



Original Article: Can Total Urine Analysis Predict Urine Culture Result?

Mehmet Zeynel Keskin* MD, Yusuf Özlem İlbey MD

Department of Urology, Tepecik Training and Research Hospital, Izmir, Turkey

***Corresponding Author:** Mehmet Zeynel Keskin, Tepecik Training and Research Hospital, Yenisehir Mah, Gaziler Cad. No: 468, 35180, Konak/Izmir/Turkey, **E-mail:** zeynel_akd@hotmail.com

Abstract

Introduction: The aim of our study was to determine the efficacy and the power of total urine analysis (TUA) in predicting culture results, hence to make our contribution in correcting a general mistake in our country of ordering TUA and urine culture tests at the same time, and try to help economic loss to reduce and support the success of empiric therapy to increase.

Material and Method: The data of 228 patients who applied to our urology clinic between January - March 2018 due to dysuria and similar urinary tract infection (UTI) symptoms and had TUA and urine culture tests at the very same day were retrospectively analysed. In the culture test results, $<10^5$ CFU/mL colony number was accepted as negative (group 1) and higher colony number as positive (group 2). TUA parameters were compared between the groups.

Results: It was determined that, nitrite, leucocyte esterase (LE) and protein in urine dipstick analysis; leucocyte and erythrocyte in microscopic examination; and evaluation of appearance in macroscopic examination of urine were found to be valuable parameters for the prediction of urine culture result.

Discussion and Conclusion: In cases where TUA parameters were determined to be negative, it was not quite necessary to perform urine culture tests thus it was possible to reduce the high cost due to urine culture and time loss by the help of TUA, and in cases where it was found to be positive however, verification was required either by combined values (along with the other TUA parameters) or by urine culture.

Keywords: TUA, Urine culture, Predictivity

1. INTRODUCTION

Urinary Tract Infection (UTI) which is one of the most common factors in visiting urology outpatient clinics can be non-complicated as in causing bladder irritation and dysuria symptoms, can also become complicated so much as to lead to hypertension in progressive stages, by causing renal parenchyma damage and renal scar tissue. Especially in female patients, 60-80% of the dysuria complaints are associated with bacteriuria (1-3). Considering that uremia was not determined in 25-30% of symptomatic UTI patients, especially in non-complicated UTI cases, ordering urine culture test has always been controversial.

Even though medical history and physical examination (FE) are valuable in UTI diagnosis, the most fundamental test to be ordered is TUA. In UTI patients the most frequent accompanying symptoms are dysuria, and urgent and frequent

desire to void. Empiric antibiotic therapy is started in these patients before ordering urine culture test (4, 5). Urine culture test is an expensive, tedious and time consuming procedure. Bacterial growth in culture media requires 18-48 hours time and this increases hospital stay period as well as treatment costs. An inexpensive test that will decrease the need for ordering urine culture test, will also decrease economic burden and increase the efficacy of the empiric treatment to be initiated. High accuracy rate of TUA used for diagnostic purpose before empiric therapy increases the efficacy of the therapy and reduces the need for culture test. Thus, TUA which is an inexpensive and quick test, can help saving time and money, and protects public assets. That's why, it is used before urine culture test routinely, for predictive purposes (6, 7).

The aim of our study was, to determine the efficacy and power of TUA in predicting culture

test results and so to make our contribution to the correction of general mistake of ordering both TUA and urine culture in our country, to give a support to reduction of economic loss and to increase success rates of empiric treatment

