspects of urinary tract infection in community?dwelling elderly women. Braz J Infect Dis 2012;16:436-41.
21. Huysal K, Budak YU, Karaca AU, Aydos M, Kahvecioglu S, Bulut M, et al. Diagnostic accuracy of UriSed automated urine microscopic sediment analyser and dipstick parameters in predicting urine culture test results. Biochem Med (Zagreb) 2013;23:211-17.
22. JEFF A. SIMERVILLE, M.D., WILLIAM C. MAXTED, M.D., and JOHN J. PAHIRA, M.D., Urinalysis: A Comprehensive Review. Am Fam Physician. 2005 Mar 15;71(6):1153-1162.
23. Evans PJ, Leaker BR, McNabb WR, Lewis RR: Accuracy of reagent strip testing for urinary tract infection in the elderly. Journal of the Royal Society of Medicine. 1991;84:598-599.
24. Pezzlo M. Detection of urinary tract infections by rapid methods. Clinical Microbiology Reviews.1988;1:268-280.
25. Thakre SS, Dhakne SS, Thakre SB, Thakre AD, Ughade SM, Kale P. Can the Griess Nitrite Test and a Urinary Pus Cell Count of ?5Cells Per Micro Litre of Urine in Pregnant Women be Used for the Screening or the Early Detection of Urinary Tract Infections in Rural India? J Clin Diagn Res 2012;6:1518-22.
26. Beer JH, Vogt A, Neftel K, Cottagnoud P. False positive results for leucocytes in urine dipstick test with common antibiotics. BMJ. 1996;313:25.
27. Zaman Z, Borremans A, Verhaegen J, Verbist L, Blanckaert N. Disappointing dipstick screening for urinary tract infection in hospital inpatients. Journal of Clinical Pathology. 1998;51:471-472.
28. Loo SY, Scottolini AG, Luangphinith S, Adam AL, Jacobs LD, Mariani AJ: Urine screening strategy employing dipstick analysis and selective culture: an evaluation. American Journal of Clinical Pathology. 1984;81:634-642.
29. Rehmani R. Accuracy of urine dipstick to predict urinary tract infections in an emergency department. J Ayub Med Coll Abbottabad 2004;16:4-7.
30. Sharp V J, Lee DK, Askeland EJ. Urinalysis: Case Presentations for the Primary Care Physician. Am Fam Physician. 2014 Oct 15;90(8):542-547.
31. Semeniuk H, Church D. Evaluation of the leukocyte esterase and nitrite urine dipstick screening tests for detection of bacteriuria in women with suspected uncomplicated urinary tract infections. J Clin Microbiol 1999;37:3051-2.

32. Bartlett RC, Zern DA, Ratiewicz I, Tetreault JZ. Reagent strip screening for sediment abnormalities identified by automated microscopy in urine from patients suspected to have urinary tract disease. Arch Pathol Lab Med 1994;118:1096-101.
33. McNair RD, MacDonald SR, Dooley SL, Peterson LR: Evaluation of the centrifuged and Gram-stained smear, urinalysis, and reagent strip testing to detect asymptomatic bacteriuria in obstetric patients. American Journal of Obstetrics and Gynecology. 2000;182:1076-1079.
34. Gerber GS, Brendler CB. Evaluation of the urologic patient: History, physical examination, and urinalysis. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, Editors, Campbell-Walsh Urology. 9th ed. Philadelphia: Saunders Elsevier; 2007. p. 81-110.
35. McPherson RA, Ben-Ezra J. Basic examination of urine. In: McPherson RA, Pincus MR, Editors, Henry's Clinical Diagnosis and Management by Laboratory Methods. 22nd ed. Philadelphia: Saunders Elsevier; 2011. p. chap28.
36. Bhavsar T, Potula R, Jin M, Truant AL. Predictability of urinalysis parameters in the diagnosis of urinary tract infection: a case study. MLO Med Lab Obs. 2015 Jan;47(1):8, 10, 12; quiz 13.
37. Laosu-angkoon _S. The sensitivity and specificity of a urine leukocyte esterase dipstick test for the diagnosis of urinary tract infection in the outpatient clinic of Rajavithi Hospital. J Med Assoc Thai 2013;96:849-53.
38. Gieteling E, van de Leur JJ, Stegeman CA, Groeneveld PH. Accurate and fast diagnostic algorithm for febrile urinary tract infections in humans. Neth J Med 2014;72:356-62.
39. Woolhandler S, Pels RJ, Bor DH, Himmelstein DU, Lawrence RS. Dipstick urinalysis screening of asymptomatic adults for urinary tract disorders. I. Hematuria and proteinuria. JAMA. 1989;262:1214-9.
40. Mambatta AK, Jayarajan J, Rashme VL, Harini S, Menon S, Kuppusamy J. Reliability of dipstick assay in predicting urinary tract infection. J Fam Med Primary Care 2015;4:265-8.
41. Memisogullari R, Yüksel H, Hayriye Ak Y?ld?r?m, Yavuz O. Performance characteristics of dipstick and microscopic urinalysis for diagnosis of urinary tract infection. Eur J Gen Med 2010;7:174-8.