

Performance Evaluation of point-of-care (POC) Testing in Diagnosis of Urinary Tract Infections.

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Abstract

Introduction: Early detection of UTI is critical for instituting effective treatment and avoiding patient complications. Unfortunately, the results of the culture are available after 24 hrs. .Thus point-of care rapid diagnostic tools are especially relevant in this setting.

Material and methods: During this trial, 800 patient samples were taken. Direct Gram staining, wet mount preparation, and Urine dipstick chemical analysis was performed. Dipstick test provides point of care information about urinary tract infection and a positive test was later confirmed by culture of the urine specimen.

Results: Nitrite test was found to have 50% sensitivity, 93% specificity,75.52% positive predictive value and 84.04% negative predictive value .Leucocyte esterase test showed sensitivity, specificity, positive predictive value, negative predictive value of 81%, 69%, 47.73%, 91.07% respectively. Sensitivity of Leucocyte esterase test was higher than the nitrite test. The Leucocyte esterase-nitrite test combination yielded the best levels of sensitivity 81% and specificity 97% as well as positive and negative predictive values of 89%, 93% respectively when compared to culture.

Conclusion: Urine culture is still the gold standard in diagnosis of UTI nevertheless it is time-consuming and expensive. pre-screening urine samples with rapid tests seem to be sensible and cost-effective approaches for identifying urinary tract infection and to decrease the workload in the laboratory in resource-limited settings, according to our research.

Keywords: Diagnosis of Urinary Tract Infections (UTI) at the Point of Care (POC), UTI dipstick test, LE test, Nitrate reductase test, urine culture, UTI gram staining, fast UTI diagnosis.

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Introduction

Detection and treatment of urinary tract infections as soon as they are discovered are the first steps in preventing urosepsis (UTIs). A bacterial urinary tract infection (UTI) can affect patients of any gender. When it comes to UTIs, women are more likely to have them than males, and the frequency varies with age and gender. Only 2% of one-year-old male and female children have a urinary tract infection (UTI). The incidence of urinary tract infections (UTIs) in males remains low until they reach the age of 60. Women are more likely to develop bacteriuria as they get older, with a prevalence of 10% to 20% [1]. Symptomatic urinary tract infections (UTIs) affect up to 60% of the female population at some point in their lives [2], and 3% of women are likely to encounter more than one UTI every year [3]. Urinary tract infections (UTIs) may be difficult to diagnose clinically since their symptoms are non-specific. To rule out a urinary tract infection, a urine sample analysis is preformed. [4]. Upper respiratory tract illness and Urinary tract infection (UTI) are by far the most frequent bacterial disease. [5,6] Urinary tract infections (UTIs) are estimated to cause over half of all nosocomial infections associated with urinary catheters, [7], and these diseases have a significant morbidity, economic cost, and research expenditure. UTIs that are more difficult to diagnose might benefit from screening tests in addition to traditional culture methods [8,9]. Detection of UTIs is essential to initiate early treatment, as delay can lead to significant morbidity.

Granulocytes, the majority of which are neutrophils, generate the enzyme leukocyte esterase (LE). It is possible to detect LE activity in urine using a strip saturated with buffered indoxyl carboxylic acid ester and a diazonium salt. It is a good indication of pyuria since it can detect both lysed and intact granulocytes in the

bloodstream. Squamous epithelial cells may cause false positive findings, as can preservatives and detergents, as well as excessive amounts of ascorbic acid or albumin in the urine (>300mg/dl) [10,11]. When dietary nitrates in the urine are converted to nitrites by nitrate-reducing bacteria, a nitrite test becomes positive [12,13,14]. It is possible for a nitrite test to produce false positive results as a result of delays in transit that allow bacteria that reduce nitrites to grow excessively or as a result of drug interference, also nitrite tests can produce false negative results if the infecting organism does not reduce nitrates (e.g. *Enterococcus* spp.) [11]. The leukocyte esterase and nitrite tests are equivocal when it comes to identifying a urinary tract infection. [2]. Urine dipstick test can confirm the diagnosis of uncomplicated cystitis in a patient with a reasonably high pretest probability. [3]

Urinary tract infection (UTI) diagnosis might be difficult in certain situations. There is a 24-hour delay before the patient's culture results are available. Urinary tract infections (UTI) can be diagnosed and treated more effectively if a point-of-care diagnostic tool for bacteriuria could be developed. In terms of quick testing, dipsticks are the most popular. Leukocyte esterase and nitrite are two typical analytes evaluated in a typical dipsticks test. One of the benefits of dipstick tests is that they are fast and simple to conduct and provide an instant results [5]. The present study was conducted to find out the sensitivity and specificity of the rapid dipstick tests in both hospital and community acquired urinary tract infections (UTIs).