2. MATERIALS AND METHODS

The data of 228 patients were retrospectively analysed, who admitted to our urology clinic between January and March 2018 for dysuria and UTI symptoms and both TUA and urine culture tests were performed on the same day. After the patients were informed about appropriate wiping method to cleanse the urethral area, midstream urine sample was taken into two sterile urine cups (one for TUA the other for urine culture test). For TUA, macroscopic, dipstick and direct microscopic examination of urine were established. For the efficacy and predictivity of TUA, culture test results were regarded as reference line. In macroscopic observation, blurred view in urine and the colors other than light yellow; in microscopic observation $>5/\text{hpf}$ value for erythrocyte and leucocyte, and $>15/\text{hpf}$ value for epithelial cell were accepted as positive. Statistical correlation was analysed by chi-square test. No threshold value was taken for mucus parameter. (Statistical correlation was analysed by Mann-Whitney U test.) In dipstick test, nitrite (>0.06 mg/dL), hemoglobin (>0.01 mg/dL), leucocyte esterase ($>25\text{hc}/\mu\text{L}$), protein (>30 mg/dL), glucose (>15 mg/dL), bilirubin (>0.02 mg/dl), urobilinogen ($>2\text{mg}/\text{dL}$), ketone (>5 mg/dL acetoacetate) values were accepted as positive and the correlation with urine culture was analysed by chi-square test. Statistical correlation of pH and density values with urine culture was analysed by Mann-Whitney U test. For culture, urine sample inoculated on blood agar was incubated at 35°C for 18-24 hours. Subsequently, $<10^5$ CFU/mL colony number was accepted as negative (group 1), and higher colony number was accepted as positive (group 2) Statistical correlation was evaluated by using IBM Statistical Package for Social Sciences (SPSS) Version 22.0 program. $P<0.05$ values were accepted as statistically significant.

3. RESULTS

Average age of 228 patients included in our study was 51.95 ± 16.59 years (51.42 ± 16.1 and 53.9 ± 18.33 years in group 1 and group 2 respectively). Statistically significant difference was not determined between the groups with respect to age ($p=0.360$). The number of patients was 179 (78.6%) in Group 1 (culture negative)

and 49 (21.4%) in group 2 (culture positive). Chi-square analysis was used in the statistical analysis of the parameters examined in urine microscopy (leucocyte, erythrocyte, epithelial cell) of culture result groups. The sensitivity of leucocyte in the microscopic analysis was determined as 53%, specificity as 81%, positive predictive value (PPV) as 44%, negative predictive value (NPV) as 86.3%, and Odds Ratio (OR) as 5 ($p=0.000$). For erythrocyte in microscopic analysis, the parameters of sensitivity, specificity, PPV, NPV and OR were determined as 44.89%, 75.4%, 33.3%, 83.3% ve 2.5 respectively ($p=0.005$). The same parameters for epithelial cell were determined as 6.1%, 94.4%, 23%, 78.6% and 1.1 ($p=0.886$). For the correlation of urine appearance (blurred or clear) with culture positivity, the same parameters were determined as 8.16%, 99.4%, 4%, 79.8% and 15.8 respectively ($p=0.008$). We determined no statistically significant relation of *urine color* with culture positivity, and the same parameters were determined as 6.1%, 92.7%, 18%, 78.3% and 0.83 respectively ($p=0.537$). The correlation between the presence of mucus cells and culture positivity was analysed by Mann-Whitney U test and no difference was determined ($p=0.487$)

Considering the relation of the Dipstick parameters with culture results, for leucocyte esterase the same parameters above were, 69.3%, 77.6%, 45.9%, 90.2% and 7.8($p=0.000$); for hemoglobin parameter, 67.3%, 63.6%, 33.6%, 87.6% and 3.6($p=0.000$); for nitrite parameter, 32.6%, 96%, 69.5%, 83.9% and 11.9($p=0.000$); and for protein parameter 53%, 81.5%, 41%, 84.8% and 3.91 ($p=0.000$) respectively.

When the other dipstick parameters were considered, according to chi-square test, *glucose, bilirubin, urobilinogen, ketone parameters* were determined to be statistically not significant in culture predictivity ($p=0.682$, $p=0.345$, $p=1.000$, $p=0.345$ respectively). Also *pH ve density values* were determined to be insignificant in predicting urine culture results (Mann Whitney-U test; $p=0.110$, $p=0.374$ respectively). (See Table 1 for all statistical results.)

