Validity of pyuria and bacteriuria (detected by Gram-stain) in predicting positive urine culture in asymptomatic female children

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Abstract

Background & Objectives: Early diagnosis and treatment of urinary tract infections is a cost effective tool in preventing harmful complications in asymptomatic children. The present study assess the validity of two simple and cost saving parameters, namely pyuria determined by general urinalysis and bacteriuria (detected by Gram-stain), in predicting urinary tract infection (established by positive urine culture).

Methods: A total of 600 healthy females children less than seven years of age were included in this study. Urine was collected by clean-catch technique. Fresh uncentrifuged urine specimens were examined for pyuria, while Gram-stained specimens were used to detect bacteriuria. Bacterial cultures were set on agar plates. A bacterial colony count of $\geq 10^5$/ml of urine was considered as an evidence of significant bacteriuria and established the diagnosis of UTI.

Results: The rate of positive urine culture tends to increase with the increasing number of pus cells detected by urinalysis. It also shows a significant positive trend with bacteriuria detected by Gram-stain. Pyuria at cut-off value of ≥ 10 pus cells/mm3 of urine provides the best working parameter for validity giving a positive predicting value (PPV) of 92.3% and a negative predicting value (NPV) of 94.2%. Bacteriuria (detected by Gram stain) at cut-off value of ≥ 3 bacteria/HPF provides the best working parameter for validity giving a positive predictive value of 85.7% and negative predictive value of 94.1%. Parallel combination of the two criteria is associated with 100% sensitivity and 100% negative predictive value. On the other hand, serial combination of both criteria is associated with 100% specificity and 100% positive predictive value.

Conclusion: It is recommended to use both significant pyuria and bacteriuria (detected by Gram-stain) in parallel combination as a screening tool for asymptomatic UTI since their joint sensitivity is 100% in addition to being cheep and easy to perform.

Key words: Asymptomatic UTI, pyuria, bacteriuria.

Introduction

Urinary tract infections represent a major health problem in many areas of the world, affecting millions of people each year; it is the most frequently encountered infection in daily practices[1,2].

Urinary tract infections in children may cause substantial morbidity and there is significant risk that urinary tract infections will give rise to serious acute illness[3, 4], and permanent renal damage[5, 6]. It can be asymptomatic or present with symptoms that can not be linked to the urinary tract[7-9]. Poor long-term prognosis is associated with delay in treatment[10]. Therefore early diagnosis and treatment is a cost effective tool in preventing harmful complications in children. The golden standard test for establishing the diagnosis of UTI is urine culture, which is time consuming and need a well equipped laboratory and personnel. Therefore the use of urine culture is unjustified in asymptomatic children as a screening tool and one needs to validate simpler tests in predicting UTI.

The present study assess the validity of 2 simple and cost saving parameters, namely pyuria determined by general urinalysis and bacteriuria (detected by Gram-stain), in predicting urinary tract infection (established by positive urine culture).

Materials & Methods

A cross-sectional study was conducted in Babel governorate for the period from the 1st December 2003 through 30th the June 2004. A total of 600 healthy females children less than seven years of age were selected from 10 primary health care centers while attending for vaccination. After obtaining an informed consent from the child's guardian, a sample of urine was obtained for analysis. Urine was collected by clean-catch technique. Preliminarily the vulva and labia were washed thoroughly, using sterile cotton pads with benzyl alcohol (0.9% in water) according to the method of Vikers et al.[11]. Urine specimen were transported in cooling box to the laboratory of Maternity and Child Hospital of Babel Governorate for urine analysis and culture.

The enhanced urinalysis technique was used in this study, urine was examined fresh for detection of WBCs and stained specimens were examined for detection of bacteria by the standard light microscopy. The standard criteria for enhanced urinalysis; include looking for pyuria (presence of at least 10 white blood cells/per cubic millimeter) by using a Neubauer hemocytometer. Bacteriuria detected by Gram stain was defined as the presence of at least one bacterium per oil immersion field on Gram-stained smear as described by other workers[12, 13].

Bacterial cultures were set on blood agar and Mac Conkey agar plates by direct streaking with a sterile calibrated platinum wire loops. Both plates were incubated overnight at 37°C. Diagnosis of bacteriuria was made by bacterial count. A bacterial colony count of $\geq 10^5$/ml of urine was considered as an evidence of significant bacteriuria and established the diagnosis of UTI as described by other workers[14, 15].

