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Assessment of urinalysis reflex to culture criteria: Impact on antimicrobial usage

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Abstract

Objectives: To assess the predictive value of the urinalysis (UA) reflex criteria's parameters and to evaluate the criteria's impact on antibiotics usage.

Methods: A prospective study using laboratory data was conducted on inpatient urine samples with orders placed for Urinalysis Reflex Culture (UARC) in a 400-bed acute care hospital. A total of 4016 urine samples were collected and examined between February and April 2020. The UA results were then subjected to the laboratory UA reflex criteria for reflecting UA to culture. Multivariable logistic regression was utilized in evaluating the effectiveness of the criteria's parameters to predict positive urine cultures.

Results: The total number of the positive UA reflex samples was 1539, which accounted for 38.3% of all the UA samples. Moreover, those positive UA samples were reflexed to urine cultures. Among the urine samples that were cultured, 45.1% (n=694) were negative urine cultures while 54.9% (n=845) were positive urine cultures. The UA reflex criteria was associated with positive predictive values for positive urine cultures between 26.30% and 92.96%.

Conclusions: The current Laboratory UA reflex criteria is not highly effective in predicting positive urine culture, thus potentially leading to the inappropriate use of antibiotics.

Keywords
Urinary Tract Infection, Urinalysis, Urine Culture, Antibiotics Usage, USA.

Introduction

Antimicrobial resistance (AR) is a serious threat to the treatment of infectious diseases, which might result in human side effects, loss of life, and huge economic impacts. Several efforts are taking place

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to combat AR and halt the spread of resistance. Laboratories play a vital role in the prevention of the spread of AR [1]. The microbiology laboratory can rapidly detect AR pathogens and inform treating physicians and infection control practitioners to help prevent the spread and protect other patients (CDC 2018). Most importantly, optimal diagnosis of various infections is essential as it ensures the appropriate antibiotic treatment and prevents unnecessary use of antibiotics. For instance, urinary tract infections (UTIs) are one of the leading conditions that require antibiotics intervention, hence contributing highly to antibiotic misuse [2]. Patients presented with the possibility of having urinary tract infection (UTI) are often screened by urinalysis (UA) to determine whether administration of antibiotics is warranted and then whether a urine culture is needed. Unfortunately, improper urinalysis reflex criteria can result in suboptimal laboratory practice and can incorrectly influence healthcare practitioners to inappropriately prescribe antibiotics [3-4].

Urinalysis is a rapid diagnostic tool utilized by healthcare providers to clarify uncertainty in the diagnosis of UTI. However, laboratories must adhere to evidence-based practices and high predictive UA diagnostic criteria to ensure providing accurate patient diagnosis and appropriate antibiotics treatment. Most laboratory practices rely on historical UA reflex criteria that have not been updated for many years, thus, they are often associated with a high rate of false positives UAs [1, 5]. This was evident in the baseline assessment during this study, where we reported high false positives due to the application of outdated UA reflex criteria applied in our laboratory. Suboptimal or improper laboratory testing is a major challenge and a serious quality problem, significantly affecting patient's outcome. In particular, the reflex criteria rely on a single UA reflex parameter to predict positive urine cultures which were associated with a low positive predictive value. Consequently, they influence the providers towards the suboptimal administration of antibiotics. According to the Centers for Disease Control (CDC), over-testing and over-treatment are linked to excessive usage of antibiotics and result in unnecessary healthcare costs of more than $1.1 billion annually [6-8].

Methods

A prospective study using laboratory data was conducted on inpatient urine samples with orders placed for Urinalysis Reflex Culture (UARC) in a 400-bed acute care hospital. A total of 4016 urine samples (2426 females, 1590 males) between age of 2 and 75 years old with a median age of 43 years. Samples were collected and examined between February and March 2020. The purpose of this study is to assess the predictive value of the UA reflex criteria's parameters and to evaluate the criteria's impact on usage of antibiotics. The study was evaluated by the hospital regulatory department, and it was determined to have the legal or ethical status of "quality improvement activity" rather than "human subject research." Urine samples were collected from patients who presented to the hospital for routine workup or possible UTIs but not necessarily with any signs or symptoms. As per Clinical and Laboratory Standards Institutes (CLSI) urinalysis guidelines (CLSI, 2009), nurses or laboratory staff provided patients with a clean-catch urine collection instruction to minimize contamination caused by bacteria on the skin. Following the instructions provided, a minimum of 5 ml urine clean-catch sample was collected from patients in a sterile urine cup which was submitted to nursing or laboratory staff in a timely manner. Samples were transported to the laboratory to be tested within two hours of collection if were unrefrigerated or within 24 hours if kept refrigerated. Urine samples were tested for urinalysis on the AUTION HYBRID AU-4050 (Arkray, Minneapolis, MN), Microscopic examination was performed if the urine was positive for any of the followings; red blood cells (2-

5), nitrite(+), protein (+) or leukocyte esterase (+). Urinalysis is defined as positive if it contains any of these parameters: nitrites+, leukocyte esterase+, bacteria present, or (0-5) white blood cells present per high-power field (hpf). UA-reflexed data statistics and antibiotic usage were recorded during the baseline period.

