Can urine dipstick test be an alternative to detect urinary tract infection in limited resource setting? – A validity study from Bangalore, India

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**Abstract**

**Background:** Diagnosis of urinary tract infection (UTI) can be challenging as symptoms are nonspecific. The gold standard for the diagnosis of urine culture is not easily available in resource constrained settings. Hence, the need for affordable point of care diagnostic test could be an inexpensive alternative for urine culture or microscopy. The objective of the study was to validate the urine dipstick test to detect UTI in a resource constrained primary care setting. **Methods:** A diagnostic accuracy study was conducted in a health center in an urban slum by Bangalore Baptist Hospital. We included 136 patients suspected to have UTI. Patients were asked to give urine samples for urine dipstick analysis, urine microscopy, and urine culture and validity of the dipstick was analyzed. **Results:** A total of 136 patients fulfilling the inclusion criteria were recruited. Nitrite had higher specificity than leukocyte esterase (95% vs. 73%). Positive predictive value for nitrite and leukocyte was 84% and 51%, respectively. A combination of fever, dysuria along with lower abdominal pain had higher specificity (92%). Most common organism that was isolated was \textit{E. coli} (56%) followed by \textit{S. aureus} (13%). \textit{E. coli} was susceptible to nitrofurantoin. **Conclusion:** Urine dipstick could be used as a simple diagnostic test in a limited resource setting for a rapid diagnosis and initiation of empirical antibiotic therapy. Urine dipstick for nitrite has a good specificity.

**Keywords:** Dipstick, limited resource setting, urinary tract infection

**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.\textsuperscript{[4]} The prevalence of UTI is found to be higher in women.\textsuperscript{[2]} The prevalence of UTI in women is about 3% at the age of 20, increasing by about 1% in each subsequent decade.\textsuperscript{[3]} Nearly 20% of UTIs are found in men.\textsuperscript{[3]} It is estimated that 150 million UTIs occur yearly worldwide and are estimated to account for over 7 million office visits per year. In the healthcare setting, approximately 40% of all nosocomial infections are UTIs.\textsuperscript{[4,5]}

Clinically, the diagnosis of UTI can be difficult as symptoms are nonspecific. The only way to reliably exclude a UTI is by the laboratory examination of a urine specimen.\textsuperscript{[6]} Urine culture could be gold standard with specificity of 99%.\textsuperscript{[2]} But it is expensive and cannot be afforded by all patients and the facility may also not be available in all the limited resource setting. UTI can be detected by urine microscopy in primary care setting. But the sensitivity and specificity of microscopy is 100% and 38.8%, respectively.\textsuperscript{[7]} Urine dipstick method which can detect nitrite and leukocyte can be a good alternate for urine culture. In the female population...
with symptoms indicative of UTI, Dutch guidelines postulate that a positive nitrite test result indicates a high probability for UTI, in which case empirical antibiotic treatment is started. In the instance of a negative nitrite test result, microscopic examination and urine culture is the next step for further analysis.[9]

Specific gravity, pH, urobilinogen, glucose, ketones, blood, leukocyte esterase, and nitrite are tested in dipstick analysis. The results are also readily available in a few minutes which will help the physicians to start the antibiotics without waiting for urine culture.[9] Nitrites are generally found in urine due to reduction of nitrite to nitrites by gram-negative bacteria such as E. coli. The detection of bacteria in urine by nitrite positive dipstick is also dependent on nitrite from the patient’s diet (vegetables) and sufficient bladder incubation time. Gram-positive uropathogens do not produce nitrite reductase and therefore when infection is due to these bacteria, the dipstick will be negative for nitrite.[9]

Leukocyte esterase is an enzyme released by neutrophils and macrophages. A urine dipstick positive for this enzyme indicates pyuria (an increased number of leukocytes). The presence of leukocyte esterase on dipstick may also be due to non-infectious renal diseases such as glomerulonephritis. Contamination of samples by vaginal secretions may cause a false-positive result.[10] Multiple references support different sensitivity and specificity numbers of urine dipstick test. For example, Campbell’s Urology states that “the specificity of the nitrite dipstick for detecting bacteriuria is over 90%. The sensitivity of the test, however, is considerably less, varying from 35% to 85%.[11]

The present study will aim to investigate the presence of UTI in a simple and inexpensive way to reduce the requirement of other expensive urine investigations. This study will also observe the validity of dipstick method in detecting the UTI in primary care setting where there is lack of gold standard tests like urine culture to investigate the presence of UTIs. Urine dipstick test is easily available and can be easily done without expertise.