4. DISCUSSION

In the studies on female patients, the prevalence of dysuria was determined as 2-5%, and the rate of bacteriuria in these patients was reported as 60-80% (1-3, 8). The tests implemented in order to determine bacteriuria can be inexpensive and

fast tests but with less accuracy like TUA, as well as expensive and time taking tests but with high accuracy like urine culture tests. Urine culture test is gold standard in revealing bacteriuria but it is expensive and requires time. Furthermore, according to studies in the literature, 52-68.3% of culture tests are known to be negative. However, there are also studies

with much higher number of cases, reporting much higher culture negativity 97.7% than these studies (7). It is essential to predict the patients with probable culture negative results in order to prevent this situation causing increased cost (9-11). Right at this point, urine dipstick test and urine microscopy (TUA) becomes important.

Table1. Demographic data and the statistical results of Culture and TUA results

			culture negative		culture positive		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	OR	p value.	Test		
			(-) Test result (%)	(+) Test result (%)	(-) Test result (%)	(+) Test result (%)									
Age (years)			4	89	51.9	16.5						0.360	mwu		
TUA	Dipstick Tests	Nitrite (>0.06 mg/dL)	172 (96.1)	7 (3.9)	33 (67.3)	16 (32.7)	32.6	96	69.5	83.9	11.9	0.000	Chi-Square		
		LE (>25hc/μL)	139 (77.7)	40 (22.3)	15 (30.6)	34 (69.4)	69.3	77.6	45.9	90.2	7.8	0.000			
		Hb (>0.01 mg/dL)	114 (63.7)	65 (36.3)	16 (32.7)	33 (67.3)	67.3	63.6	33.6	87.6	3.6	0.000			
		Protein (>30 mg/dL)	146 (81.6)	33 (18.4)	26 (53.1)	23 (46.9)	53	81.5	41	84.8	3.91	0.000			
		Glucose (>15 mg/dL)	173 (96.6)	6 (3.4)	47 (95.9)	2 (4.1)	4	96.6	25	78.6	1.2	0.682			
		Ketone (>5 mg/dL asetoasetat)	173 (96.6)	6 (3.4)	49 (100)	0 (0)	0	96.6	0	77.9	0.77	0.345			
		Bilirubin (>0.02 mg/dl)	173 (96.6)	6 (3.4)	49 (100)	0 (0)	0	96.6	0	77.9	0.77	0.345			
		Urobilinogen (>2mg/dL)	176 (98.3)	3 (1.7)	48 (98)	1 (2)	2	98.3	25	78.5	1.22	1.000			
		Min.	Max.	Ave.	SS										
			pH											0.110	mwu
	Density										0.374				
	Mucus (number)										0.487				
Microscopic findings			culture negative		culture positive		Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	OR	p value.	Test		
		(-) Test result (%)	(+) Test result (%)	(-) Test result (%)	(+) Test result (%)										
		Leukocyte(>5/hpf)	146 (81.6)	33 (18.4)	23 (46.9)	26 (53.1)	53	81	44	86.3	5	0.000	chi-square		
		Erythrocyte (>5/hpf)	135 (75.4)	44 (24.6)	27 (55.1)	22 (44.9)	44.8	75.4	33.3	83.3	2.5	0.005			
		Epithelium(>15/hpf)	169 (94.4)	10 (5.6)	46 (93.9)	3 (6.1)	6.1	94.4	23	78.6	1.1	0.886			
Appearance (clear, blurred)	178 (99.4)	1 (0.6)	45 (91.8)	4 (8.2)	8	99.4	4	79.8	15.8	0.008					
Color (light yellow, red etc.)	166 (92.7)	13 (7.3)	46 (93.9)	3 (6.1)	6.1	92.7	18	78.3	0.83	0.537					

According to the results of our study leucocyte esterase, nitrite, protein and hemoglobin were found to be significant in regard to predicting urine culture positivity. In the meta-analysis, Deville et al (12) examined the effectivity of nitrite test in predicting culture result and the sensitivity and specificity were determined as 50% and 82% respectively in the general population (the data of 15 studies). The same parameters were determined to be 59% and 97% in the population of urology patients (data of 3 studies) as 59% and 97%. In the study of Kayaalp et al (7) these values were found to be 17.7% and 90.1 % in general population

respectively. And in the study of Yüksel et al (11) these values were 36.1% and 95.4%. In our study however, these values were determined as 32.6% and 96%, and OR was 11.9. We can say that, in the cases where nitrite test was negative, urine culture was also negative at such a high rate of 96% (specificity).

