

Reliability of dipstick assay in predicting urinary tract infection

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ABSTRACT

Aims: Urine dipstick analysis is a quick, cheap and a useful test in predicting Urinary Tract Infection (UTI) in hospitalized patients. Our aim is to evaluate the reliability (sensitivity) of urine dipstick analysis against urine culture in the diagnosis of UTI. **Materials and Methods:** Patients admitted to our hospital suspected of having UTI, with positive urine cultures were included in this study from a 2-year period (January 2011 to December 2012). Dipstick urinalysis was done using multistix 10 SG (Siemens) and clinitek advantus analyzer. The sensitivity of dipstick nitrites, leukocyte esterase and blood in these culture-positive UTI patients was calculated retrospectively. **Results:** Urine dipstick analysis of 635 urine culture-positive patients was studied. The sensitivity of nitrite alone and leukocyte esterase alone were 23.31% and 48.5%, respectively. The sensitivity of blood alone in positive urine culture was 63.94%, which was the highest sensitivity for a single screening test. The presence of leukocyte esterase and/or blood increased the sensitivity to 72.28%. The sensitivity was found to be the highest when nitrite, leukocyte and blood were considered together. **Conclusions:** Nitrite test and leukocyte esterase test when used individually is not reliable to rule out UTI. Hence, symptomatic UTI patients with negative dipstick assay should be subjected to urine culture for a proper management.

Keywords: Urinary tract infection, urine culture, urine dipstick assay

Introduction

Urinary tract infections (UTIs) are the most common bacterial infections seen in the general population. In hospitalized patients, the second most common cause of bacteremia is UTI.^[1] The prevalence of UTI is found to be higher in women. Nearly 20% of UTIs are found in men.^[2] The predominant pathogen responsible for UTI is *Escherichia coli* followed by *Staphylococcus saprophyticus*. Less frequently identified isolates are *Klebsiella*, *Enterobacter* and *Proteus* species.^[3,4]

The diagnosis of UTI is not straight forward making it a challenging task. Dysuria is most common symptom in UTI, experienced by one in four women every year. Dysuria is also the presenting complaint in vaginitis, chlamydial urethritis and pyelonephritis.^[5] Sometimes patients with UTI are asymptomatic or have atypical symptoms and signs. Hence, laboratory investigations are required to diagnose UTI. There are several

tests available for the diagnosis of UTI. An ideal test is one which is cheap, needs less time and expertise, with high accuracy enabling a reliable and rapid diagnosis in high-risk patients. Though urine culture is the gold standard for the diagnosis of UTI, it is expensive and time consuming, requiring at least 48 hours to produce results. The above-mentioned limitations have made urine analysis a preferred first-step investigation among clinicians.

Urine analysis is a quick and inexpensive screening method requiring limited expertise. Physical, chemical and microscopic examination constitutes a complete urine analysis. In some hospitals urine culture is performed only in the presence of abnormalities in urine dipstick tests. Specific gravity, pH, urobilinogen, glucose, ketones, blood, leukocyte esterase and nitrite are tested in dipstick analysis. Negative urine dipstick analysis was found to be valuable in ruling out UTI by a few studies.^[6] However, a meta-analysis has shown that a negative dipstick analysis is insufficient to rule out UTI.^[7] Hence, there exists an on-going debate on the accuracy of urine analysis. There are different opinions regarding the need for urine analysis or urine culture as routine.

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The purpose of our study is to evaluate the reliability of dipstick urine analysis in the diagnosis of UTI.

Materials and Methods

We evaluated urine dipstick analysis of 635 urine culture-positive patients admitted in our hospital in the department of medicine from January 2011 to December 2012. The study was done after obtaining institutional ethical committee clearance. We excluded patients less than 14 years of age, intensive care unit (ICU) patients and pregnant women.

Urine dipstick chemical analysis

Dipstick urinalysis was done using multistix 10 SG (Siemens) and clinitek advantus analyzer. The reagent strip contains tests pads for protein, blood, leukocyte, nitrite, glucose, ketone, pH, specific gravity, bilirubin and urobilinogen. In our study the parameters considered in dipstick analysis were nitrites, leukocyte esterase and blood. Reading time for nitrites and blood was one min and two min for leukocyte esterase. Cut-off values for a positive result was trace or more of leukocyte esterase, blood (+) and nitrite (+).

