Evaluation of Urine Dipstick For Leukocyte Esterase Test For Diagnosis of Urinary Tract Infection
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Abstract

Background: General urine examination (GUE) and urine culture are the most requested tests by clinicians for patients with symptoms suggestive of urinary tract infections (UTI). However, they are laborious methods. So dipstick probably become rapid diagnostic alternative.

Objective: To determine the sensitivity, specificity, positive and negative predictive values of dipstick for leukocyte esterase (LE) test compared with gold standard urine culture for diagnosis of UTI.

Patients and Methods: A total of 150 mid-stream urine samples were collected from adult patient with clinically diagnosed or suspected UTI, during the period from 1st September to 1st December, 2018. Urine culture, general urine examination (GUE) and dipstick for LE were performed for each sample.

Results: In the 150 urine samples, 126 (84%) were culture positive, and the prevalence of UTI among female (84.13%) was significantly higher than the prevalence among males (15.87%). Approximately, half of urine culture grew E.coli 70 (46.67%) followed by Klebsiella spp. 55 (36.67%), and Staphlococcus aureus 1(0.67%). The sensitivity, specificity, positive and negative predictive values of dipstick for LE test were 86.5%, 87.5%, 97.3% and 55.25%, respectively. However, the values can be enhanced by combination with GUE.

Conclusion: Both general urine examination (GUE) and dipstick for leukocyte esterase (LE) methods are with predictive value in diagnosis of UTI. Because urine culture is an expensive and delayed test, rapid test could be a good substitution to reduce the workload and a good screening method.

Keywords: Urine dipstick, Leukocyte esterase, UTI predictor test.

Introduction

Urinary tract infection (UTI) is one of the commonest health conditions in both hospital and the community [1]. Although UTI is encountered at all ages, it has an important association in human female, the highest incidence of UTI occur in child bearing age and this has been linked to sexual activity and aging [2].
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In Iraq, UTI represent a public health problem with impact on quality of life [3,4], and attributed to fetal complications when occurred during pregnancy [5].

Urinalysis and urine culture are the most requested tests by clinicians for patients with symptoms suggestive of UTI, such as dysuria, urinary incontinence and hematuria. Although the urine culture is a benchmark to determine presence or absence of UTI, it is an expensive and time-consuming method [6]. The decision about the best screening test of bacteriuria has always been based on the balance between the cost of screening and its sensitivity and specificity [7].

In addition, the validity of the laboratory test is crucial in reducing the unnecessary prescription of drug or inappropriate management by determining the individual status [8,9]. Urinary biochemical parameters can be evaluated using the urine dipstick screening test. Although the value of urine dipstick has been questioned, it is an inexpensive and rapid diagnostic alternative, [10,11,12,13]. The dipstick test detects urinary parameters such as glucose, protein, nitrite and leukocyte esterase (LE). Leucocyte esterase is a specific leukocyte protein, its presence in urine indicates pyuria. Nitrates are produced by the bacterial breakdown of dietary nitrates.

Even though not all microorganisms have the ability to reduce nitrate to nitrite, the combination of nitrite and LE in urine may indicate the presence of UTI [14]. Dipstick test therefore, could be a useful qualitative tool for diagnosis of UTI and have the advantage of being easy to perform, requires less time, does not need a highly trained personnel and result can be obtained immediately [15].

Patients and Methods

A total of 150 mid-stream urine samples were collected from adult patient with clinically diagnosed or suspected UTI in sterile, wide-mouth bottle, during the period from 1st September to 1st December, 2018. Culture and non-culture methods for laboratory diagnosis of UTI were done for all cases. The study protocol was approved by University of Diyala/ College of Medicine and verbal informed consent was taken from each participant before enrollment in this study and after explanation of urine collecting methodology.

At the time were the sample was collected, participant were asked to complete a brief questionnaire about demographic information. Urine culture were performed by inoculation of 0.02 μl urine on blood agar and MacConkey agar plates (Himedia, India).