Methodology

A diagnostic accuracy study was conducted by Community Health Division of Bangalore Baptist Hospital at Urban Health Centre in Deverajeevanahalli, an urban slum in Bangalore. This Community Health Centre provides primary care to predominantly underprivileged population. Considering the 89% specificity of urine dipstick test, the sample size was calculated as 136.[12] Patients who visited the centre with symptoms of UTI with age group from 18 to 60 years were included and those with history of recurrent UTI, complicated UTI, and taken antibiotics in last 2 weeks were excluded. A questionnaire with demographic details, clinical profile was administered by the interviewer after an informed consent. Participants were asked to give urine samples for urine dipstick analysis, urine microscopy, and urine culture and sensitivity. They were educated to collect the urine sample by mid stream urine specimen collection method and sample was collected in a sterile container provided by laboratory and then it was handed over to the laboratory in aseptic condition as soon as possible.

The urine strip was acquired from the manufacturer “Siemens Multisitix and SD Urorcolor” and it comprised of 10 chemical pads or reagents which could analyze various parameters including nitrates and leucocytes. The test can often be read in as little as 60–120 s after dipping. Urine microscopy was done by a standard method. The sample was inoculated for semi-quantitative culture on cystine-lactose-electrolyte-deficient (CLED) media using a calibrated loop. The culture plate was incubated at 37°C for 18–24 h under aerobic conditions. Identification of bacterial growth was determined by Gram’s staining and standard microbiology techniques. Antibiotic susceptibility was performed by the Kirby-Bauer disc diffusion method on Mueller Hinton agar. Cultures were considered positive if the culture showed greater than 100,000 colonies of a single pathogen.[12]

The data collected from the patients was entered in Microsoft Excel 2010 and analyzed in SPSS Version 16.0. The sensitivity, specificity, negative predictive value, and positive predictive values were calculated for nitrite and leucocyte in dipstick. Patients were informed about all aspects of the study in their understandable language and written informed consent was taken. Voluntary participation was ensured and no care was denied even the patients who did not agree to participate in the study. In this study, there is no conflict of interest with the company, the tool was selected as it was used in the hospital. This study was approved by the Institutional Review Board of Bangalore Baptist Hospital on 25/07/2017.

Urine dipstick

Urine dipstick, obtained from a mid-stream sample, is used as a first-line screening. Once a urine sample is collected, a specially treated chemical strip (dipstick) will be placed in to urine. Patches on the dipstick will change color to indicate the presence of such things as white blood cells, protein, nitrite, or glucose.

Urine microscopy

Urine will be examined under a microscope. It can be used to examine the cells of urinary tract, blood cells, crystals, bacteria, parasites, and cells from tumors. This test is often used to confirm the findings of other tests or add information to a diagnosis.

Urine culture positive

A “positive” or abnormal test is when bacteria or yeast are found in the culture. This likely confirms the UTI or bladder infection.

Results

A total of 136 patients fulfilling the inclusion criteria were recruited. We predominantly (81.61%) had women. Nearly half of the study population were from the age group of 31–50 years (48.53%) and most of the patients were nondiabetic (88.3%) [Table 1]. Dysuria was the most common
symptom (83%) followed by painful micturation (53.6%) and lower abdominal pain (53.6%). Itching around genital region was the least common symptoms (20.5%) among the patients [Table 2].

Sensitivity of the urine dipstick test for nitrite (40%) was lower than dipstick test for leukocyte esterase (65%), while nitrite had higher specificity than leukocyte esterase (95% vs. 73%). Positive predictive value (PPV) was also higher with nitrite than leukocyte (84% vs. 51%). When nitrite and leukocyte were combined the sensitivity (40%) and specificity (95%) did not improve significantly. Similarly, PPV and NPV remained that of dipstick for leukocyte. Urine microscopy had higher sensitivity (86%) and lower specificity (39%) and lower PPV (46%) and higher NPV (82%) [Table 3].

When symptoms were combined and tested for validity, a combination of fever, dysuria along with lower abdominal pain had higher specificity (92%), followed by fever and abdominal pain (82%) [Figure 1]. Dysuria, fever, and lower abdominal pain along with positive urine dipstick has increased the sensitivity to 98%. Similarly, dysuria had higher sensitivity (86%) followed by fever (57%) and lower abdominal pain [Table 4].

