

Cut-off Values of Bacteriuria and Leukocyturia for the Diagnosis of Urinary Tract Infections in Pediatric Patients

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ABSTRACT

The diagnosis of Urinary Tract Infection (UTI) in infants and children is often missed. There have been no studies on diagnostic tests using automated urine analyzer in pediatric patients. This study aimed to determine the cut-off values of bacteriuria and leukocyturia using the automated urine analyzer Sysmex UX-2000 to diagnose UTI with the gold standard of automated urine culture using VITEK 2 in pediatric patients at Dr. Moewardi Hospital, Surakarta. An observational analytical study with the cross-sectional design was during August-October 2019 at the Clinical Pathology Laboratory and Clinical Microbiology Laboratory of Moewardi Hospital, Surakarta. Eighty-four patients sample were collected. This study's dependent variable was the diagnosis of urinary tract infections in pediatric patients established with positive culture results (bacterial count of ≥ 105 CFU/mL urine). This study's independent variables were the number of urine bacteria (BACT) and the number of urine leukocytes (WBC) from urinalysis using the Sysmex UX-2000 automated urine analyzer. A diagnostic test was used for data analysis. The best cut-off value for leukocyturia was 37 cells/ μ L with a 61.1% sensitivity, 63.6% specificity, a positive predictive value of 31.4%; a negative predictive value of 85.7; positive likelihood ratio of 1.64; negative likelihood ratio of 0.595, and accuracy of 63%. The best cut-off for the number of bacteria was 143 cells/ μ L with a sensitivity of 66.7%; specificity of 71.2%, the positive predictive value of 38.7%, the negative predictive value of 88.7%; positive likelihood ratio of 2.14; negative likelihood ratio of 0.432 and an accuracy of 70.2%. A cut-off of 37 cells/ μ L for leukocyturia and 143 cells/ μ L for bacteriuria using an automated urine analyzer can be used for UTI screening in pediatric patients.

Keywords: Urinary tract infections, children, leukocyturia, bacteriuria, Sysmex UX-2000

INTRODUCTION

Urinary Tract Infections (UTI) are among the most dominant infectious diseases and have an essential financial burden in the community. The incidence of urinary tract infections in children varies greatly depending on age and gender. UTI's risk in the first decade after males' birth is 1%, and females are 3%. At least 5% of girls and 0.5% of school-age boys experience one episode of UTI. Urinary tract infection was more commonly found in Male babies less than three months old compared to female babies.¹

The diagnosis of UTI in infants and children at primary health care is often missed. This fact is due to the lack of awareness and limited facilities to rule out UTI. Symptoms of UTI in children tend to be less specific. The diagnosis process, which requires quite a long time and expensive costs, is another obstacle in diagnosing UTI.² Clinical symptoms of UTI in children are usually mild and non-specific, and fever is often the only symptom. Hypothermia, lethargy, irritability, decreased appetite, vomiting, diarrhea,

jaundice, failure to thrive, sepsis, or foul-smelling urine are other symptoms that may be found.^{2,3}

There has been no study about bacteriuria and leukocyturia's diagnostic performance using an automated urine analyzer in pediatric patients. The definitive diagnosis of UTI is considered very important to provide appropriate treatment to patients. The gold standard is still considered costly and requires a long time of processing. In this study, researchers compared the detection of bacteria and leukocytes using the Sysmex UX-2000 to the gold standard, urine culture, particular attention to cut-off values for bacteriuria leukocyturia, to carry out a fast and reliable diagnosis of UTI.⁴

METHODS

This study was a diagnostic test using a cross-sectional design and urine culture as the gold standard. This research was performed at the Clinical Pathology Laboratory and Microbiology Laboratory of Dr. Moewardi Hospital, Surakarta. The inclusion

criteria were pediatric patients with clinical suspicion of UTI, aged 1-18, who came to the Pediatric Outpatient Clinic or were treated in the Pediatric Ward at Dr. Moewardi Hospital between October 2018 and October 2019. Urine culture was done using VITEK 2, and automated urinalysis using Sysmex UX-2000. The informed consent was taken from all subjects. Exclusion criteria were patients with an incomplete test. Clinical data were taken from the patient's medical record. The culture results were obtained from the register of VITEK 2 from the Microbiology Laboratory. The number of bacteria (BACT) and the number of leukocytes (WBC) were obtained from the record of Sysmex UX-2000 automated urine analyzer from the Clinical Pathology Laboratory. The Receiver Operating Characteristics (ROC) curves for WBC and BACT were plotted, sensitivity (SE), specificity (SP), Positive Predictive Value (PPV), Negative Predictive Value (NPV), likelihood ratios, and accuracy were then evaluated. The data were analyzed using STATA version 14.2.