Statistical analyses were computer assisted using SPSS ver 13 (Statistical Package for Social Sciences). Frequency distribution for selected variables was done first. The statistical significant of association between two categorical variables was assessed by Chi-square test. P value less than 0.05 was considered statistically significant.

Results

The rate of positive urine culture increased from 5.4% in those with no pyuria to 6.7% in those having one to ten pus cells /mm3 of urine, and further to 90.9% in those having 11-20 pus cells/mm3 of urine and then increased to 100% in those having more than 20 pus cells/mm3 of urine as revealed by general urine examination. The increase in the rate of positive urine culture tends to increase with the increasing number of pus cells, this association was statistically significant (Table1).

Regarding bacteriuria, as detected by Gram-stain, the rate of positive urine culture increased from 5.6% in those with no bacterium to 10% in those having one to two bacteria, reaching 50% in those with three to four bacteria and then increased to 100% in those having more than four bacteria/HPF. The increase in the rate of positive urine culture with the increasing number of bacteria was also statistically significant (Table 1).

Table 1: The rate of positive urine culture by the magnitude of pyuria and bacteriuria (detected by Gram-stain).

	Total	**Positive urine culture**	
	No.	**No.**	**%**
Pyuria (Count of pus cells / mm^3 urine)			
0 (negative)	368	20	5.4
1-10	180	12	6.7
11-20	44	40	90.9
≥21	8	8	100
P < 0.001			
Bacteriuria detected by Gram stain (Bacteria/HPF)			
0	504	28	5.6
1-2	40	4	10
3-4	16	8	50
≥5	40	40	100
P <0.001			

As shown in Table 2; the validity of pyuria (count of pus cells/mm^3) in predicting positive urine culture was assessed at three cut-off value (≥1/mm^3, ≥10/mm^3 and ≥21/mm^3 of urine). The sensitivity of pyuria increased from 10% at the highest cut-off value of ≥21/mm^3 of urine to 75% at the lowest cut-off value (≥1/mm^3), while the specificity increased from 66.9% at the lowest cut-off value of ≥1/mm^3 to 100% at the highest cut-off value of ≥21/mm^3 of urine. Pyuria at cut-off value of ≥ 10 pus cells/mm3 of urine provides the best working parameter for validity giving a positive predicting value (PPV) of 92.3% and a negative predicting value (NPV) of 94.2%. Therefore, this cut-off value will be used as significant pyuria for purpose of detection of significant bacteriuria by urine culture.

The validity of bacteriuria detected by Gram-stain was tested at 3 cut-off values of ≥ 1 bacteria/HPF, ≥ 3 bacteria/HPF and ≥ 5 bacteria/HPF in predicting positive urine culture. The sensitivity of bacteriuria increased from 50% at the highest cut-off value (≥ 5 bacteria/ HPF) to 65% at the lowest cut-off value (≥ 1 bacteria/HPF), while the specificity increased from 91.5% at the lowest cut-off value to 100% at the highest cut-off value. Bacteriuria at cut-off value of ≥ 3 bacteria/HPF provides the best working parameter for validity giving a positive predictive value of 85.7% and negative predictive value of 94.1%.Therefore this cut-off value will be labeled as significant bacteriuria for purpose of detection of positive urine culture.

To improve validity of significant pyuria and significant bacteriuria (detected by Gram-stain) in predicting UTI (significant bacteriuria detected by positive urine culture), these two criteria will be used in combination. To improve the sensitivity of predicting UTI, a female child is considered as positive for UTI if the test is positive on any of the two criteria (pyuria or bacteriuria) as this combination is associated with 100% sensitivity and 100% negative predictive value. On the other hand, to increase the specificity, a female child is considered as positive for UTI if the test is positive on both criteria (pyuria and bacteriuria) as this combination is associated with 100% specificity and 100% positive predictive value.

Table 2: Validity parameters of pyuria and bacteriuria (detected by Gram-stain) at different cut off values in predicting positive urine culture.

