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Evaluating the diagnostic value of nitrite test in comparison with U/S results in patients with urinary tract infection symptoms: A cross-sectional study

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Abstract

Objective: The purpose of this study is to evaluate the diagnostic value of nitrite test in comparison with urine culture (U/C) results in patients with Urinary tract infection (UTI) symptoms.

Methods: This cross-sectional study was performed on 203 patients with UTI symptoms. Middle urine sample was taken into sterile plastic containers, and simultaneously the urine sample and the nitrite test were done by the use of urine dipstick test. Data were analyzed using SPSS software version 23.

Results: The results of the urine culture test indicated that the highest excreted organisms in both sexes were *E. coli* (58.8%), *Candida* (17.6%), *Klebsiella* (8.8%), *E. coli* (MDR) (5.9%), *Pseudomonas* (2.9%), *Enterococcus* (2.9%) and *Acinetobacter* (2.9%). The results showed that there was a significant correlation between U/C and urine analysis (U/A) test results ($P = 0.01$), and in U/C positive results, U/A results were significantly positive for UTI. Other findings showed a significant relationship between the results of nitrite one and nitrite two tests ($P = 0.001$). There was a significant correlation between urinary, and nitrite1 levels ($P = 0.04$). Also, in this study, the sensitivity and specificity of diagnostic tests for U/A and nitrite 1 and 2 with U/C were calculated as the Golden Standard method.

Conclusion: Overall, the results of this study showed that the negative nitrite test and urine dipstick test could be performed in emergency cases to prevent ectopic dysfunction and inadequate diagnosis. Also, it can reduce the unreasonable expenses for U/A.

Keywords: Urinary tract infection, Urine culture, Nitrite test, Urine analysis test

Introduction

Urinary tract infections (UTIs) include a clinical spectrum of bacterial absence in the urine to severe kidney infections and infections caused by it. About 150 million people die due to UTI every year (1). UTIs are one of the main causes of nosocomial infections (2-4) and also one of the most common infections in all age groups. Lack of diagnosis and timely treatment can cause severe complications such as urinary tract disorders, blood pressure, Uremia, and in pregnant women may cause premature labor and even abortion (2-4). The increased risk of UTI in pregnant women, patients with injured spinal cord, diabetic patients, patients with sclerosis, and subsequent use of urinary catheters and AIDS were reported more than others (2,4). The disease is more common in women than in men, and the rate of infection in women is sometimes reported to be threefold higher than men. However, half of the female population is infected with this disease at least once in their lives (2). The studies conducted in different communities in the world show that most of the etiologic factors of UTI are intestinal bacteria (Enterobacteriaceae family), among which the most common is *Escherichia coli* (4). Also, many other bacteria including gram-positive species, viruses, and even fungi are able to contribute to it (5). The most important symptoms that support UTI are the presence of 10 leukocytes in 1 mL of urine and nitrite in urine analysis (U/A) (3,6). However, several studies have identified the presence of the two above-mentioned factors in urine as a desirable marker for bacteriuria, but evidence shows that urine culture and the determination of antibiotics susceptible into isolated species are necessary (7-10). Although urinary culture helps to detect bacteria, it is a costly and time-consuming process, and at least 24 hours of time is needed to identify the microorganisms grown in the culture sample. On the other hand, there are studies that demonstrate unnecessary urinary culture demands, and effective screening tests before urinating urine can prevent waste of time, cost and unnecessary drug

treatments. In this study, we sought a solution that could be a better alternative to urinary culture for the diagnosis of UTIs, so that it could be achieved faster by this method and begin the treatment as soon as possible for patients with UTI symptoms. Another reason for this study was to conduct an emergency nitrite test on the urine specimen of patients before sending it to the laboratory and comparing its results with the results of laboratory test nitrite.

Methods

In this cross-sectional study, the statistical population was 203 patients referring to Imam Reza hospital in Mashhad in 2018.

Inclusion criteria encompassed patients with UTI symptoms who were over 16 years of age. Exclusion criteria were patients who had Gross hematuria, patients with Foley catheter, urinary system anomalies, pregnant women, patients who had a history of antibiotic use in the past month before giving a sample, cases in which the sampling was done inappropriately and patients who did not consent to participate in the study.

After explaining the research plan for eligible people and obtaining informed consent in order to collect samples, patients were asked to wash and dry their external genitals before urinating. Then, Middle urine sample (Mid-stream) was taken from these patients in a sterile plastic container, and at the same time nitrite testing was performed. Dipstick and results can show blood or hemoglobin, urobilinogen, bilirubin, protein, nitrite, ketone, glucose, leukocyte specific gravity and PH. Subsequently, the samples were sent to the laboratory for urine analysis and urine culture, and then the results were extracted separately and compared.