Research permission was obtained from the Health Research Ethics Committee of the Dr. Moewardi General Hospital with number 883/VII/HREC/2019.

RESULTS AND DISCUSSION

The subjects' characteristics, including age, gender, comorbidities, and urine sources, can be seen in Table 1. The number of subjects in this study were 84, consisting of 55 hospitalized subjects (65.5%) and 29 subjects (34.5%) with Outpatients care. The number of samples from female subjects was equal to male subjects. There were 18 samples

(21.4%) with positive culture (i.e. bacterial count of > 105 CFU/mL) and 66 samples (78.6%) with negative culture (i.e. no growth or bacterial count of < 105 CFU/mL). Among samples with positive culture result, seven samples (38.9%) were *Klebsiella pneumoniae*, four samples (22.2%) were *Escherichia coli*, two samples (11.1%) were *Pseudomonas aeruginosa*, three samples were Gram-positive cocci (*Staphylococcus aureus*, *Streptococcus haemolyticus*, and *Enterococcus faecalis*), 2 other samples were *Stenotrophomonas maltophilia* and *Salmonella sp.*

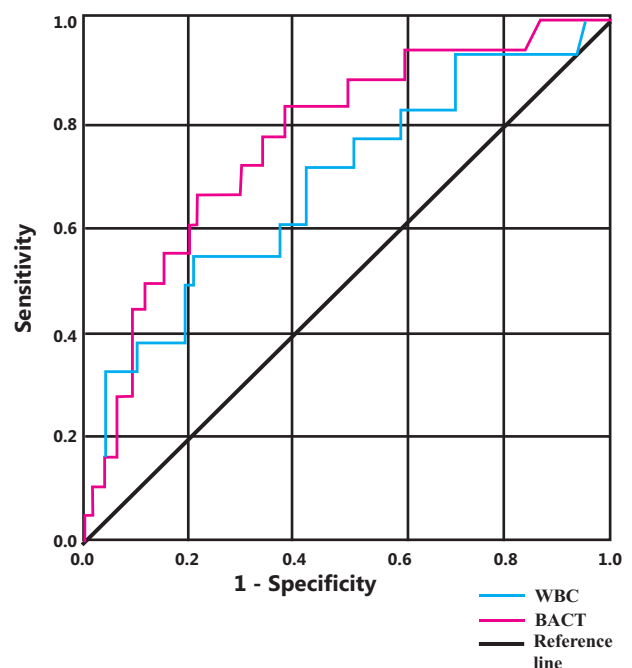


Figure 1. Receiver operating characteristics curve of WBC and BACT to diagnose urinary tract infection

Table 1. Characteristics of research subjects

Characteristics	Culture (+)		Culture (-)		Total	
	n	%	n	%	n	%
Age (year)						
1-5	6	23.1	20	76.9	26	30.85
6-18	12	20.7	46	79.3	58	69.05
Gender						
Female	11	26.2	31	73.8	42	50
Male	7	16.7	35	83.3	42	50
Comorbidities						
Malignancy	4	13.3	26	86.7	30	35.7
Non-malignancy	14	25.9	40	74.1	54	64.3
Source of urine						
Mid-stream	16	20.8	61	79.2	77	91.7
Catheterized	2	28.6	5	71.4	7	8.3

From the ROC curve (Figure 1), the Area Under Curve (AUC) of WBC and BACT was 0.701 (95%CI 0.559-0.843) and 0.779 (95%CI 0.658-0.899), respectively. The AUC of BACT had a higher value than the AUC of WBC ($p=0.009$).

Tables 2 and 3 showed the sensitivities and specificities of various cut-off values for WBC and BACT. As shown in Tables 2 and 4, the best cut-off value for WBC was 37 cells/ μ L with a sensitivity of 61.1% and a specificity of 63.6%. This cut-off also gave a PPV of 31.4%, a NPV of 85.7%, a positive likelihood ratio of 1.64, and an accuracy of 63%. Table 3 and 4 also showed the best cut-off value of 143 cells/ μ L for BACT with a sensitivity of 66.7%; specificity of 71.2%; a positive predictive value of 38.7%; a negative predictive value of 88.7%; positive likelihood ratio of 2.14; and an accuracy of 70.2%.