Urine culture

The cultures were done using blood agar and MacConkey agar plates. The cultures were read after 24 h of incubation at 37°C. The growth of $\geq 10^5$ colony forming unit (CFU) per ml of urine was considered to be a positive culture. Samples that grew more than one microorganism were considered to be mixed growth and were excluded from the study. This is the gold standard against which the screening tests were compared.

Results

In our study, the urine dipstick analyses of 635 urine culture-positive patients were studied retrospectively. Patients with suspected UTI ranged from 15 to 89 yrs. The mean age of the patients was 50 yrs. Among 635 patients, 53.13% were male patients and 46.87% were female patients. Of the 635 culture positives, *E. coli* (62.8%) was the predominant isolate followed by *Enterococcus species*, *Klebsiella species*, *Candida species* and others [Table 1].

The sensitivity of blood alone for positive urine culture was 63.94%, which was the highest sensitivity for a single screening test and the least sensitive was nitrite test (23.31%). The sensitivity of leukocyte esterase test alone was less (48.5%). The presence of leukocyte esterase and/or blood increased the sensitivity to 72.28%. The sensitivity was found to be the highest when nitrite, leukocyte and blood were considered together (74.02%) [Table 2].

Discussion

UTI is among the most common infections affecting all age groups, especially women of the reproductive age group. Higher prevalence of UTI in adult women compared to men has been reported in various studies and is mainly due to anatomical factors,^[8] but in our study there was a mild male predominance

Table 1: Organisms causing UTI among hospitalized patients

Organisms	Number isolated	Percentage (%)
<i>E. coli</i>	399	62.8
<i>Enterococcus species</i>	90	14.1
<i>Klebsiella species</i>	43	6.7
<i>Candida species</i>	41	6.4
<i>Pseudomonas aeruginosa</i>	18	2.8
<i>Staphylococcus aureus</i>	11	1.7
<i>Citrobacter species</i>	9	1.4
<i>Enterobacter species</i>	9	1.4
<i>Acinetobacter species</i>	5	0.78
<i>Proteus species</i>	4	0.62
<i>Streptococcus agalactiae</i>	3	0.47
<i>Staphylococcus saprophyticus</i>	2	0.31
<i>Streptococcus pyogenes</i>	1	0.15
Total	635	100

UTI: Urinary Tract Infection

Table 2: Sensitivity of tests used for screening UTI

Parameters	Sensitivity (%)
Nitrite test	23.31
Leukocyte esterase test	48.5
Blood test	63.94
Nitrite and/or leukocyte esterase	53.1
Leukocyte esterase and/or blood	72.28
Nitrite and/or blood	68.66
Nitrite and/or blood and/or leukocyte esterase	74.02

UTI: Urinary tract infection

(53.13%). This may be because pregnant patients were excluded and UTI in elderly males is common among those with prostatomegaly and neurogenic bladder.^[9]

A history of dysuria, increased frequency, change in the color of urine, suprapubic pain, etc. along with urine culture help in the diagnosis of UTI. However, to reduce the cost and time to diagnose UTI, the usefulness of screening tests is being evaluated.

Commercially available dipstick screening tests are used to assess pyuria and bacteriuria. In dipstick analysis, the intensity of the reaction color may diminish with urinary protein excretions >500 mg/dL and urinary glucose >2 mg/dL, as can high doses of cephalexin/gentamicin or boric acid as preservative.^[10] However, a negative dipstick in the presence of a strongly suggestive history of UTI cannot reliably rule out an infection in such cases.

