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Evaluation of Leukocyte esterase, Nitrite and Blood in urine by dipstick as a point of care test in cases of UTI in a resource limited country.

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Abstract

Urinary Tract Infection is the most common infection encountered in clinical practice. Quick, reliable and cheap methods for diagnosis of UTI is of great importance as it will reduce the misuse of antibiotics and financial burden on the society. We aim to evaluate the reliability of urine dipstick analysis against urine culture which is the gold standard in the diagnosis of UTI. We evaluated 420 urine samples from both outpatient and inpatient departments of our hospital which came into our Bacteriology laboratory for urine culture during one-month duration (March 2019). Urine dipstick analysis was done using Orinasys B10 (ACON Biotech, *Hangzhou*, China) and urine culture was done on CLED medium. The sensitivity of leukocyte esterase alone for positive urine culture was 53.8% followed by blood (50%) and nitrite (42.3%). The sensitivity (80.8%) and negative predictive value (78.3%) was found to be the highest when nitrite, leukocyte esterase and blood were considered together. In a resource limited country like India, nitrite test, leukocyte esterase test and detection of blood can be used to rule out UTI when all three are considered together.

Keywords: Urine dipstick, Urinary Tract Infection, Leukocyte esterase, Nitrite, CLED medium

Introduction

Urinary tract infection (UTI) is amongst the most common infections encountered in clinical practice. There is adequate literature available to suggest that about 50% of all women experience at least one episode of urinary tract infection during their lifetime.[1] In females, anatomical factors play an important role in the pathogenesis of UTI. The shortness of the urethra, with its close relationship to the anus, makes it easy for bacteria to ascend in the urinary tract, thus making *E. coli* the most common causative organism causing this infection.[2]

Because this problem is so common and so significant in routine clinical practice, a high level of diagnostic accuracy is essential which creates a huge economic and administrative burden on the public system. In a study done in the United States stated that about 100 million urinalysis are performed each year at a total cost exceeding half a billion dollars.[3]

For UTI, many diagnostic tests are available but urine culture is the gold standard which takes around 48 hours

and requires well-equipped laboratory and trained staff to give a reliable result. Evidence suggests that about 70-80% of the urine specimens received in a clinical laboratory are found to be free from evidence of infection in the urinary tract. Microbiologists have been trying to identify methods which may be used to rule out such infections clinically, without the need to send these samples for more sophisticated, time consuming and expensive procedures. Various chemical and automated methods have been tried for the detection of the negative specimens, but none has yet been generally accepted as sufficiently reliable.[4]

Many screening procedures (eg urine dipstick analysis) were also developed to quickly identify urine specimens that will be negative on culture and circumvent excessive use of media, technical staff and the overnight incubation period.[5] Rapid diagnosis or exclusion of urinary tract infection is valuable both to the general practitioner and to the hospital physician as it will also decrease unnecessary use of antibiotics.[6] Few studies suggest that negative urine dipstick analysis was found to be valuable in ruling out urinary tract infection.[7]

The reagent strip of the urine dipstick contains tests pad for leukocyte esterase, nitrite, glucose, ketone, pH, blood, specific gravity, bilirubin and urobilinogen. Nitrate reducing enzymes are produced by the most common urinary tract pathogens which reduce nitrate to nitrites. It is used in conjunction with leukocyte esterase which is produced by polymorphonuclear cells. In dipstick analysis, the intensity of the reaction color may diminish with urinary protein excretions >500 mg/dL and urinary glucose >2 mg/dL.[6] However, a negative dipstick in the presence of a strongly suggestive history of UTI cannot reliably rule out an infection in such cases.[8]

This study was conducted to assess the usefulness of leukocyte esterase (LE), nitrate reductase (NIT) and blood (B) in rapidly diagnosing urinary tract infections, thereby providing a cost-effective method for urinalysis.

5. Material and Methods: This was a hospital-based cross-sectional study, purposive sampling was done and the study was carried out in the Department of Microbiology, Uttar Pradesh University of Medical Sciences, Saifai, Etawah (U.P). Patients of both genders, irrespective of their age, suspected of UTI, were included in the study.

We evaluated 420 urine samples from both outpatient and inpatient departments of our hospital which came into our Bacteriology laboratory for urine culture during one-month duration (March 2019). Most of the urine samples included clean catched mid-stream urine and were collected in disposable, sterile, neutral containers with screw lids. Urine culture was done within 2 hours of sample collection. After seeding the urine sample on cysteine-lactose electrolyte deficient (CLED) medium, the sample was transferred to a sterile glass test tube and urine dipstick analysis was done following the manufacturer's instructions. The results of urine dipstick analysis and culture were correlated the next day.

The study was conducted after obtaining institutional ethical committee clearance.

Urine dipstick chemical analysis: Dipstick urinalysis was done using Orinasys B10 (ACON Biotech, *Hangzhou*, China). The reagent strip contained tests pad for leukocyte esterase, nitrite, glucose, ketone, pH, blood, specific gravity, bilirubin and urobilinogen. In our study, the parameters considered were nitrites, leukocyte esterase, pH and blood. After doing culture from the urine sample it was transferred to a sterile glass test tube in which the strip's reagent area was completely immersed and was removed after 2 seconds. The reagent area was compared to the corresponding colour blocks on the canister label at a specified time. Reading time was one minute for nitrites, pH and blood and two minutes for leukocyte esterase. Cut-

off values for a positive result were trace or more for leukocyte esterase, blood (+), nitrite (+) and pH (5-7).