All plates were incubated at 37°C for 24 hours. Bacterial identification was done according to standard bacteriological criteria. Clinically significant bacteriuria was defined as positive if 105 cfu/mL of urine was found. Culture considered as gold standard to assess the performance characteristic of dipstick test. LE tests were examined by insertion of multi-reagents strip(URIPATH-UK) into un-centrifuged samples as manufacturer's instructions. For general urine examination, urine samples were centrifuged at 3000 rpm
for five minutes and the supernatant were discarded. The sediment re-suspended in the remaining liquid was examined under 40 hp in 10 microscopic fields. Pus cell count less than 5 was considered negative. Other findings (RBC, epithelial cells, casts and crystals) were detected.

Thereafter, antimicrobial susceptibility tests of bacterial isolates against 7 clinically usable agents (Nitrofurantoin, Amikacin, Ceftriaxone, Azithromycin, Piperacillin, Amoxicillin and Ofloxacillin) were done by Kirby-Bauer disk diffusion method on Muller Hinton, which was accepted by Clinical and Laboratory Standards Institute (CLSI, 2002), employed it as described by [16].

Statistical analysis
The results accumulated during study period were transformed into computerized database. The SPSS (Statistical Package of Social Science) version 18 was used. Evaluation of the sensitivity, specificity, and positive and negative predictive values were performed. Qualitative parameters are expressed as percentages. Chi square was used for paired and group comparison. Differences were considered significant whenever p-value less than 0.05.

Results
Among the 150 patients included in this study, 122 (81.33%) were females and 28 (18.67%) were males. The results indicated that, significant highest rate of the patients 59 (39.33%) were aged between 25-34 years, followed by 45 (30%) and 22 (14.67%) were between 15-24 and 35-44 years, respectively, Table (1).

Table (1): Demographic description of patients

| Age group | 15-24 | 25-34 | 35-44 | 45-54 | 55-64 | 65-74 | Total |
|-----------|-------|-------|-------|-------|-------|-------|-------|
| Gender    |       |       |       |       |       |       |       |
| Male      | 3     | 10    | 9     | 4     | 1     | 1     | 28    |
|           | (10.7%) | (35.7%) | (32.1%) | (14.28%) | (3.57%) | (3.57%) | (18.67%) |
| Female    | 42    | 49    | 13    | 11    | 5     | 2     | 122   |
|           | (34.4%) | (40.1%) | (10.65%) | (10.65%) | (4.09%) | (1.6%) | (81.33%) |
| Total     | 45    | 59    | 22    | 15    | 6     | 3     | 150   |
|           | (30%) | (39.33%) | (14.67%) | (10%) | (4%) | (2%) | (100%) |

* X^2= 16.304, P-value= 0.000

In Regarding the prevalence of UTI, Table (2) shows the prevalence among females were significantly higher than prevalence of UTI among males.

Table (2): Prevalence of UTI among study groups

| Gender | Positive culture | Percentage % |
|--------|-----------------|--------------|
| Male   | 20              | 15.87%       |
| Female | 106             | 84.13%       |
| Total  | 126             | 100%         |

* X^2 = 16.754 ;P=0.000
Analysis of data recorded in Table (3), revealed that the majority grew E. coli 70 (46.67%), while only one grew Staphylococcus aureus (0.67%). The highest number of true positive results was seen in GUE followed by (123/126) in dipstick test, Table (4).

**Table (3): Frequency of bacterial isolates**

| Type of microorganism | No. of isolates | Percentage % |
|------------------------|-----------------|--------------|
| E. coli                | 70              | 46.67%       |
| Klebsiella             | 55              | 36.67%       |
| S. aureus              | 1               | 0.67%        |

**Table (4): UTI diagnosis by urine culture compared to dipstick and GUE**

| Urine culture | Dipstick leukocyte esterase | GUE |
|---------------|----------------------------|-----|
|               | Positive   | Negative | Total | Positive | Negative | Total |
| Positive      | 109        | 17       | 126   | 123      | 3        | 126   |
| Negative      | 3          | 21       | 24    | 1        | 23       | 24    |
| Total         | 112        | 38       | 150   | 124      | 26       | 150   |

Regarding the reliability of standard dipstick testing for the detection of leukocyte esterase (as a marker of bacteriuria) compared to urine culture (assumed as the gold standard for bacteriuria), Table (5) shows the combination of dipstick testing and GUE has the highest sensitivity 99.67%. However, specificity, positive and negative predictive values of only GUE were the highest 95.8%, 99.19% and 88.46%, respectively. Whereas sensitivity, specificity, positive and negative predictive values of dipstick test were 86.5%, 87.5%, 97.3% and 55.25%, respectively.

