URICULT TRIO AS A SCREENING TEST FOR BACTERIURIA IN PREGNANCY

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Objective. To establish the effectiveness in an indigent urban population of Uricult Trio as a screening test for asymptomatic bacteriuria in pregnancy and in diagnosing urinary tract infections (UTI) in symptomatic pregnant women. Likelihood ratios were established for positive and negative Uricult Trio test results.

Subjects. Two populations of patients from the Pretoria region were involved: (*i*) asymptomatic pregnant women attending the antenatal clinic for the first time or presenting in labour; and (*ii*) pregnant women with symptoms suggestive of UTI.

Method. A midstream urine specimen was collected from the two populations of patients, plated onto the Uricult Trio and sent to the laboratory for culture.

Results. The prevalence of asymptomatic bacteriuria in this population was 23%, and for women with symptoms suggestive of UTI, 29%. The likelihood ratios for a positive test were 1.8 and 1.5 for asymptomatic and symptomatic patients respectively. The likelihood ratios for a negative test were 0.35 and 0.44 for asymptomatic and symptomatic patients respectively. *Escherichia coli* was the causative agent in 36% of cases.

Conclusion. Uricult Trio is not effective as a screening test for asymptomatic bacteriuria in pregnancy or for diagnosing UTIs in women with symptoms suggestive of infection.

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Asymptomatic bacteriuria is a common and potentially dangerous medical condition when it occurs during pregnancy.[1] Between 15% and 45% of untreated pregnant women with asymptomatic bacteriuria will develop pyelonephritis. The incidence of asymptomatic bacteriuria is reported as being between 2% and 10%.[2] The prevalence was found to be 11% in a local study[3] conducted in the Pretoria region. Effective antibiotic treatment of pregnant women with asymptomatic bacteriuria reduces the incidence of premature labour and low-birth-weight babies with attendant complications as well as the occurrence of pyelonephritis.[2,4] Therefore screening for asymptomatic bacteriuria is worthwhile during pregnancy.

Previous studies[2,5-11] have been performed using urine reagent sticks with the aim of finding an appropriate screening test for asymptomatic bacteriuria. In a study in the Pretoria region[3] the sensitivity of reagent sticks ranged from 18% to 67%, with the best sensitivity being with the combination of leucocytes, nitrates or proteins. The specificity, however, decreased with any attempt to increase the sensitivity and it was considered not to be an effective screening test. In the same study urine was plated on site onto blood agar before transporting it to the laboratory. This had an excellent sensitivity of 94% and specificity of 95%. These results were very similar to those of an earlier study by Hall and Theron[11] in the Western Cape. Blood agar plates are not commercially available. This means that any screening of asymptomatic bacteriuria is dependent on sending midstream urine specimens to a laboratory for culture. This is often inaccurate because of the time taken to transport the specimens from a clinic to the laboratory, especially in the case of primary health care (PHC) clinics. Furthermore, arranging transport to achieve an acceptable transfer time to the laboratory makes the process very expensive.

Consequently there is still no commercially available, practical and cost-effective screening test available for asymptomatic bacteriuria in pregnancy, especially in the PHC setting. Uricult Trio was investigated for this purpose. Uricult Trio consists of three growth mediums, namely CLED, MacConkey and *Escherichia coli*, and is manufactured by Orion Diagnostica in Finland. The company distributes a chart illustrating the different types of organisms that can be identified as well as interpretation of the size of the colonies. Uricult Trio is designed mainly for the detection of *E. coli* and all the literature distributed with the system cites only studies investigating the detection of *E. coli*.

METHODS

Patients attending the Kalafong Hospital's antenatal clinic for the first time and admitted to hospital with symptoms suggestive of a urinary tract infection (UTI) were requested to participate in the study. They were then divided into symptomatic and asymptomatic groups. The symptomatic group included any woman who had symptoms or clinical signs that would include UTI in the differential diagnosis. After an explanation, patients collected their own midstream urine specimens. The Uricult Trio slide was then dipped into the urine and placed directly in the incubator, while the rest of the specimens were sent to the laboratory for culture. Basic demographic data were collected for each patient. The Uricult

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Trio specimens were incubated for 16 - 24 hours according to the manufacturer's instructions, and were interpreted by one investigator (AG). The colony size was recorded on the information sheet. The result of the Uricult Trio was then compared with the laboratory culture after 3 days or as soon as the results were available. Where the laboratory result indicated a UTI, the patient was contacted and treated with nitrofurantoin.

The laboratory test was regarded as significant if there was a growth reported of 10^5 colony-forming units (CFU)/ml or more, while the Uricult Trio was regarded as positive if there was a growth of 10^3 CFU/ml or more according to the manufacturer's chart.

