ORIGINAL PAPER

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Diagnostic value and cost utility analysis for urine Gram stain and urine microscopic examination as screening tests for urinary tract infection

Abstract The aim of this study was to evaluate the diagnostic properties of urine Gram stain and urine microscopic examination for screening for urinary tract infection (UTI), and to perform an additional cost utility analysis. This descriptive study was performed on 95 urine samples sent for urine culture to the Department of Microbiology, Faculty of Medicine, Chulalongkorn University. The first part of the study was to determine the diagnostic properties of two screening tests (urine Gram stain and urine microscopic examination). Urine culture was set as the gold standard and the results from both methods were compared to this. The second part of this study was to perform a cost utility analysis. The sensitivity of urine Gram stain was 96.2%, the specificity 93.0%, the positive predictive value 94.3% and the negative predictive value 95.2%. False positives occurred with a frequency of 7.0% and false negatives 3.8%. For the microscopic examination, the sensitivity was 65.4%, specificity 74.4%, positive predictive value 75.6% and negative predictive value 64.0%. False positives occurred with a frequency of 25.6% and false negatives 34.6%. Combining urine Gram stain and urine microscopic examination, the sensitivity was 98.1%, specificity 74.4%, positive predictive value 82.3% and negative predictive value 97.0%. False positives occurred with a frequency of 25.6% and false negatives 1.9%. However, the cost per utility of the combined method was higher than either urine microscopic examination or urine Gram stain alone. Urine Gram stain provided the lowest cost per utility. Economically, urine Gram stain is the proper screening tool for presumptive diagnosis of UTI.

Introduction

Urinary tract infection (UTI) is an important health problem affecting millions of people each year. Women are especially prone to UTI. Affected women often complain of uncomfortable pressure above the pubic bone and some men experience a feeling of fullness in the rectum. UTI in men is not common, but it can be very serious. In young children and infants, the symptoms of a UTI may be overlooked or mistakenly attributed to other conditions. The symptoms in such patients include irritability, change in eating habits, unexplained fever that does not go away, urinary incontinence or change in urinary pattern, and loose stools [1, 2, 3].

The evaluation of suspected UTI involves a detailed history and physical examination. A laboratory investigation is also required for the diagnosis and evaluation of the disease. Analysis of a collected urine sample in suspected UTI is very useful [4]. Common screening tests for bacteriurias, indicating UTI, include urine Gram stain and a microscopic examination [4]. Here, we report our evaluation of the diagnostic value and cost utility of these screening methods in medical laboratory practice.

Materials and methods

Screening and confirmation test

Two screening tests, urine Gram stain and microscopic examination, were evaluated in this study. Confirmation involved urine culture. All tests were performed according to the standard protocol described in laboratory medicine textbooks [4, 5].

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Study of the diagnostic property

This descriptive study was performed during 2000. A total of 95 urine samples from suspected UTI cases sent to the Department of Microbiology, Faculty of Medicine, Chulalongkorn University were included. All were sent to the Microbiology Laboratory for urine culture tests. After the routine culture technique, we used the remainder of the samples for further laboratory analysis. Each urine sample was divided into two parts. The first part was centrifugated and a urine smear was made of the sediment. The smear was then stained with by Gram stain and examined for the presence of bacteria under a microscope (×1,000 magnification). Then second part was sent for routine microscopic examination, centrifuged and examined under the microscope (×400 magnification). White blood cells, red blood cells, organisms, crystals and casts were looked for. Those investigating the Gram stain and microscopic examinations were blinded to the culture results. According to our study, the primary assumption that the urine culture be accepted as the gold standard is correct. Sensitivity (the probability that the test is positive when given to a group of patients with the disease), specificity (the probability that the test will be negative among patients who do not have the disease), false positive (the probability that the test will be positive among patients who do not have the disease), false negative (the probability that the test is negative when given to a group of patients with the disease), positive predictive value (the probability that the patient has the disease when restricted to those patients who test positive) and negative predictive value (the probability that the patient will not have the disease when restricted to all patients who test negative) were calculated for each test.

The operative definition for positive and negative for each test [4, 5] were defined as:

1. urine Gram stain: positive means the presence of ≥1 bacteria/field (×1,000), negative means <1 bacterium/field
2. urine microscopic examination: positive means the presence of bacteria and pyuria; >5 white blood cells or white blood cell clumps/fieldobjective (×400), negative means <5 white blood cells ir clumps/field
3. urine culture: positive means the presence of colony forming unit (CFU) of 10^5/ml or more, negative means <10^5 CFU/ml

Cost utility analysis

The cost in baht for performing each test was reviewed. The cost used was set as the price of each test at the laboratory, King Chulalongkorn Memorial Hospital. The utility of each method was defined as the rate of ability to detect an abnormal result (confirmed by urine culture). The cost utility analysis was then performed. The operative definition of cost utility is cost divided by the utility.