**Table (5): Sensitivity, Specificity, Positive Predictive value and Negative predictive value of Dipstick test and GUE**

| Test       | Sensitivity | Specificity | Positive predictive value | Negative predictive value |
|------------|-------------|-------------|---------------------------|----------------------------|
| Dipstick test | 86.5%       | 87.5%       | 97.3%                     | 55.25%                     |
| GUE        | 97.6%       | 95.8%       | 99.19%                    | 88.46%                     |
| Dipstick and GUE | 99.67%    | 83.82%      | 98.09%                    | 62.45%                     |

**Discussion**

Urinary tract infection is one of the most common types of bacterial infections and account for a significant part of the workload in clinical microbiology laboratories. In fact, in many clinical laboratories, urine cultures are the most common type of culture, as well as being an expensive and time-consuming
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The present study indicates that the prevalence of UTI in female was significantly higher (84.13%) than males (15.87%). The current results actually not surprising since there were numerous studies have indicated that UTIs occur more often in female than male at a ratio of 8:1 [17, 18]. The high rate of UTI in female may be attributed to short urethra and its close proximity to anus and vagina, sexual contact, hormonal changes, as well as vaginal microbial flora that play a critical role in encouraging vaginal colonization with coliforms.

The predominant rate of UTI in females (40.1%) was in the age group 25-34 years, followed by (34.4%) in age group 15-24 years. Almost similar results were reported by other workers [17, 18, 19]. This may actually reflecting the relationship between sexual activity and UTI, especially that the age of marriage in Iraq ranges between 15-35 years.

As it expected the predominant bacterial isolate was E. coli with frequency of (46.67%, 70/126). Despite of this rates was inconsistent with previous international studies, which reported superiority of E. coli in > 85% of UTI. However, our results agree with other local studies [18, 20].

Surprisingly, the frequency (36.67%, 55/126) of Klebsiella spp. was very high compared to previous local and international studies [18,20,21,22]. A reasonable explanation is that the local isolate are probably becoming more virulent.

Numerous studies discuss the utility of dipstick for LE individually or in combination to other markers to indicate the presence of UTI, the challenge comes with interpretation since gold standard continues to be the delayed urine culture. In the current study, the sensitivity (86.5%) of dipstick was slightly lower than specificity (87.5%), whereas, the positive predictive value was high (97.3%). Although, the values still less than GUE, but almost acceptable and can be enhanced by combination to GUE. However, dipstick method is considered as useful alternative when microscopy is not feasible. Our results are inconsistent with Alsamarai, [18], but relatively comparable with Memişoğlu, [6].

In antibiotic resistant era, the wise use of antibiotic necessitate the medical provider to decide based on rapid test results treating the patient or wait for the culture result. Prior research results suggest that dipstick for LE has been found to improve diagnostic accuracy above clinical assessment alone [23]. In addition, this methodology is simple and relatively inexpensive, for GUE which is a more laborious test and must be performed by trained professionals.

Conclusions

The study has suggested that both urinalysis and dipstick for LE methods are predictive in diagnosis of UTI and when interpreted in combination. Because urine culture is an expensive test particularly in institutions and settings with limited resources, rapid tests such as dipstick for LE may be used for rapid diagnosis and urine
screening, especially in childhood and pregnancy. Specifically, the results can be applied in primary healthcare centers in rural areas where microscopy is not readily available, experiencing power outage, and symptoms are vague. Therefore, unnecessary antibiotic prescriptions will reduced.

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