In contrast to this study, Pratistha reported a higher cut-off of 52.8 cells/ μ L for leukocyturia with a sensitivity of 82.3%, a specificity of 76.3%, PPV of

85%, NPV of 72.5%, and accuracy of 84.6%.⁵ Similar research by Bargotya *et al.* reported a lower cut-off value of 19.8 cells/ μ L with a sensitivity of 82.3%, a specificity of 80.9%, PPV of 54.3%, and NPV of 93.5%.⁶ Giesen *et al.* reported that the flow cytometry method resulted in a lower cut-off of leukocyturia (≥ 31.8 cells/ μ L) with a sensitivity of 89%, a specificity of 79%, PPV of 38%, and NPV of 98%.⁷ Agpaoa *et al.* obtained cut-off of ≥ 27 cells/ μ L for leukocyturia, with a sensitivity of 84.6%; specificity of 65.4%; PPV of 71% and NPV of 81%. The cut-off value for WBC obtained in this study was similar to that of Agpaoa *et al.*⁸

The best cut-off for the bacterial count (BACT) for the diagnosis of UTI was 143 cells/ μ L with a sensitivity of 66.7%, a specificity of 71.2%; PPV of 38.7%; NPV of 88.7%; positive likelihood ratio LR of 2.14, and accuracy of 70.2%. Bargotya *et al.* determined a higher cut-off of 198.8 cells/ μ L with a sensitivity of 82.1%, a specificity of 79.5%, a PPV of 54.3%, and NPV of 92.7%.⁶

Variations in the cut-off values of leukocyturia and bacteriuria can be caused by differences in study populations, characteristics of study samples in inclusion criteria, and differences in the interpretation of positive urine cultures.⁵ The high NPV values of leukocyturia and bacteriuria in this study indicated these two parameters' ability to predict negative urine culture results of 85.7% and 88.7%, respectively, to exclude UTI diagnosis. Based on the study results, it could be concluded that the cut-off value of 37 cells/ μ L for WBC and 143 cells/ μ L for bacteriuria (BACT) can be used for UTI screening in pediatric patients.

This study was the first research that determined the cut-off value of bacteriuria and leukocyturia in

Table 2. Sensitivity and specificity for WBC at various cut-off values

	Cut-off Value for WBC (cells/ μ L)		
	35.3	35.8	37
Sensitivity	61.1%	61.1%	61.1%
Specificity	59.1%	62.1%	63.6%

Table 3. Sensitivity and specificity for BACT at various cut-off values

	Cut-off Value for BACT (cells/ μ L)		
	99.35	112.4	143
Sensitivity	72.2%	66.7%	66.7%
Specificity	69.7%	69.7%	71.2%

Table 4. Sensitivity, specificity, PPV, NPV, accuracy, and likelihood ratios for WBC at a cut-off of 37 cells/ μ L and BACT at a cut-off of 143 cells/ μ L

	WBC at Cut-off 37 cells/ μ L	BACT at Cut-off 143 cells/ μ L
Sensitivity (95% CI)	61.1% (35.7%-82.7%)	66.7% (41%-86.7%)
Specificity (95% CI)	63.6% (50.9%-75.1%)	71.2% (58.7%-81.7%)
PPV (95% CI)	31.4% (16.9%-49.3%)	38.7% (21.8%-57.8%)
NPV (95% CI)	85.7% (72.8%-94.1%)	88.7% (77%-95.7%)
Positive likelihood ratio (95% CI)	1.64 (0.892-3)	2.14 (1.09-4.18)
Accuracy	63%	70.2%

pediatric patients aged 1-18 years using automated urinalyzer Sysmex UX-2000. As a retrospective study, this study had several limitations, such as no proper control of urine sampling procedures for urinalysis and urine culture and no consideration of the history of antibiotics prescribed to patients, which increased false-negative results of urine cultures.

CONCLUSION AND SUGGESTION

The best cut-off leukocyturia for UTI diagnosis was 37 cells/ μ L with a sensitivity of 61.1%; specificity of 63.6%; PPV of 31.4%; NPV of 85.7%; positive likelihood ratio of 1.64; and accuracy of 63%. The best cut-off for bacteriuria 143 cells/ μ L with a sensitivity of 66.7%; specificity of 71.2%; PPV of 38.7%; NPV of 88.7%; positive likelihood ratio of 2.14; and an accuracy of 70.2%. This study's cut-off values can be used to rule out a UTI diagnosis in pediatric patients due to the high negative predictive value obtained, which was 85.7% for bacteriuria and 88.7% for leukocyturia. Further research using a prospective research design and consideration of antibiotics prescribed to patients as needed.

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