Most common organism that was isolated was E. coli (50%) followed by S. aureus (13%). The antibiotic sensitivity pattern is shown in Table 5. Among the parenteral administered antibiotics, meropenem (100%), imipenam (100%), and amikacin (95.2%) were highly sensitive to E. coli. Nitrofurantoin, one of the most common antibiotic which is commonly prescribed in primary care setting was the most sensitive orally administered antibiotic against E. coli. S. aureus was moderately sensitive to commonly used oral antibiotics such as amoxicillin clavulanic acid (80%) and cefazolin (80%). Enterobacter which was isolated in 10% of samples was highly sensitive to ciprofloxacin (100%) [Table 5].

We had an increased number of women in our study group than men. It has been well documented that women are more prone for UTI than men across the globe. The most common presenting symptom was burning sensation (83.09%) followed by pain while passing urine (53.68%) and lower abdomen (53.68%). A similar study by Devaraja et al reported a similar observation in which 87.5% of the patients had dysuria and abdominal pain which slightly differs from the findings of our study, whereas Chandrasekar et al observed only 48.6% of the patients who had community acquired UTI presented with dysuria. In our study, the sensitivity of dysuria (86%) is higher than that of fever (57%) and lower abdominal pain (57%). However, Mishra et al observed suprapubic pain (89%) had a higher sensitivity than dysuria (81%).

Mambatta et al did a validity study in Tamil Nadu and reported that the sensitivity of nitrite alone and leukocyte esterase alone were 23.31% and 48.5%, respectively, which are similar to our findings with slightly higher sensitivity (40% and 65%) in both tests. The reason for low sensitivity of nitrite test could be false-negative test due to lack of dietary nitrate, dilution of urine, or non-reducing bacteria in the urine. Moreover, first voided urine sample which is more accurate for nitrate is not always possible in all the patients. The nitrite in the urine has been shown to increase the PPV in our study and it was also observed in earlier studies. Previous researches have reported sensitivity for nitrite varying from 23 to 81%. Findings from other studies have showed sensitivity of leukocyte esterase from 48.5% to 77%. Our finding corroborates with these existing evidences and falls in this range. Urine contaminated with bacteria, esinophils, or trichomonas are known to show false positives with leukocyte strip.
When nitrite and leukocyte were combined, the sensitivity (40%) and specificity (95%) did not improve significantly. The findings of our study was also slightly similar to the study done by Cairas et al. with low sensitivity and high PPV with nitrite. Rehmani observed the specificity reduced when both tests were combined. Wilson et al. reported the combination of positive nitrite or positive leukocyte esterase tests had improved sensitivity (85%) and specificity (84%). Dunnagai et al. also observed a similar findings in patients with spinal cord injuries and these findings were inconsistent with ours.

Leman et al. reported that urine microscopy alone was sensitive (100%) but nonspecific (38.9%), whereas in our study, the urine routine test had sensitivity of 86.54% and specificity of 39.29%.

Most common organism that was isolated was *E. coli* (56%) followed by *S. aureus* (13%). The findings of our study corroborate with many of the other studies. *E. coli* was susceptible with oral nitrofurantoin which is consistent with literature. The sensitivity pattern of parenteral antibiotics also corroborates with existing evidences.

In a study by Marsha et al., the most common isolated pathogen was *E. coli*, which was detected in 283 (74.9%) isolates which corroborates with our findings. They have reported that resistance rate was higher in the nitrite positive group for trimethoprim/sulfamethoxazole and ampicillin with or without sulbactam. We found that the resistance rate of nitrite positive group to 2<sup>nd</sup> generation cephalosporins was followed by ampicillin (38.4%).

This is a unique study which looked into the validity of using dipstick test for diagnosis of UTI in a resource constrained primary care setting. We have used an appropriate gold standard test. We had few limitations in our study. There could be good number of patients who have used antibiotics before coming to the health center and it could have altered the test result. Our definition of positive culture was >10<sup>5</sup> CFUs and moderately significant bacteria was considered as negative culture.

Urine dipstick nitrite is a good test that can be used to detect UTI in primary care setting where urine microscopy and culture is not available. This can also be an inexpensive alternative for primary care physicians.

