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Validity of the urinary dipstick test in the diagnosis of urinary tract infections in adults

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ABSTRACT

INTRODUCTION. Utility of dipstick analysis must be investigated in patients admitted to the emergency department. The aim of this study was to evaluate if urine dipstick analysis can be used to detect significant bacteriuria. The cross-sectional study was performed in the Emergency Department of Copenhagen University Hospital – Herlev Hospital, Denmark.

METHODS. We recorded urine dipstick analysis of 500 adult patients admitted to the Emergency Department. Dipstick results were compared with urinary culture.

RESULTS. Sensitivity for leukocyte esterase (LE) was 80.9%, but specificity was 58%. The sensitivity of nitrite was 46.5%, and specificity was 90%. The positive predictive value (PPV) and negative predictive value (NPV) of LE for women were 54.5% and 75.9%; for men, 50.0% and 91.6%. PPV and NPV for nitrite in women were 85.9% and 66.8%; for men, 62.9% and 88.7%. Positive LE and positive nitrite had a PPV of 90.2% for women and 70.4% for men. Negative LE and negative nitrite had an NPV of 80.9% for women and 93.3% for men.

CONCLUSIONS. No single parameter or combination of parameters on the urine dipstick analysis can be used reliably to predict positive urine culture in women. The most accurate predictor of negative urine culture in men is the combination of negative nitrites and negative LE. To minimize unnecessary use of antibiotics, treatment can be delayed in female patients with positive urine dipstick until urine culture results are available.

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Urinary tract infections (UTI) are a common cause of referral to the emergency department (ED) and hospitalisation. UTI account for 21.2% of hospital-acquired infections [1]. The prevalence of UTI among females in the ED setting has been found to vary from 40% to 60% [2]. UTI diagnosis is based on clinical symptoms supported by urinalysis and urine culture findings. The clinical symptoms lack sensitivity and are often absent in elderly patients [3, 4]. This is a clinical challenge since elderly patients may have unspecific symptoms due to other reasons. Positive urine culture has been found to be only slightly higher in elderly patients with vague symptoms attributable to UTI than in patients treated for other diagnoses, which suggests that a positive urine culture may reflect asymptomatic bacteriuria rather than UTI [4]. Urine culture provides clinicians with information about the pathogen and any antibiotic resistance. This method is, however, costly, labour intense and requires at least 24 hours before results are known. Extensive use of antibiotics has increased antibiotics resistance, which was identified in 20% of laboratory specimens in the UK [5]. The urine dipstick analysis is an

inexpensive and rapid testing method used extensively in the ED worldwide. If dipstick urine analysis could be used to guide further diagnostics and antibiotic treatment, this may considerably reduce laboratory workload and decrease unnecessary use of antibiotics. This study aimed to evaluate whether urine dipstick analysis may determine bacteriuria. Several other articles have tested the urine dipstick, but most only studied female or male populations [5, 6] and had small sample sizes [4, 7, 8].

METHODS

This was a cross-sectional study performed in the ED of Copenhagen University Hospital – Herlev Hospital, Denmark. The inclusion period started on 15 September 2019 and concluded on 16 November 2019. This was a quality control study; no changes were made in the treatment or diagnosis of any patients; and permission from the local Ethical Committee was not required. Patient characteristics were obtained from electronic patient files. We evaluated the urine dipstick analyses of 500 patients who had performed a urine culture while admitted to the Internal Medicine Emergency Department. The author screened patient files from the patients admitted to the emergency department both with symptoms suggestive of UTI and with non-specific symptoms (fever, dehydration, dyspnoea, malaise) as it is known that especially elderly patients often present with atypical symptoms [2, 4, 9]. Consecutive adults (≥ 18 years) with data on urine dipstick analysis and urine culture were included in the study. Patients with indwelling catheters were excluded. Preferably, midstream urine samples were collected by an emergency nurse who performed a dipstick analysis, which was read automatically with the urinalysis analyser Siemens Clinitek Status +®.

Subsequently, the urine culture was processed during 24 hours in the Microbiology Department. Laboratory technicians were not blinded to the results of urine dipstick analysis. The gold standard of microbiologically confirmed UTI diagnosis is growth of uropathogen in the urine culture. Significant bacteriuria was defined as growth of a minimum of 10^3 colony-forming units per ml (cfu/ml) for primary uropathogens such as *Escherichia coli* and *Staphylococcus saprophyticus* and > 10^4 cfu/ml for the secondary uropathogens *Enterococcus species (*spp.), *Klebsiella* spp. and *Pseudomonas aeruginosa,* which was used to compare the results of dipstick analysis.