The information was completed and analyzed by SPSS software version 23. Data were analyzed using chi-square or Fisher exact tests as well as independent samples test. The statistical significance level was considered 5%.

Results

In this study, 203 patients including 104 males (51.2%) and 99 women (48.8%) referred to the emergency department of Imam Reza hospital in Mashhad during 2018. The mean age of patients was 57 years (range of 16 years and older). Also, 50 patients (24.8%) had diabetes mellitus, and 153 patients (75.2%) had no diabetes mellitus. The results showed that there was a significant difference between the mean age of the patients with the outcome of positive and negative urine culture test ($P=0.002$), and the mean age of patients with positive urine culture was higher than the mean age of patients with urinary culture (Table 1).

The results of urine test showed that the highest excreted organisms in both genders were *E. coli* (58.8%), *Candida* (17.6%), *Klebsiella* (8.8%), *E. coli* (MDR) (5.9%), *Pseudomonas* (2.9%), *Enterococcus* (2.9%) and *Acinetobacter* (2.9%) (Figure 1).

The results of urine culture test showed 16.7% positive and 83.3% negative U/C. Also, the results of urine analysis showed 19.30% positive and 80.7% negative U/A. The results of the statistical test revealed that there was a significant correlation between urinary culture and urine analysis ($P = 0.01$), indicating that U/A was more positive than urinary culture, so that 46.2% of those who had U/A positive; their cultivation was positive; compared with 9.2% of U/A patients who had a positive culture result. Therefore urinary analysis results were significantly positive for UTI (Table 2).

Other results also showed that there was a significant relationship between urinary culture and positive or negative variables of diabetes mellitus ($P=0.01$), bacteria ($P=0.01$), WBC ($P=0.01$), nitrite 1 ($P=0.01$) and nitrite 2 ($P=0.005$), but there was no significant relationship between urine culture with gender ($P=0.3$) and positive or negative RBC ($P=0.1$) (Table 3). Also, there was a significant relationship between the results of nitrite 1 and

Table 1. Mean and standard deviation of age in patients with positive and negative urine culture (U/C)

U/C	Positive	Negative	*P* value
Age	63.21±16.39	52.29±21.85	0.002

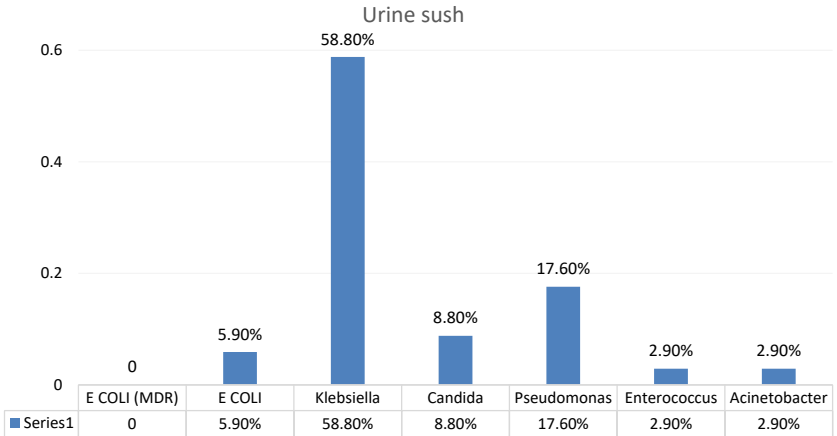

Figure 1. Distribution of urinary tract infections.

Table 2. Relationship between urine culture (U/C) and urine analysis (U/A)

U/A	U/C		*P* value
	Positive	Negative	
	No. (%)	No. (%)	
Positive	18 (46.2)	21 (53.8)	
Negative	15 (9.2)	148 (90.8)	0.01
Total	33 (16.3)	169 (83.7)	

nitrite 2 tests ($P=0.001$). Other results indicated that there was no significant correlation between urinary tract and RBC levels ($P=0.7$), WBC ($P=0.3$), nitrite 2 ($P=0.9$) and bacteria ($P=0.2$). But there was a significant correlation between urinary flow and nitrite 1 levels ($P=0.04$).
Also, in the present study, the sensitivity and specificity of diagnostic tests for urine analysis and nitrite 1 and 2 with urinary culture were calculated as gold standard method. The results showed that urinary analysis included 54% sensitivity and 87% specificity. In addition, nitrite 1 included 20% sensitivity and 97% specificity, and nitrite 2 included 20% sensitivity and 94% specificity (Table 4).