The Ethics Committee of the University of Pretoria approved the study.

Data were analysed using the standard sensitivity, specificity, positive and negative predictive values as well as by calculating the likelihood ratios for the positive and negative tests.[12] A likelihood ratio of 1 indicates that a test has no predictive value for the outcome of interest. In order for conclusive prediction of the outcome event of interest to be achieved, a likelihood ratio of more than 10 or less than 0.1 is required for a positive and negative test result, respectively. Moderate prediction is achieved with likelihood ratio values of 5 - 10 and 0.1 - 0.2, whereas likelihood ratios of 1 - 5 and 0.2 - 1 generate only minimal prediction. Fagan's[13] nomogram was used for interpreting the test results.

Results

A total of 453 patients were recruited for the study. Fig. 1 illustrates the patient distribution. Laboratory specimens for 79 of the 453 patients never reached the laboratory, with the result that only 374 patients were included in the study. The 79 lost specimens were recorded as having been placed in the laboratory specimen collection boxes, but there was no record of their having been received at the laboratory. This unacceptably high lost specimen rate underlines the importance of finding sensitive on-site tests.

The symptomatic group consisted of 127 patients and the asymptomatic group of 247 patients. The prevalence of significant bacteriuria in the asymptomatic group was 23%, and in the symptomatic group 29%. The sensitivity, specificity, positive and negative predictive values as well as the likelihood ratios for the Uricult Trio are summarised in Table I. For the prediction of a significant laboratory culture of an organism in the asymptomatic group, the likelihood ratio for a positive Uricult Trio was 1.8 and the likelihood ratio for a negative Uricult Trio 0.35. In other words, using the Fagan nomogram[13] the likelihood of an asymptomatic pregnant woman having significant bacteriuria where the Uricult Trio indicated an infection was increased from the basic prevalence

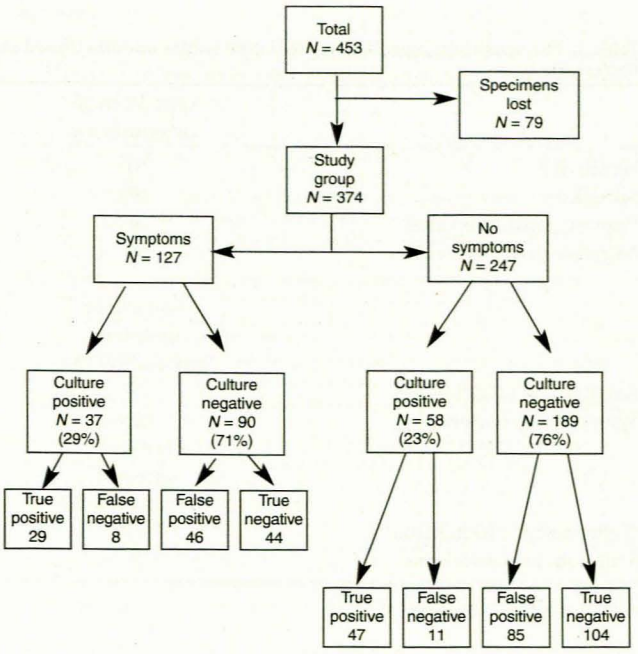

Fig. 1. Outcome of patients entered in the trial.

rate in the population (23%) to a 36% chance of having an infection, whereas the likelihood decreased to 10% if the Uricult Trio was negative. For the prediction of a significant laboratory culture of an organism in the symptomatic group the likelihood ratio for a positive Uricult Trio was 1.5 and the likelihood ratio for a negative Uricult Trio 0.44. In the symptomatic pregnant women the chance of having a significant culture from the laboratory where the Uricult Trio was positive increased from the pre-test probability (prevalence) of 29% to a post-test probability of 39%, whereas the chance decreased to 13% if the Uricult Trio was negative.

All the organisms that were cultured and those missed by the Uricult Trio are given in Table II.

Discussion

The Uricult Trio performed poorly in terms of sensitivity and positive predictive value or after the likelihood ratios were calculated. The likelihood ratios calculated all fall within the minimal prediction category.[12] This is illustrated by the following interpretation of the data. In screening a population for asymptomatic bacteriuria, changing the pre-test probability (prevalence of asymptomatic bacteriuria in the population) from 23% to a post-test probability of 36% for women with a positive Uricult Trio and to 10% for a negative test, is not clinically useful. A clinician would not treat a woman for asymptomatic bacteriuria if she only has a 36% chance of having an infection; laboratory culture of the urine would have to be done for those women with positive tests. This would not

Table I. The sensitivity, specificity, predictive values and likelihood ratios for Uricult Trio in women with asymptomatic and symptomatic bacteriuria