Only the presence of primary and secondary uropathogens in the urine culture as defined by the European Guideline for Urinalysis counted as positive urine culture [10]. Used test strips showed a range of leukocyte esterase (LE) concentrations from 0 to 4+. LE > 0+ was counted as positive. Nitrite reaction on dipsticks was categorised as either present or absent. The sample size for the present study was estimated by Buderer's formula, considering the following assumptions: expected sensitivity for LE 0.80, expected specificity for LE 0.60, prevalence of bacteriuria 0.35, precision 0.07 and confidence level 95%. LE sample size was calculated to 359. For nitrites, the following was assumed: sensitivity 0.45, specificity 0.85, prevalence 0.35, precision 0.07 and a confidence level of 95%. The sample size for nitrite was 538 [11]. Assumptions were based on existing literature analysed prior to the study. Two-by-two tables were constructed to calculate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of LE, nitrite and a combination of both those parameters using standard formulas against urine culture. The prevalence of bacteriuria in the study population was also calculated.

Trial registration: not relevant.

RESULTS

Table 1 shows study subjects. This study population was characterised by a preponderance of women (66.8%).

The mean age for women and men was 64 (18-101 years) and 70 (19-94 years), respectively. A total of 187 patients had a positive urine culture, corresponding to a prevalence of 37.6% within the study population. Positive urine culture was found in 44% of women and in 24% of men. In all, 116 (34.7%) women and 38 (22.9%) men had urinary symptoms, and the most frequent symptoms were pollakiuria, dysuria and abdominal pain. Overall, LE sensitivity was 80.9%, whereas specificity was only 58%. The sensitivity of nitrite was 46.5% and the specificity was 90%. Due to the difference in the prevalence of bacteriuria for each gender, the PPV and NPV were calculated separately for men and women. The PPV and NPV for LE for women were 54.5% and 75.9%, respectively; 50.0% and 91.6% for men, respectively. PPV and NPV for nitrite in women were 85.9% and 66.8%, respectively; 62.9% and 88.7% for men, respectively. Positive LE combined with positive nitrite had a PPV of 90.2% for women and 70.4% for men. A negative LE combined with negative nitrite had a NPV of 80.9% for women and 93.3 % for men (**Table 2**).

TABLE 1 Study subjects and urine test results.

	Males	Females
Age, yrs, mean (range)	70 (19-94)	64 (18-101)
Subjects, n	166	334
Positive culture, n	39	148
Positive nitrite, n	42	76
Positive leukocyte esterase, n	60	223
Symptoms, n	38	116
Symptoms, positive culture, n	15	68

TABLE 2 Study results of dipstick urine analysis. The values are %.

	Nitrite	Leukocyte esterase	Nitrite and leukocyte esterase	
			positive	negative
Sensitivity	46.5	80.9	-	-
Specificity	90	58	-	-
Females				
PPV	85.9	54.5	90.2	-
NPV	66.8	75.9	-	80.9
Males				
PPV	85.9	50.0	70.4	-
NPV	88.7	91.6	-	93.3

NPV = negative predictive value; PPV = positive predictive value.

DISCUSSION

This study showed a moderate sensitivity and a low specificity of LE in the dipstick urine analysis. Conversely, nitrites had a low sensitivity and a high specificity. The low specificity of LE may be attributed to the fact that leukocytes can be present in the urine in various other conditions, as for example, vulvovaginitis, urethritis, urinary lithiasis and diabetes mellitus, which may contribute to false positive results [3, 12]. The NPV for LE in women was 75.9%. Together with the moderate sensitivity of LE, this means that LE cannot be used to exclude a suspected UTI. The NPV for LE for men was higher at 91.6% and may be used to rule out significant bacteriuria. The nitrite test detects nitrate-reducing bacteria. Nitrate-reducing bacteria include all the *Enterobacteriaceae* and most of the non-fermenters, but *Candida* and streptococci including enterococci do not reduce nitrates [12]. A negative nitrite test in patients with positive urine culture may be found when a UTI is caused by a microorganism that does not contain nitrite reductase. In the present study, this occurred in 100 patients corresponding to 54% of the patients with a positive urine culture. Furthermore, at least four hours are required for the bacteria to reduce nitrate to nitrite, and frequent urination during UTI can lead to false negative results [3].