Discussion

The aim of this study was to evaluate the diagnostic value of nitrite test in comparison with urinary culture results in patients with UTI symptoms. Contrary to other studies indicating that women are more likely than men to have UTI (7-10), in this study the ratio between men and women was almost the same and with little difference in favor of men. This contradiction is due to the fact that men in our study have become important and more concerned with UTIs or because of the prevalence of UTIs in women and past experiences in this area, women are more likely to self-medication. Also, according to other literature in this field, at the age of less than one year and more than 50 years, UTIs are more common in male than female (2). In this study, the average age of patients is more than 50 years old. Other results showed that there was a significant difference between the mean age of the patients with the positive and the negative test ($P = 0.002$) and the mean age of the patients with positive urine culture was higher than the mean age of the patients with negative urine culture. The results of urine test showed that the highest excreted organisms in both genders were *E. coli* (58.8%), *Candida* (17.6%), Klebsiella (8.8%), *E. coli* (MDR) (5.9%), *Pseudomonas* (2.9%), *Enterococcus* (2.9%), and *Acinetobacter* (2.9%). The results of this study indicated that the majority of isolated bacteria were related to the antibiotic family, which is consistent with other reports (7-10). The study by Platt in the United States indicated that antibiotics are responsible for 90% of UTIs (11). A report published by the UK Health Center showed that the prevalence of *E. coli* in outpatients is 80% and in hospitals is 40% (12). It seems that the cause of the abundance of *E. coli* in the development of the UTI is its presence in the intestine and its ability to stick with the Fimbriae to the mucous membranes of the ureter (2). Besides, this bacterium exhibits topical resistance to IgA in the ureter and neutralizes its effect as a strong bactericide (13,14). After *E. coli*, *Klebsiella, Proteus,* and *Enterobacter* are the most important causes of UTIs (7-10). In the present study, the frequency of urinary tract pathogens in

Table 3. Evaluation of the relationship between urine culture result and gender, diabetes mellitus, bacteria, RBC, WBC, nitrite 1 and nitrite 2

		Urine Culture		*P* value
		Positive	Negative	
Bacteria	Positive	29 (31.5)	62 (68.5)	<0.01
	Negative	5 (4.5)	106 (95.5)	
	Total	34 (16.7)	169 (83.3)	
RBC	Positive	18 (20.7)	69 (79.3)	0.1
	Negative	16 (13.8)	100 (86.2)	
	Total	34 (16.7)	169 (83.3)	
WBC	Positive	22 (23.7)	71 (76.3)	0.01
	Negative	12 (10.9)	98 (89.1)	
	Total	34 (16.7)	169 (83.3)	
Nitrite 1	Positive	7 (58.3)	5 (41.7)	0.01
	Negative	27 (14.1)	164 (85.9)	
	Total	34 (16.7)	169 (83.3)	
Nitrite 2	Positive	7 (41.2)	10 (58.8)	0.005
	Negative	27 (14.5)	159 (85.5)	
	Total	34 (16.7)	169 (83.3)	
Gender	Male	15 (14.4)	89 (85.6)	0.3
	Female	19 (19.2)	80 (80.8)	
	Total	34 (16.7)	169 (83.3)	
Diabetes mellitus	Have not	16 (10.5)	136 (89.5)	< 0.01
	Have	17 (34)	33 (66)	
	Total	33 (16.3)	169 (83.7)	

Table 4. Sensitivity and specificity of the diagnostic method of urinalysis

		Urine Culture		
		Positive	Negative	Total
Urinalysis	Positive	18	21	39
	Negative	15	148	163
	Total	33	169	202
Nitrite 1	Positive	7	5	12
	Negative	27	164	191
	Total	34	169	203
Nitrite 2	Positive	7	10	17
	Negative	27	159	186
	Total	34	169	203

Sensitivity Urinalysis = 18/33 = 54%, specificity Urinalysis = 148/169 = 87%
Sensitivity Nitrite 1= 7/34 = 20%, specificity Nitrite 1= 164/169 = 97%.
Sensitivity Nitrite 2= 7/34 = 20%, specificity Nitrite 2= 159/169 = 94%.