Table 1 Diagnostic property of UTI by urine Gram stain and urine microscopic examination. Positive for both methods indicates by either urine Gram stain or urine microscopic examination

Screening	Urine culture	
	Positive	Negative
Urine Gram stain		
Positive	50	3
Negative	2	40
Urine microscopic examination		
Positive	34	11
Negative	18	32
Both methods		
Positive	51	11
Negative	1	32

Results

The diagnostic property

From the total urine samples in this study, the prevalence of UTI from urine culture was 54.7% (52 cases). Urine Gram stain and urine microscopic examination could accurately detect 50 (96.2%) and 34 (65.4%) of positive cases, respectively (Table 1). Of 50 Gram stain positive cases, there were two Gram positive uropathogens and 48 Gram negative uropathogens. The findings using Gram stain were identical to those of culture (Table 2). The sensitivity of urine Gram stain was 96.2%, the specificity 93.0%, the positive predictive value 94.3% and the negative predictive value 95.2%. False positive was 7.0% and false negative 3.8%. For the urine microscopic examination, the sensitivity was 65.4%, specificity 74.4%, positive predictive value 75.6% and negative predictive value 64.0%. False positive was 25.6% and false negative 34.6%. Combining urine Gram stain and urine microscopic examination, the sensitivity was 98.1%, specificity 74.4%, positive predictive value 82.3% and negative predictive value 97.0%. False positive was 25.6% and false negative 1.9%.

Cost utility analysis

The cost and utility of each method are shown in Table 3. The cost per utility of the combination method was higher than either urine microscopic examination or

Table 2 Total bacterial spectrum from 52 positive urine culture

Types of organism	Number (%)
Gram negative uropathogens	
Escherichia coli	36 (69.2%)
Proteus mirabilis	8 (15.5%)
Klebsiella pneumoniae	6 (11.5%)
Gram positive uropathogens	
Staphylococcus saprophyticus	2 (3.8%)

Table 3 Cost utility analysis. Cost indicates cost from the Financial Unit, King Chulalongkorn Memorial Hospital, utility indicates the number of abnormal cases/number of total cases

Test	Cost (baht)	Utility (rate)	Cost/utility (baht)
Screening			
Urine Gram stain	50	0.923	54.17
Urine microscopic examination	50	0.654	76.45
Both methods	100	0.981	101.94
Confirmation	150	1.000	150.00

urine Gram stain. Urine Gram stain provided the lowest cost per utility.

Discussion

UTI is an everyday clinical problem [6]. The pathogenesis of UTI is complex and influenced by many host biological and behavioral factors and by properties of the infecting uropathogens [7]. The populations at risk for UTI include the newborn, prepubertal girls, young boys, sexually active young women, elderly males, and elderly females [6, 7]. UTI is mainly caused by bacterial infection [6, 7, 8]. In general, diagnosis is made with regard to typical symptoms and an additional laboratory investigation. Urine culture is a confirmation test which requires a long waiting time and might be omitted in real clinical practice [8].

Some screening tests, such as the urine Gram stain and urine microscopic examination are used for UTI. Urine Gram stain has been reported to have a sensitivity of about 90% [9, 10], and urine microscopic examination of about 80% [11, 12]. We obtained a similar sensitivity for both urine Gram stain and urine microscopic examination. An improvement in sensitivity for the presumptive diagnosis of UTI by the combination of the two methods was reported by Hussain et al. [13]. However, according our study the combination of the two screening methods adds only a little to the sensitivity, but markedly reduces the specificity. Therefore, combination of the two methods seems not to be recommendable.

According to present concepts in laboratory medicine, not only the diagnostic properties of the test but also its cost utility should be considered. Here, we also performed the cost utility analysis for both the urine Gram stain and urine microscopic examination methods. According to our results, there was a higher cost per utility, reflecting that the method costs more for the detection of a UTI case. The cost per utility for urine Gram stain is the lowest, and therefore, this choice should be the best.

Urine Gram stain examination is an economically proper screening for the presumptive diagnosis of UTI.

However, some limitations of our study should be declared. Firstly, the total number of subjects in our study was few. Secondly, we used specimens from suspected cases, not from the general population under evaluation. Thirdly, the cost utility is mainly based on our laboratory setting. Therefore, further study is recommended. Finally, the sensitivity of Gram stain is only so high if $CFU \geq 10^5$/ml is taken as the breakpoint. In some cases of UTI, however, a lower CFU may also be diagnostic, e.g. in acute cystitis with 10^3/ml and sometimes even 10^2/ml. If bladder puncture urine is taken, a lower CFU is also considered diagnostic.

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