Material and methods:

The Government Medical College Srinagar's Department of Microbiology did this 1 year cross-sectional investigation. During the trial, 800 participants were

enrolled. For the urine culture and sensitivity test, random samples were taken from the urine specimens collected at the laboratory. Patients above the age of 2 years with suspected urinary tract infection (both from community (OPD) as well as (IPD) hospitalized), catheterized patients, patients who had undergone surgical instrumentation and patients on antibiotics were included in this study. Suprapubic aspiration, percutaneous nephrostomy (PCN), Cystoscopy, and Ileal conduit samples were not included in this investigation. Patients were advised to collect the midstream clean catch urine. For indwelling catheter standard procedure for collection of sample was followed while maintaining the integrity of closed drainage system. Urine was transported to the laboratory as soon as possible. It was cultured as early as possible after collection, preferably within 2 hours. In case of delay, it was refrigerated up to a

maximum of 24 hours before plating. If delay was expected to be for more than 24 hours then transport media were used. Direct Gram staining was performed following the standard operating procedure of our laboratory. After gram staining plating of culture plates was done, the specimen tubes were returned to the refrigerator, where they were kept between 2 and 8°C until the final report was completed. After that, the smear was investigated under oil immersion field (1000x). At least one or five bacteria per oil immersion field (OIF) suggest significant bacteriuria. Due to the rapid degradation of leukocytes in old urine, the Gram stain could not be relied upon to identify PMNs. By Wet mount preparation microscopy the presence of pyuria was verified in all specimens. More than five pus cells per high-power field (hpf) was considered as pyuria.

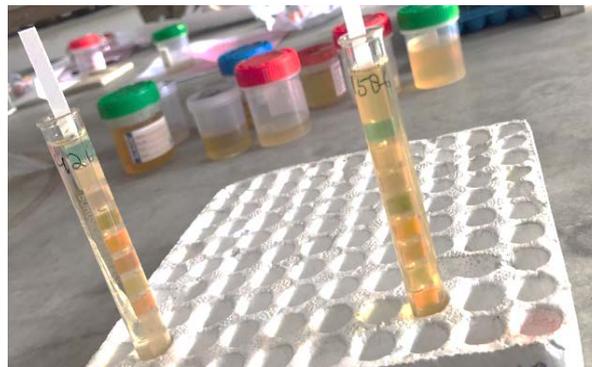


Plate 2: Showing Urine dipstick chemical analysis

Urine dipstick chemical analysis: This test provides point-of-care information about urinary tract infection; a positive test was confirmed by culture of the urine specimen. Urinalysis reagent strips (Rapid Diagnostic Pvt Ltd.) were used for screening of the urine samples. The reagent strips were allowed to reach the room temperature before testing. After the strip was removed from the canister it was used immediately by completely immersing the strip in the labeled tube containing urine sample. After taking the strip out of urine sample it was kept on

adsorbent paper and Reagent regions were checked against the canister label color blocks at predetermined intervals. Following the manufacturer's instructions, the data were examined and analyzed. (Plate: 2) The two most important tests from infection point of view in the dipstick are leukocyte esterase test (LE) and nitrate reductase test or Greiss test (NR). Granulocytes, the majority of which are neutrophils; generate the enzyme leukocyte esterase (LE). Leukocyte esterase activity in urine may be identified using this reagent strip, which is covered

with buffered indoxyl carboxylic acid ester and diazonium salt. Leucocytes esterase activity is detected even if the leucocytes

are not viable. Since most of the organisms (family Enterobacteriaceae) causing UTI reduce nitrates to nitrites. (Plate: 4)