This may explain the low sensitivity of nitrites found in our study. Owing to its high specificity and moderately high NPV, nitrite may be used to rule out bacteriuria in men, but not in women. Combining positive LE and nitrites on dipstick analysis produced a high PPV (90.2%) for women, which may be used to rule in a possible bacteriuria. However, this combination cannot be used for men. The combination of a negative LE and nitrites on dipstick analysis yields a moderate NPV for women and a high NPV for men (93.3%), which may be used to rule out bacteriuria. Laboratory technicians were not blinded to the results of the dipstick analysis, and they might be prone to assigning a positive urine culture to a patient with a positive dipstick analysis, leading to false

positive results. The clinical value of the urine dipstick remains debated since various studies have provided somewhat conflicting evidence about its use. Gieteling et al. [7] studied the use of urine dipstick in an ED setting. They found that urine dipstick analysis could not be used in the diagnosis of UTI, but positive nitrites could be utilised to rule in a urinary infection.

A review by Meister et al. [2] concluded that no single test or combination of tests based on dipstick analysis could be used to reliably exclude urinary infection in symptomatic female patients. Eidelman et al. [8] did not find any parameter in dipstick analysis that was sufficiently sensitive to exclude UTI in high-risk populations in the ED. Furthermore, Ducharme et al. [4] found that the reagent strip was not accurate enough to identify UTI in elderly patients in the ED setting. A meta-analysis by Devillé et al. [13] concluded, however, that dipstick analysis was highly sensitive and that a negative LE and nitrites could exclude UTI in study populations with a high pre-test probability of UTI. Additionally, a retrospective study by Marques et al. [14] found that negative urine culture could be predicted by negative nitrite and leukocyte urine dipstick analysis. Finally, a review by Little et al. [5] suggested targeting antibiotic treatment by positive leukocytes and nitrites as a good predictor of UTI.

The conclusions in our study with respect to the sensitivity and specificity for LE are in accordance with those of the above-mentioned studies. The sensitivity of LE spanned from 59% to 89%, and the specificity was found to fall in the 64-95% range; sensitivity of nitrites varied from 28% to 48% and specificity from 64% to 99% [3, 7, 8, 14, 15]. This may be attributed to the wide heterogeneity of the studies, including different cut-off values for the dipstick analysis, reference standards for UTI, patient inclusion criteria (only male or female study population, ED or general practice) and study designs. These differences limit comparability between studies. A positive urine culture does not always represent UTI. Differentiating UTI from asymptomatic bacteriuria is important as it may contribute to diminishing unnecessary antibiotic treatment.

Strengths and limitations

One of the strengths of this study was its large sample size, which improves the statistical power of our findings. The study population represents a typical patient group admitted to the ED, mimicking the average patient mix in the ED in most countries. Furthermore, specific exclusion criteria were described precisely. One possible limitation is the retrospective study design, which introduces several biases. We cannot exclude that this study may have enrolled patients with asymptomatic bacteriuria and not UTI. Data were collected retrospectively. Thus, information about how urine samples were collected is lacking. Urine samples from the entire container may be contaminated with leukocytes, which can contribute to false positive LE results.

CONCLUSIONS

Our study showed that a negative LE in urine dipstick analysis cannot be used to exclude bacteriuria in female patients in the ED. Conversely, a negative LE in men may be used to rule out bacteriuria. The combination of positive LE and nitrite in urine dipstick analysis may be used to rule in bacteriuria in women, but not in men. Negative nitrites may be used to predict a negative urine culture in men owing to their high specificity and relatively high NPV, but not in women. The diagnostic accuracy of ruling out bacteriuria is further strengthened by combining negative leukocyte and nitrites, which results in high NPV for men, but less so in women. No single test or combination of tests on dipstick analysis may be used to reliably detect bacteriuria in women, and diagnosis of UTI in females must always be confirmed by a urine culture. Urinary dipstick analysis must not be used unselectively due to the risk of over-treating patients with asymptomatic bacteriuria. In sum, urinary dipstick analysis cannot be used to reliably guide further treatment of suspected UTI in all ED patients.

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