The Griess Nitrite test used for the detection of significant bacteriuria picks up the sodium nitrite in concentration of as little as 0.1 μ g/ml to give a positive result. Normally urine should not show any trace of nitrite. The nitrite test is an indirect measure of nitrate-reducing bacteria, provided the urine contains sufficient dietary nitrates and has been retained in the bladder for more than 4 hrs. Most bacterial species causing UTI reduce nitrate in the urine to nitrite.^[11] Nitrate-reducing bacteria includes all the Enterobacteriaceae and most of the non-fermenters, but *Candida* and Streptococci including *Enterococci* do not reduce

nitrate. Though our study population had predominantly *E. coli* (62.8%) similar to other studies,^[12-14] 21.2% of the uropathogens comprised of *Candida*, *Enterococci*, *Streptococcus agalactiae* and *Streptococcus pyogenes*. *Enterococcus* as the second most common uropathogen was described by various authors usually as a nosocomial pathogen.^[15,16]

The first voided urine specimen has been proven to be accurate for nitrate, but such sample collection was not possible in all the patients. Lack of dietary nitrate, dilution of nitrite in urine or non-nitrate-reducing bacteria cause a false negative test. Hence, an absence of urinary nitrite cannot rule out a UTI. These maybe the possible reasons for the very low sensitivity of nitrite test in our study. The presence of nitrite has a high positive predictive value of 94%.^[17] Also, the presence of nitrites is highly specific for bacteriuria (96.6–97.5%) with a low sensitivity of 0–44% for 10³–10⁵ CFU/ml bacteriuria.^[18,19] The sensitivity of nitrites in other studies varied between 39% and 81%.^[12,20-25]

Proteins with esterolytic activity hydrolyze ester substrates, which is the basis of LE tests. Leukocyte esterase reacts with agents on the dipstick to produce a blue colour. Human neutrophils produce proteins with esterolytic activity. The advantage of this test is that esterases released after cell lysis as well as esterases in intact leukocytes can be detected. Hence, a positive result may be obtained even if the specimen is not properly preserved. Positive value of the test correlates with a minimum number of WBC/hpf, and can vary from trace to many. Trace of LE activity may be considered a positive result for predicting UTI. However, a positive test result is not very specific for UTI as there are many other conditions causing pyuria. Conditions like chlamydial urethritis, analgesic nephropathy and bladder tumors can produce WBC in the urine. The above-mentioned reason causes the positive predictive value of the LE test to vary from 19% to 88%.^[19,26] The negative predictive value is between 97% and 99%, in the absence of leukocyte esterase activity with <10³ CFU/ml in urine culture.^[19] False positives are seen in conditions when the urine is contaminated with bacteria, eosinophils or trichomonas and when the test strip reacts with formalin or oxidizing agents. As obvious from above, leukocytes when considered alone as a parameter for diagnosing UTI is not as sensitive as when it is combined with nitrates and blood in urine. This finding was different from other studies where the sensitivity of leukocyte esterase was high and varied between 61.7% and 77%.^[21,22,24,25,27,28] The reasons for low sensitivity of leukocyte esterase in our study may be attributed to the treatment initiated in these patients with drugs like gentamycin, nitrofurantion or tetracycline leading to false negative test results. False negative LE test may also be due to proteinuria, vitamin C in the urine and technical error due to inadequate time allowed for the dipstick reading.^[29,30]

The dipstick test for hematuria is a screening test and not used for diagnosis. Oxidation of a test-strip reagent causes a color change and is considered a positive result. Microscopic examination of urine is required to confirm dipstick hematuria.

Microscopic hematuria is commonly defined as the presence of three or more RBCs per high power field in spun urine sediment. The common causes of hematuria are UTI, ureteric calculus, glomerular diseases, malignancy and medications. Hemoglobinuria, myoglobinuria, menstrual blood, concentrated urine, and strenuous exercise can cause a false-positive result on a dipstick test.^[29] The presence of oxidizing contaminants such as hypochlorite and povidone can lead to false-positive result. False negative results are seen if the dipsticks are exposed to air, pH of urine is less than 5.1 and ascorbic acid is present in the urine. Blood test was the highest sensitive single test in our study. When any of the three (nitrite/leukocyte esterase/blood) were positive, the sensitivity increased to 74.02%, which was comparable with a similar study by Ramazan *et al.* with a sensitivity of 80%.^[10]

Conclusion

We found that the sensitivity of nitrite test and LE test when used alone was low and cannot rule out UTI in most patients. Hence, urine dipstick assay is not reliable in predicting UTI and we suggest performing urine culture for patients admitted with suspected UTI in tertiary hospitals. The dipstick analysis may find its use in outpatient settings and primary health centers as a first-level screening test and should be clinically correlated.

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