Urine culture: Urine was cultured within 2 hours of specimen collection using CLED agar. The urine was mixed thoroughly, and the plates were inoculated using a calibrated loop of 0.01ml. The culture was read after overnight incubation at 37°C and growth of $\geq 10^5$ colony forming unit (CFU) per ml of urine was considered as culture positive. Cultures with more than two micro-organisms were considered to be contaminated and were excluded from the study. For species identification, different biochemicals (catalase test, oxidase test, urease test, citrate test, etc.) were used. This is the gold standard against which the screening test was compared.

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 23.

Results & 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]

In our study, we evaluated 420 urine samples suspected of causing UTI out of which only 100 (23.8%) showed significant colony count ($\geq 10^5$ CFU/ml) on CLED medium and were considered as culture positive. Out of the total positive patients, 65% were females and 35% were males. The mean age was 32.35 years ranging from 2 years to 95 years.

Table 1: Organisms isolated in urine culture	
E. coli	66%
Klebsiella spp.	10%
Citrobacter	8%
Pseudomonas	6%
Enterococcus	4%
Acinetobacter	3%
Acinetobacter & E. coli	1%
Enterococcus & Citrobacter	1%
E. coli & Citrobacter	1%

Table 1 shows that among the culture positive cases, the most common organism isolated was *E. coli* (66%) followed by Klebsiella spp. (10%), Citrobacter spp. (8%), Pseudomonas spp. (6%), Enterococcus spp. (4%), Acinetobacter spp. (3%). Three percent of the urine samples showed growth of two type of colonies on culture. Cloudiness was seen in 72.8% of the total samples. The mean pH of the urine was 6.17±0.92.

Use of dipsticks as a screening test decreases the cost, and may also help in earlier initiation of treatment. Although culture is the gold standard for diagnosis of UTI, it has some disadvantages. Urine culture takes at least 48 hours, well equipped laboratory and trained staff to give a reliable result. Whereas dipstick tests have the advantage of being rapid and easy to carry out and can be performed even in small laboratories by staff with limited training. In this study, we compared urine culture which is the gold standard for diagnosis of UTI with urine dipstick analysis.

Table 2: Sensitivity, specificity, PPV, NPV, false positive and false negative for screening UTI

Screening test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	False positive (%)	False negative (%)
Nitrite	42.3	79.3	47.8	75.4	52.18	57.69
LE	53.8	55.2	46.15	72.7	65	46.15
Blood	50	56.9	34.2	71.7	65.79	50
Nitrite &/or LE	23.08	91.38	54.55	72.60	45.45	76.92
Nitrite &/or Blood	23.08	87.93		71.83	53.84	76.92
LE &/or Blood	30.77	74.14	34.78	70.49	65.22	69.23
Nitrite &/or LE &/or Blood	80.8	31	34.4	78.3	65.57	19.23

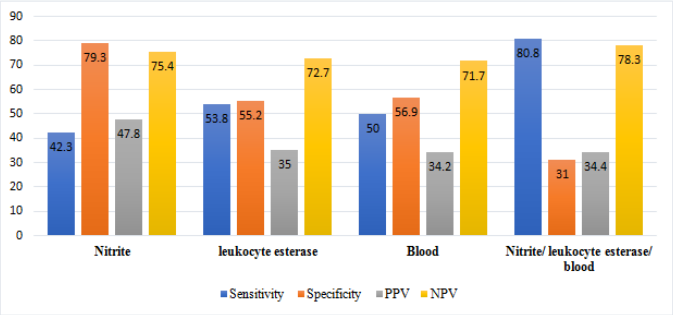

Fig 1: Sensitivity, specificity, PPV and NPV for screening UTI

Table 2 and Fig 1 shows that the sensitivity of leukocyte esterase alone for positive urine culture was 53.8%, which was the highest sensitivity for a single screening test and the least sensitive was nitrite test (42.3%). The sensitivity of blood alone was 50%. The sensitivity (80.8%) and negative predictive value (78.3%) was found to be the highest when nitrite, leukocyte esterase and blood were considered together.

A number of previous studies have shown a correlation between positive LE, NIT and culture results. Fernandes DJ, et al. in their study conducted at Karnataka in 2018 found that the sensitivity of urine dipstick against urine culture for combined nitrite and leukocyte esterase was 31.58%.[10] Another study conducted by Najeeb S, et al. [11]in 2015 at Pakistan, analyzed this sensitivity at 75.74%, whereas our study reported it to be 23.1%.

Mambatta AK, et al. [12] in their study done at Tamil Nadu in 2015 found that the sensitivity of nitrite test, LE and blood was 23.3%, 48.5% and 64% respectively when done alone but increased to 74.2% when all the parameters were taken together, which in our study was 80.8%.

Screening methods are insensitive at levels below 10^5 CFU/mL, therefore are not acceptable for urine specimens collected by suprapubic aspiration, catheterization or cystoscopy and may also fail to detect significant number of infections in symptomatic patients with low colony counts.[5] Results showed that urine dipstick analysis could be considered for rapid analysis of UTI when all the three parameters viz. nitrite, leukocyte esterase and blood were combined together.

Conclusion

Though urine culture remains the gold standard but, in a resource limited setup, where the facility of culture is not available, urine dipstick can be used to rule out urinary tract infection in order to avoid unnecessary use of antimicrobials.

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