Statistical data were extracted through the laboratory information system (TD Synergy) a product of Tech Data, Inc,USA, and the pharmacy electronic inventory system (SRX-Allscripts) a product of All scripts Health care Solutions, Inc. Multivariable logistic regression was utilized to evaluate the predictive value of UA criteria's parameters and to identify the highest predictive reflex indicators with clinical significance that resulted in true positive urine cultures. The statistical analysis of the results was analyzed and interpreted using IBM SPSS Statistics software (V25.0).

Results

A total of 4016 patients participated with samples in the study, among which 60.4% (n=2426) were females and 39.6% (n=1590) were males. The total number of the negative UA reflex samples was 2477 which accounted for 61.7% of all the UA reflex samples. In addition, 38.3% of all the UA positive samples (n=1539) were reflexed to urine culture. Among the urine samples that were cultured, 45.1% (n=694) were negative urine cultures, while 54.9% (n=845) were positive urine cultures. See **Table 1**.

Table 1. Summary of the study descriptive statistics.

Characters	Frequency	Percent
Gender		
Female	2426	60.4
Male	1590	39.6
Total no.	4016	100
UA Reflex Samples		
Negative	2477	61.7
Positive	1539	38.3
Total no.	4016	100
UC		
Negative	694	45.1
Positive	845	54.9
Total no.	1539	100

Evaluation of bacteria presence as a single parameter to predict positive urine culture

Bacteriuria is the presence of bacteria in urine and when accompanied by symptoms will most likely be an indication of a urinary tract infection. Gram negative rod bacteria such *Escherichia coli* is the most common cause of UTIs. Bacteria presence in urine as a single UA parameter with a cut-off value of (0-1) showed 30.1% PPV for positive urine culture; (214/(214+498)=30.1%, while bacteria presence with a cut-off value of >1 showed 76.3% PPV for positive urine culture; (631/(631+196)=76.3% as described in **Table 2**.

Table 2. Bacteria prediction for positive urine cultures.

Urine cultures	Bacteria (hpf)			
	0-1		>1	
	Count	%	Count	%
Negative	498	69.9	196	23.7
Positive	214	30.1	631	76.3
Total no.	712	100	827	100

Evaluation of nitrite as a single UA parameter to predict positive urine culture

Normal urine contains a chemical called nitrate and the presence of certain bacteria; mostly Gram-negative organisms can convert nitrate into nitrite. Therefore, the presence of nitrite gives us indication of the presence of certain bacteria in the urine which indicate the possibility of UTI. In the present study, nitrite negative UAs that resulted

in positive urine culture showed 41.0% PPV; (462/(665+462)=41.0%, while positive nitrite UAs with positive urine culture showed 92.96% PPV; (383/(383+29)=92.96% as described in **Table 3**.

Table 3. Nitrite prediction for positive urine cultures.

Urine cultures	Nitrite			
	Negative		Positive	
	Count	%	Count	%
Negative	665	59	29	7.04
Positive	462	41	383	92.96
Total no.	1127	100	412	100.0

Evaluation of esterase as a single UA parameter to predict positive urine culture

The presence of esterase in the urine indicates the presence of WBCs, which indicate possible UTI. In the present study, trace or few esterase presence in the UA had 33.7% PPV for positive urine culture; (299/(299+588)=33.7%, while moderate or large esterase had 83.7% PPV for positive urine culture; (546/(546+106)=83.7% as described in **Table 4**.

Table 4. Esterase prediction for positive urine cultures.

Urine cultures	Esterase			
	Trace or Few		Moderate or Large	
	Count	%	Count	%
Negative	588	66.3	106	16.3
Positive	299	33.7	546	83.7
Total no.	887	100	652	100

Evaluation of the WBCs as a single UA parameter to predict positive urine culture

The presence of WBCs in the urine is indication of a possibility of UTI. In the present study, UA samples with WBCs (0-5) showed 26.30% PPV for positive urine cultures; (96/(96+269)=26.30%, while UA samples with WBCs >5 showed 85.09% PPV for positive urine cultures; (999/(999+175)=85.09% as described in **Table 5**.