			Validity parameters				
	No. Negative	**No. Positive**	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
Pyuria (count of pus cells / mm^3) at cut off value:							
(≥1 / mm^3)			75.0	66.9	25.9	94.6	68.0
Negative	348	20					
Positive	172	60					
Significant Pyuria (≥11 / mm^3)			60.0	99.2	92.3	94.2	94.0
Negative	516	32					
Positive	4	48					
(≥21 / mm^3)			10.0	100.0	100.0	87.8	88.0
Negative	520	72					
Positive	0	8					
Bacteruria detected by Gram stain at cut off value:							
(≥1/mm^3)			65.0	91.5	54.2	94.4	88.0
Negative	476	28					
Positive	44	52					
Significant bacteruria (≥3/mm^3)			60.0	98.5	85.7	94.1	93.3
Negative	512	32					
Positive	8	48					
(≥5/mm^3)			50.0	100.0	100.0	92.9	93.3
Negative	520	40					
Positive	0	40					
Microscopical definition of UTI based on urinalysis							
Significant bacteruria detected by Gram stain ***OR*** significant pyuria)			100.0	97.7	87.0	100.0	98.0
Negative (both criteria negative)	508	0					
Positive (any of the 2 criteria positive)	12	80					
Significant bacteruria detected by Gram stain ***AND*** significant pyuria)			20.0	100.0	100.0	89.0	89.3
Negative	520	64					
Positive (both criteria positive)	0	16					

Discussion

The golden standard for establishment of the diagnosis of UTI is the presence of a pure bacterial growth of $\geq 10^5$ colony forming unit/ml of urine[14, 15]. Detection of pyuria by simple urinalysis and bacteriuria by Gram stained smear is however, much simpler techniques that can be used to screen for possible diagnosis of UTI in urine.

In the present study the pretest probability of having UTI (positive urine culture) in an apparently healthy (asymptomatic) female child is 13.3%[16]. This low pretest probability will definitely affect the interpretation of the results of pyuria and bacteruia in predicting UTI in a clinical setting.

The present study showed that the optimal cut-off value of pyuria used to differentiate between infected and non-infected urine in asymptomatic female children was set at the level of $\geq$ 10 pus cells/mm3 of urine, which provides a sensitivity of 60.0% and a specificity of 99.2%. A positive test result will be associated with a PPV of 92.3%, while a negative test would have a NPV of 94.2% in a subject in whom the pretest probability of having UTI is 13.3%. The specificity of the test is very high which therefore resulted in a high predictive value of the positive test in establishing the diagnosis of UTI, even-though the diagnosis of UTI have a low pretest probability in asymptomatic females. On the other hand although the sensitivity of the test is low, the value of negative test in excluding a possible diagnosis of UTI remains high, as the pretest probability of having UTI in asymptomatic females is low.

The results of present study, revealed that the bacteriuria detected by Gram-stained smear at the optimum cut-off value of $\geq$ 3 bacteria/ HPF provides the best working parameter for validity: sensitivity is 60%, specificity is 98.5%, PPV is 85.7% and NPV is 94.1%. The specificity of the test is very high, which therefore resulted in a reasonably high predictive value of the positive test in establishing the diagnosis of UTI, even though the diagnosis of UTI have a low pretest probability in asymptomatic females. On the other hand although the sensitivity of the test is low, the value of negative test in excluding a possible diagnosis of UTI remain high, as the pretest probability of having UTI in asymptomatic females is low.

Other workers studied the performance of pyuria and bacteriuria in diagnosis of UTI and reported comparable results, taking into account the method of urine collection, laboratory procedures, definition of positive urine culture, the cut-off value used and pretest probability of having UTI (prevalence rate of the disease)[17-23].

The results of present study, revealed that combination of significant pyuria ($\geq$ 10 pus cells/mm^3) and significant bacteriuria ($\geq$ 3 bacteria/HPF) detected by Gram-stained smear can increase the sensitivity and NPV to 100% when used in parallel combination, considering the test as positive if any of the two criteria was positive. In this manner the combination of two criteria is useful in screening, a point that was stressed in other literatures[12, 24]. On the other hand using the two criteria in serial, i.e. considering the test as positive only if both criteria were positive can increase the specificity to 100% and PPV to 100% in diagnosis of UTI in asymptomatic female children. Similar conclusions were raised by other workers[12, 25].

It can be concluded from this study that pyuria at cut-off value of 10 pus cells/mm^3 and bacteriuria (detected by Gram-stain) at cut-off value of 3/HPF are highly specific resulting in a high PPV (>90%) for each tests. It is recommended to use both criteria in parallel combination as a screening tool for asymptomatic UTI since their joint sensitivity is 100% in addition to being cheep and easy to perform.

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