	Asymptomatic bacteriuria (%)	Symptomatic bacteriuria (%)
Sensitivity	81	78
Specificity	55	49
Positive predictive value	36	39
Negative predictive value	90	85

	Prevalence (pre-test probability) (%)	Likelihood ratio for positive test result	Post-test probability (%)
Asymptomatic bacteriuria	23	1.8	36
Symptomatic bacteriuria	29	1.5	39

	Prevalence (pre-test probability) (%)	Likelihood ratio for negative test result	Post-test probability (%)
Asymptomatic bacteriuria	23	0.35	10
Symptomatic bacteriuria	29	0.44	15

Table II. All organisms cultured by the laboratory

Organism	Symptomatic	Asymptomatic	Total	Organisms missed by Uricult Trio
Acinetobacter iwoffi	4	5	9	2
Enterobacter spp.	8	7	15	5
Klebsiella pneumoniae	1	6	7	3
Enterococcus faecalis	2	1	3	2
Acinetobacter baumanni	4	5	9	3
Non-haemolytic streptococci	1	3	4	1
Staphylococcus epidermidis	1	2	3	1
Pseudomonas aeruginosa	0	2	2	1
Escherichia coli	12	20	32	2
Proteus mirabilis	3	4	7	1
Alpha haemolytic streptococci	1	0	1	1
Staphylococcus saprophyticus	0	1	1	
Flavobacterium	2	1	3	
Citrobacter koseri	0	2	2	
Citrobacter freundi	3	3	6	
Alcaligenes faecalis	1	1	2	
Staphylococcus aureus	1	0	1	
Beta haemolytic streptococci	1	1	2	
Klebsiella oxytoca	0	2	2	
Mixed culture (> 3 organisms)	2	13	15	

be cost effective, negating the use of the Uricult Trio as an on-site screening test for asymptomatic bacteriuria. In pregnant women with symptoms of UTI, the Uricult Trio is again disappointing. The post-test probability of not having a UTI if the Uricult Trio test was negative was 13%, which is still a significant chance of having an infection and further cultures would need to be performed in order not to miss an infection. Again this would negate the value of Uricult Trio as a screening test. The post-test probability of a UTI was not much higher than the pre-test probability (35% and 29% respectively). Hence the clinician is left with the decision to treat on the basis of symptoms alone, or to perform another laboratory culture. The Uricult Trio did not add anything in terms of managing the patient more efficiently. This illustrates the value of using

likelihood ratios in determining the effectiveness of a test.

The prevalence of significant urine cultures in both groups was much higher than expected. This is the best-case scenario for the Uricult Trio. With lower prevalence rates of significant urine culture, the post-test probability would differ even less from the pre-test probability. Thus the Uricult Trio is not useful for screening asymptomatic bacteriuria or for diagnosing UTIs in women with symptoms suggestive of an infection.

The manufacturer tested the Uricult Trio in a population where *E. coli* was the causative organism for UTIs in 90% of cases. In two European studies[14,15] the sensitivity for detecting *E. coli* was 92% and 95%. This is borne out by our study because the sensitivity for detecting *E. coli* was 94% and only two *E. coli* infections were missed. However, *E. coli* was the causative agent in only 36% of infections in this study compared with 80 - 90% in the European studies.[14,15]

In order to find a reason for the poor sensitivity of the test the organisms responsible for the false-negatives were analysed. Organisms missed included *E. coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, common urinary pathogens, although none were missed consistently (Table III). This explains the poor results of the Uricult Trio in our population. It is interesting to note that the organisms cultured in the urine of the population were very similar to those cultured in infants who develop acute respiratory or diarrhoeal illness. We hypothesise that there may be a link between the two.

The advantage of this on-site test is that none of the Uricult Trio specimens got lost, as opposed to 79 laboratory specimens in this study. This highlights the value of an on-site test. Another advantage of the Uricult Trio is that one can potentially obtain the result sooner and more easily than with a conventional laboratory culture, which would also have a great impact on the cost of hospitalisation. Hence, although the Uricult Trio was not effective, the search for an effective on-site screening test for asymptomatic bacteriuria must continue.

The prevalence of HIV/AIDS has increased significantly in the Pretoria region since the original prevalence study of asymptomatic bacteriuria in 1996; at this stage one can only speculate whether it is exerting an influence on the prevalence of bacteriuria in pregnancy as well as on the causative pathogens.

Conclusion

The Uricult Trio cannot be recommended — either as a screening test for asymptomatic bacteriuria in pregnancy or as a diagnostic test for UTI in pregnant women with symptoms. The reason for the failure was the diversity of organisms found in the urine culture in our population.

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