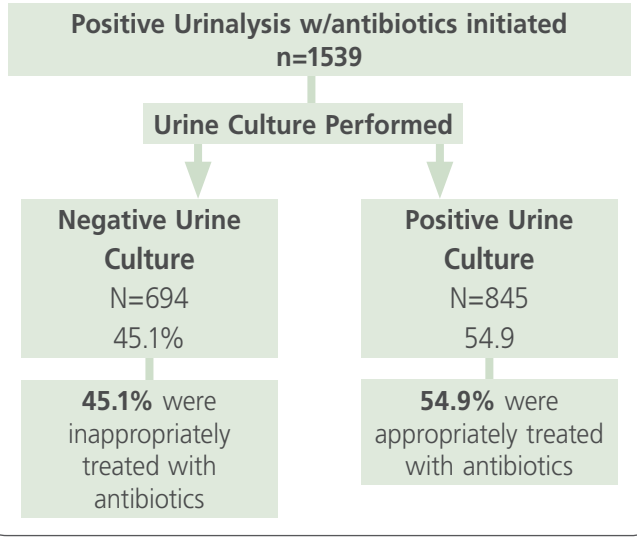
Table 5. WBCs prediction for positive urine cultures.

Urine cultures	WBCs			
	0-5		>5	
	Count	%	Count	%
Negative	269	73.70	175	14.91
Positive	96	26.30	999	85.09
Total no.	365	100.00	1174	100.00

Evaluation of the UA reflex criteria's impact on antibiotics usage

A total of 1539 urine samples that produced positive UA were reflexed to urine culture. Results demonstrated that only 54.9% (n=845) of the reflexed urine samples showed positive urine culture, which indicated that reliance on the current UA reflex criteria had led to appropriate treatment with antibiotics to 54.9% of those treated patients. The obtained findings also demonstrated that 694 urine samples with positive UAs yielded negative urine cultures. Consequently, the reliance on the current UA reflex criteria resulted in the inappropriate treatment with antibiotics to 45.1% of those treated patients. In conclusion, current UA reflex criteria is not optimal and significantly lead to inappropriate use of antibiotics. See **Figure 1**.

Figure 1: Effectiveness of the current UA reflex criteria on antibiotics usage.



Discussion

Urinalysis is a rapid and relatively simple tool in providing important clinical information for the early diagnosis and treatment of urinary tract infections [9-10]. UTIs are one of the leading conditions that require antibiotics intervention, therefore contributing highly to antibiotic misuse [3, 4, 11-12]. Optimal diagnosis of infections is very vital to ensure appropriate antibiotic treatment and patient recovery [13-14]. On the contrary, suboptimal laboratory test results can generate misleading diagnoses and influence the treating physicians to unnecessarily prescribe antibiotics, consequently leading to the development of antimicrobial resistance [6, 15].

Most laboratory practices depend on standard UA reflex criteria that have not been updated for many years; thus, they are often associated with high numbers of false positives [7, 16]. For example, using cut-off values of <1 for bacteria, or any positive nitrite test, or presence of few or less esterase and <5 WBCs was associated with low positive predictive values (between 11.4% and 45.3%). The observed low predictive values are associated with the laboratory procedures that are based on reflexing UA for culture if any of the parameters are positive. Although the low predictive values that are associated with the considered parameters (<1 for bacteria, any positive nitrite test, presence of few or less esterase, and <5 WBCs) have been previously reported among outpatients [12, 17-18]. Our study also demonstrated that the criteria are ineffective in preventing unnecessary urine cultures among inpatients as well.

In the present study, we demonstrated that the UA reflex criteria are not effective in predicting positive urine cultures. The observed low predictive values are associated with the laboratory current UA reflex policy. Although the low predictive values that are associated with the considered parameters;(presence for bacteria, any positive nitrite test, the presence of trace or few esterase, and the presence of WBCs) have been previously reported among out patients, this present study also demonstrated that the same criteria are ineffective in preventing unnecessary antibiotics therapy among inpatients as well [3, 16-17].

The study assessments pointed out the high rate of misuse of antibiotics when using suboptimal laboratory practices [18-19]. In particular, the data analysis indicated that a total of 45.1% of antibiotics were unnecessarily administrated, thus compromising patient safety and adding the risk of developing antibiotic resistance pathogens [20-24].

In conclusion, the current Laboratory UA reflex criteria is ineffective in predicting positive urine culture, thus potentially leading to the inappropriate use of antibiotics. Additionally, the assessment of the historical current UA reflex criteria confirmed the need for the refinement of the laboratory UA reflex practice to improve the quality of laboratory results and to provide accurate and reliable results to ensure adequate and optimal patient treatments.

Conflict of Interest

None declared

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