**Conclusion**

Urine dipstick could be used as a simple diagnostic test in a limited resource setting for a rapid diagnosis and initiation of empirical antibiotic therapy. Urine dipstick for nitrite has a good specificity. However, dipstick test should not be used as a screening tool as it has a very low sensitivity. *E. coli* is the most common etiological organisms for UTI in our community and nitrofurantoin could be used as a first line oral antibiotic in community acquired UTIs.

**Informed consent**

All informed consent was obtained from all individual participants included in the study.

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**Table 3: Validity of diagnostic tests**

| Tests                          | Sensitivity (95% CI) % | Specificity (95% CI) % | PPV (95% CI) % | NPV (95% CI) % | + LR         | -LR         |
|-------------------------------|------------------------|------------------------|----------------|----------------|--------------|--------------|
| Nitrite                       | 40 (27-53)             | 95 (90-99)             | 84 (69-98)     | 72 (63-80)     | 8.4 (3.0-23.3) | 0.62 (0.49-0.78) |
| Leucocyte esterase            | 65 (51-80)             | 73 (64-82)             | 51 (38-65)     | 83 (75-91)     | 2.5 (1.67-3.74) | 0.46 (0.29-0.72) |
| Combined (both positive)      | 40 (27-53)             | 95 (90-99)             | 84 (69-98)     | 72 (63-80)     | 8.4 (3.0-23.3) | 0.62 (0.49-0.78) |
| Combined (Either Nitrite or Leucocyte positive) | 51 (38-65) | 83 (75-91) | 65 (51-80) | 73 (64-82) | 3.11 (1.80-5.3) | 0.57 (0.42-0.77) |
| Routine analysis              | 86 (77-95)             | 39 (28-49)             | 46 (36-56)     | 82 (70-94)     | 1.4 (1.1-1.7)  | 0.34 (0.16-0.71) |

**Table 4: Validity of symptoms in detecting UTI**

| Tests                          | Sensitivity (95% CI) % | Specificity (95% CI) % | PPV (95% CI) % | NPV (95% CI) % |
|-------------------------------|------------------------|------------------------|----------------|----------------|
| Dysuria                       | 0.86 (0.77-0.95)       | 0.19 (0.10-0.27)       | 0.39 (0.30-0.48) | 0.69 (0.50-0.88) |
| Fever                         | 0.57 (0.44-0.71)       | 0.63 (0.52-0.73)       | 0.49 (0.36-0.61) | 0.70 (0.6-0.8)  |
| Lower abdominal pain          | 0.57 (0.44-0.7)        | 0.54 (0.44-0.65)       | 0.44 (0.32-0.55) | 0.67 (0.56-0.78) |
| Painful micturation           | 0.51 (0.38-0.65)       | 0.45 (0.34-0.55)       | 0.36 (0.25-0.48) | 0.60 (0.48-0.72) |
| Change in colour of urine     | 0.55 (0.42-0.69)       | 0.47 (0.36-0.58)       | 0.39 (0.28-0.50) | 0.63 (0.51-0.73) |
| Dysuria + Fever               | 0.5 (0.36-0.63)        | 0.6 (0.59-0.78)        | 0.5 (0.36-0.63) | 0.69 (0.59-0.78) |
| Dysuria + Lower abdominal pain| 0.51 (0.38-0.65)       | 0.64 (0.54-0.74)       | 0.47 (0.34-0.56) | 0.68 (0.58-0.78) |
| Dysuria + Change in colour of urine | 0.46 (0.32-0.59) | 0.6 (0.50-0.71) | 0.42 (0.29-0.54) | 0.64 (0.54-0.75) |
| Fever + Lower abdominal pain  | 0.30 (0.18-0.43)       | 0.8 (0.73-0.90)        | 0.51 (0.34-0.69) | 0.65 (0.56-0.74) |
| Diabetes + dysuria            | 0.29 (0.14-0.38)       | 0.76 (0.67-0.85)       | 0.41 (0.24-0.57) | 0.62 (0.53-0.72) |
| Diabetes + dysuria + fever    | 0.15 (0.05-0.25)       | 0.92 (0.87-0.98)       | 0.57 (0.31-0.83) | 0.63 (0.55-0.72) |
| Fever + dysuria + dipstick    | 0.19 (0.85-0.29)       | 0.98 (0.96-1.01)       | 0.90 (0.73-1.07) | 0.66 (0.58-0.74) |
Conflicts of interest

There are no conflicts of interest.

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