positive urine culture showed that 20 (58.80%) cases were *E. coli* and 6 (17.60%) cases were *Candida*. Also, in the present study, the sensitivity and specificity of diagnostic tests for urine analysis and nitrite 1 and 2 with urinary culture were calculated as the standard golden method. The results showed that urinary analysis included 54% sensitivity and 87% specificity. Also, nitrite 1 encompassed 20% sensitivity and 97% specificity, and nitrite 2 included 20% sensitivity and 94% specificity. Kayalp et al studied the effectiveness of urine analysis in reducing the urinary culture demands in a study on the results of urine analysis and culture of 32998 patients. In general, 758 (2.3%) patients had positive urine culture. Of the positive urine culture samples, the ratio of results for leukocyte esterase and nitrite was 71% (n = 538) and 17.7% (n = 134), respectively. Additionally, the results of the positive microscopic analysis for WBC and bacteria were 68.2% (517 people) and 78.8% (597 people), respectively. But the negative predictive value of leukocyte esterase, nitrite, bacteriuria and WBC was close to 100%. Finally, it was concluded that in most of the samples, no bacteria had grown, and dipstick and microscopic urine analysis can well reject UTI, and urine analysis is a more feasible and faster screening method (15). In our study, the findings showed 87% urine analysis and 97% nitrite 1 and 2 respectively. Lenke and Van Dorsten studied the effectiveness of nitrite test and microscopic U/A in predicting urination results in a study in the United States. They examined 146 urine cultures in which 111 were negative cultures, 18 positive cultures, and 17 infected cultures. Nitrites were not detectable in negative or contaminated culture. Pyuria was also present in 14% of the negative cultures and 24% of the infected cultures. Of the 18 positive cultures, nitrite was found to be 22%, Bacillus 61%, and Pyuria 67%. They asserted that positive culture cannot be accurately predicted by microscopic analysis and nitrite dip-steak, and urinary culture should be analyzed as part of the evaluation of UTI (16). Based on our results, the sensitivity of the diagnostic tests for urine analysis was 54%, and sensitivity of nitrite 1 and 2 was 20%. This confirms the inability of these tests to detect positive cases of UTI. This is in line with the study conducted by Lenke and Van Dorsten. Also, the findings of the present study did not find any significant correlation between nitrite urine 2 levels and urine output, which is also confirmed by the studies conducted by Lenke and Van Dorsten in the United States (16). Najeeb et al conducted a comparative study between urine specimen diabetic test and urinary culture for diagnosis of UTI. Of the 300 samples studied, 136 had the positive urine culture, and 164 had the negative urine culture. Out of 136 cases with positive cultures, 103 cases had positive dip-stick, and 33 cases had negative dip-stick. Sensitivity, specificity, positive predictive value and negative predictive value of both nitrite and leukocyte esterase tests were 75.7%, 68.9%, 66.6% and 77.4%, respectively, concerning the culture of urine as a standard golden method. Finally, results showed that the dip-stick test was sensitive and specific for the diagnosis of esterase and nitrite leukocytes and can be used to diagnose UTIs (17). This finding contradicts with the results of our study. In the Ninama and Shah's study, out of 1000 urine specimens of patients, 186 cases (18.6%) had significant bacterial culture. Sensitivity and specificity of bacterial microscopic urine were 96.7%, and 98.5%, respectively. While in the dip-stick test, the sensitivity and specificity of the nitrite test were 90% and 97%, in the leukocyte esterase test, they were 87%, and 95%, respectively. The sensitivity and specificity of Catalase test for bacteriuria were 88.6%, and 75.8%, as well. Finally, it was concluded that dip-stick test could be used as a very effective method in areas where microscopic examination and urinary culture tests are not available for the diagnosis of UTIs (18). Our study on the effect of the dip-stick test is in contradiction with Ninama study. Therefore, there are many contradictory findings regarding the use of diagnostic tests for urine analysis and nitrite in the diagnosis of UTIs in patients and further studies are needed in this regard. Overall, the purpose of this study was to find a solution that could be a better alternative to urinary culture for the diagnosis of UTIs, so that it can be achieved faster by this method and begin treatment as soon as possible for patients with UTI symptoms. Another reason for this study was to perform an emergency nitrite test on the patient's urine specimen before sending it to the lab and comparing its results with the results of the nitrite lab test. Overall, the results of this study and its comparison with other studies showed that the negative effects of nitrite test and urine dip perspiration test could detect in emergency cases, to avoid misleading and inappropriate diagnosis. Regarding the treatment of patients based on clinical signs and urine analysis results, regardless of urinary culture, it should be noted that, urine analysis parameters cannot confirm the UTI by one hundred percent. Thus, the proper treatment of the patients and prevention of unnecessary antibiotic use, in addition to its complications, also causes bacterial resistance. For a definitive diagnosis, urine analysis should be considered as a golden standard along with urine analysis. Finally, it is suggested that further studies be done to confirm the findings of this study. There is also a need for further studies on the impact of factors affecting the results for future research. Also, due to the wide area of the country and the prevalence of various infections, more investigations are needed to evaluate the correlation between the test results and the type of bacteria.

Limitations

This study has its own limitations. First, we conducted this study in a single center. In this regard, it is evident that generalizability of the results can be reduced. Another limitation of this study was the average age of patients.

Conclusion

In general, the results of this study and its comparison with previous researches showed that the negative nitrite test and urine dipstick test could detect emergency cases, prevent misuse and misdiagnosis, and also unreasonable expenses for U/A can be reduced.

Authors' contribution

Concept and design of study, acquisition of data, analysis and interpretation of data: (HZM, FM, ME, MF). Drafting the article or revising it critically for important intellectual content: (HZM, FM, ME, MF).

Ethical issues

This research was approved by the Committee on Organizational Ethics of the Faculty of Medical Sciences of Mashhad (IR.MUMS.FM.REC.1395.638).

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