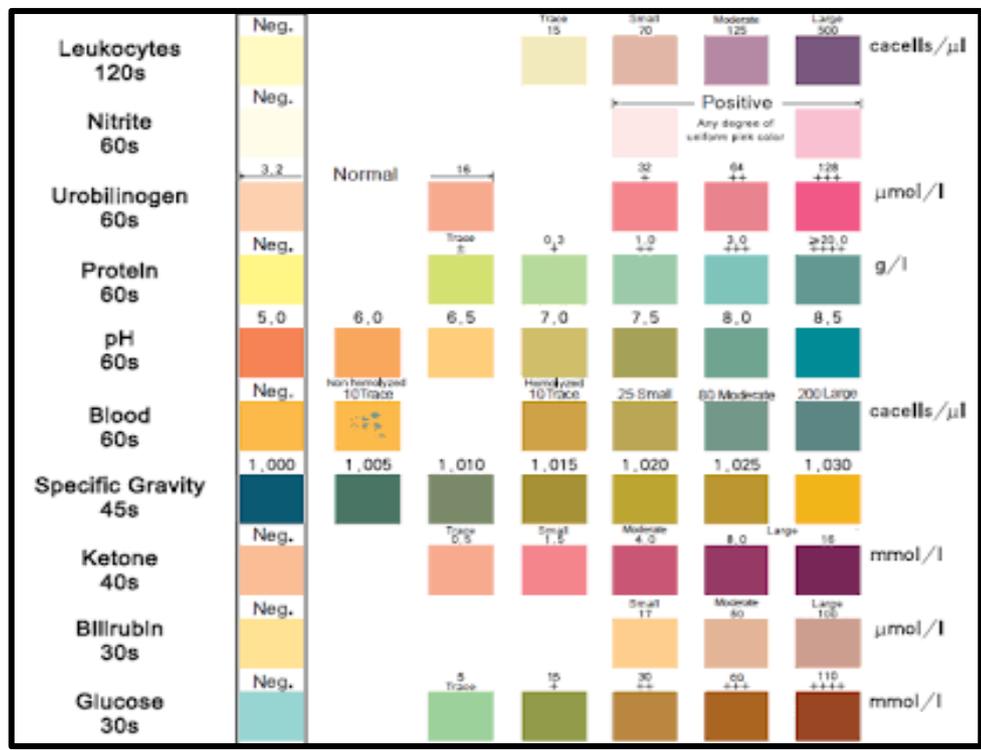


Plate 4: Showing parameters of dipstick

On the basis of growth quantity and purity, the outcomes of the culture were categorised. A cut off (10^5 cfu/mL) was taken as significant above which the organisms is more likely to be a pathogens. A genuine urinary tract infection is more likely to arise over this threshold. the organism in higher number was sub cultivated for cultures that comprised two organisms, one in low

numbers (less than 100 colonies) and the other in high numbers (more than 100 colonies).If more than two organisms were isolated, then further processing was not done since this is highly likely to be a contaminant. Identification and antimicrobial susceptibility testing was done using conventional and vitek -2 automated identification system.

Results:

Table 1: Leucocyte esterase test Versus Culture

		Culture			PPV	NPV
		Positive	Negative	Total		
LE	Positive	168	184	352	47.73%	91.07%
	Negative	40	408	448		
Total		208	592	800		
Sensitivity 81%						
Specificity 69%						

Table 2: Nitrate Test Versus Culture

		Culture			PPV	NPV
		Positive	Negative	Total		
NT	Positive	103	39	142	72.52%	84.04%
	Negative	105	553	658		
Total		208	592	800		
Sensitivity 50%						
Specificity 93%						

Table 3: Leucocyte esterase + Nitrite Test Versus Culture

		Culture			PPV	NPV
		Positive	Negative	Total		
LEU+N IT	Positive	169	20	189	89.42%	93.62%
	Negative	39	572	611		
Total		208	592	800		
Sensitivity 81%						
Specificity 97%						