In the meta-analysis of Deville et al (12) sensitivity and specificity rates for leucocyte esterase in general population was 62% and 70%, and for urologic population as 86% and 93%, respectively. These values were determined to be 71% and 83.6% respectively in general population, in the study of Kayaalp et al

(7). In the same study, OR value for leucocyte esterase was determined to be at a much higher rate with respect to nitrite (For nitrite and for LE as 2 and 12.5 respectively) (7). And these values were 86.1% and 65.5% respectively in the study of Yüksel et al (11). In our study however, these values were determined as 69.3% and 77.6%, and OR as 7.8. According to our results, although the sensitivity of leucocyte esterase was higher in comparison to nitrite test, OR value was determined to be lower (OR values for nitrite and LE as 11.9 and 7.8 respectively).

In the meta-analysis of Deville et al (12) nitrite and/or leucocyte esterase negative tests results in general population were determined to be very significant, for positive tests however, the cases with positive results in both test were considered as significant, and the cases with only one positive result, they reported that further assessments were required.

In the study of Yüksel et al (11) Hb and protein parameters among dipstick parameters were considered, and sensitivity and specificity rates were determined to be 70.3% ve 56.7% for HB, and 51.9% ve 67.8% for protein, respectively.

In our study, Hb and protein parameters were found to be diagnostically significant, and sensitivity, specificity and OR values were 67.3%, 63.6% and 3.6 for Hb; and 53%, 81.5% and 3.91 for protein. In our study, the specificity of proteinuria in determining bacteriuria was found to be significantly higher with respect to Hb parameter. In the other dipstick tests, these values were 4%, 96.6% and 1.2 for glucose; 2%, 98.3% and 1.2 for urobilinogen; and 0%, 96.8%, and 0.77 for ketone and bilirubin, respectively; and none of these were found to be statistically significant in predicting urine culture results.

In our study, >5 leucocyte or erythrocyte at every field was regarded as positive. In our study leucocyte and erythrocyte parameters analysed in urine microscopy were found to be statistically significant in regard to predicting culture test results. In the study of Kayaalp et al (7) the sensitivity, specificity and OR values of microscopic leucocyte parameter were found as 68.2%, 87.8% ve 15.5 respectively. In the study of Yüksel et al (11) however, sensitivity and specificity values for leucocyte were found as 88% and 61.8 %, and for erythrocyte as 74.1% and 54.6% respectively. In our study however, these values for leucocyte were determined to be 53%, 81% and OR as 5, and for erythrocyte 44.8%, 75.4% and OR as 2.5 respectively.

According to our results, diagnostic value of leucocyte was higher with respect to erythrocyte. These values for epithelial cell were determined as 6.1%, 94.4% and 1.1, hence not statistically significant. Since there was no threshold value for mucus parameter, Mann-Whitney U test was implemented and found to be statistically insignificant in regard to predicting urine culture.

As for urine macroscopy, the sensitivity, specificity and OR values were 8%, 99.4% ve 15.8 for urine appearance parameter and found to be statistically significant in predicting urine culture. For color parameter these were 6.1%, 92.7% and 0.83, and not valuable in predicting urine culture.

In conclusion, nitrite, LE protein in dipstick tests; leucocyte and erythrocyte in microscopy parameters, and urine appearance parameter in macroscopy, were determined to be significant in predicting urine culture results. It is clear that specificity values of TUA parameters were very high, sensitivity values however were relatively low. Final conclusion to be deduced from that is, it was not quite necessary to conduct urine culture in cases where TUA parameters were specified as negative, thus high cost and time loss due to urine culture could be reduced by the help of TUA, but in cases where TUA was positive, it was necessary to make verification by combined values (in conjunction with the other TUA parameters) or by urine culture.

We also would like to highlight that recent reports in the literature noted bacteria were isolated by PCR and bacterial genomic identification (16S rRNA sequencing) methods in the cases with negative urine culture and this led to the controversy of whether urine samples were sterile or not (13, 14). It is clear that randomized and prospective studies with higher patient numbers are required in order to illuminate this issue which will be of a center of interest in the near future.

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