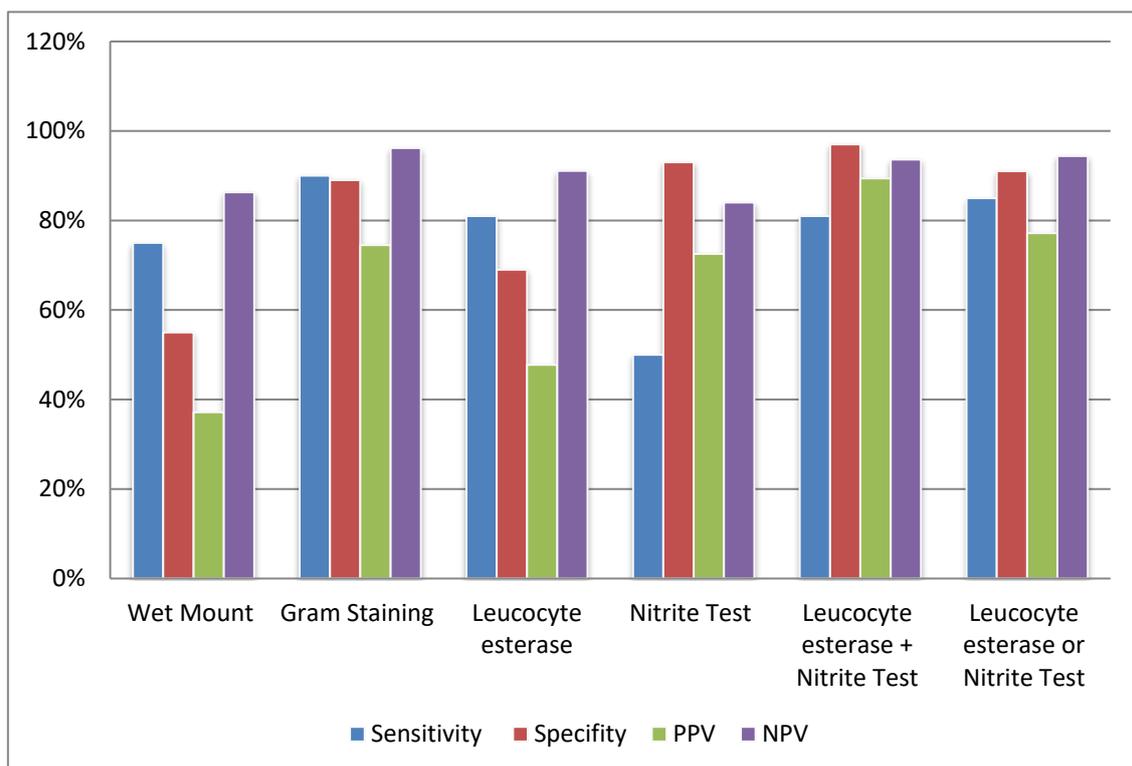


Fig. 1: Reliability of wet mount, gram staining, leucocyte esterase and Nitrite test in laboratory diagnosis of UTI.

Discussion:

Urinary tract infection (UTI) may be diagnosed using urine culture; however this procedure is costly and time-consuming. Using fast diagnostic tests at a hospital may be more efficient and cost-

effective. [15] . In current study leucocyte esterase test of dipstick showed sensitivity, specificity, positive predictive value, negative predictive value of 81%, 69%, 47.73%, 91.07% respectively. A similar study conducted by Little P et al [16] reported sensitivity, specificity, positive

predictive value, and negative predictive value of leucocyte esterase as 89%, 52%, 75% and 72% respectively, also Demilie et al [17] showed the sensitivity and specificity of leukocyte esterase as 50% and 89.1% for pregnant women with asymptomatic UTI (ASB) and 71.4% and 86.7% for symptomatic UTI respectively. Bellazreg F. et al [18] in their study reported leucocyte esterase 87% sensitive and 64% specific. In most of the studies leucocyte esterase test is found to have good sensitivity and higher negative predictive value and hence can be relied on in the diagnosis of urinary tract infection. Nitrite test was found to have 50% sensitivity, 93% specificity 75.52% positive predictive value, and 84.04% negative predictive value, which is in concordance to findings reported by May Mohamed Ali et al [19] who found that sensitivity for nitrite test was 39.3% while specificity and PPV were 87.6% and 74% respectively. In a similar study conducted by Subramanian R et al [20] they reported sensitivity of 36.6%, specificity 99.9%, positive predictive value 98.3%, negative predictive value 87.8% of nitrite test. [21] A study conducted by Evans PJ et al [22] reported nitrite test 83% sensitive and 100% specific. This difference in results may be because of different sample population or different brands of strips used. It may also be because of delay in processing of samples allowing colonizing bacteria to multiply, giving false positive results, or because of drug interference. false negative results of nitrite test can be seen if the causative organism inherently does not reduce nitrates (e.g., *Enterococcus* spp.) [11] The sensitivity of leucocyte esterase test was higher than the nitrite test, which can be explained by the fact that a minimum of 4 hours is required for a pathogenic bacteria to reduce nitrate to nitrite which is unlikely to be positive in the random urine sample so the first morning voided specimen is an ideal specimen for nitrite test. specificity of

leucocyte esterase was lower as compared to nitrite test because leucocyte esterase test (LE) test may be falsely positive due to contamination with squamous epithelial cells or due to effects of preservatives and detergents⁽³⁰⁾. In our study, both leucocyte esterase and nitrite test together showed sensitivity, specificity, positive predictive value, negative predictive value as 81%, 97% 89.42% and 93.62% respectively. Khanna et al [23] reported that combination of both leucocyte esterase and nitrite test had maximum sensitivity of 93.3% with maximum negative predictive value of 98% making reagent strip a good test to rule out UTI. A study conducted by Najeeb S et al [24] has shown that on combining these two dipstick tests sensitivity and specificity increased to 75.74% and 68.90% respectively. They concluded that dipstick tests for the detection of leukocyte esterase and nitrite in urine are sensitive and specific and can be used reliably for the detection of UTI in resource limited setup. Another study by Hiraoka et al [25] found the combined tests to have a sensitivity and negative predictive value of 100%.

The comparison of rapid tests and conventional culture in our study concluded that using the screening methods (dipstick tests) appears to be rational and cost effective approach towards diagnosing urinary tract infection and can be used reliably for the detection of UTI in resource limited setup. The strategy of the pre-screening of urine samples by rapid tests ensures a high diagnostic performance, potential cost savings and also reduces the laboratory workload considerably.

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