Reagent Strip Testing is Not Sensitive for the Screening of Asymptomatic Bacteriuria in Pregnant Women

PISAKE LUMBIGANON, M.D., M.S.*, BUNDIT CHUMWORATHAYEE, M.D.*,
CHOMPILAS CHONGSOMCHAI, M.D., M.H.S.*, JADSADA THINKHAMROP, M.D., M.Sc.*

Abstract

The objective of the study was to assess the diagnostic performance of the reagent strip in screening for asymptomatic bacteriuria in pregnant women using urine culture as a gold standard. This study comprised 204 asymptomatic pregnant women who attended their first antenatal care at Srinagarind Hospital, Khon Kaen University from April 1, 1999 to June 30, 1999. Women with symptoms of urinary tract infection, antibiotic treatment within the previous 7 days, pregnancy-induced hypertension, bleeding per vagina and history of urinary tract diseases were excluded. Urine specimens were collected by clean catched midstream urine technique for urinalysis, reagent strip test and urine culture. Diagnostic performance of reagent strip in terms of sensitivity, specificity, positive and negative predictive value was analyzed. Urine reagent strip test had a sensitivity of 13.9 per cent, a specificity of 95.6 per cent, a positive predictive value of 46.1 per cent, a negative predictive value of 80.6 per cent in detecting asymptomatic bacteriuria in pregnant women.

Key word : Reagent Strip, Asymptomatic Bacteriuria, Pregnancy

LUMBIGANON P, CHUMWORATHAYEE B, CHONGSOMCHAI C, THINKHAMROP J
J Med Assoc Thai 2002; 85: 922-927

Asymptomatic bacteriuria (ASB) is defined as the presence of $\geq 10^5$ colony forming units of single type bacteria per milliliter of urine detected by mid stream urine culture in asymptomatic patients[1-3]. The reported prevalence of ASB during pregnancy ranged from 2.5 per cent to as high as 23.9 per cent [4-7]. Results of the meta-analysis of 17 cohort studies showed an association between ASB and low birth weight and preterm birth[8]. Without appropriate management 25 per cent of pregnant women with

* Department of Obstetrics and Gynecology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

ASB will develop acute pyelonephritis later on during pregnancy which can lead to sepsis[9]. This acute pyelonephritis is also one of the risk factors of preterm delivery and low birth weight[10]. Accurate diagnosis and appropriate management of ASB is very crucial in preventing its potential serious consequences. There was evidence from meta-analysis that antibiotic treatment was effective in clearing ASB and the incidence of pyelonephritis was also reduced. Furthermore, antibiotic treatment was also associated with a reduction in the incidence of preterm delivery or low birth weight[11]. Routine urine culture for all pregnant women is recommended for the detection of ASB[9]. This is costly and not feasible in many parts of the world. Simple urinalysis by looking for the presence of white blood cells was shown not to be sensitive in the screening for ASB in pregnant women[7]. There was a report indicating that reagent strip test might be useful as a screening test for ASB[12]. The authors aimed to confirm the diagnostic performance of reagent strip test as a screening test for ASB in pregnant women.

MATERIAL AND METHOD

Pregnant women who attended their first antenatal care at Srinagarind Hospital, Khon Kaen University from April 1999 to June 1999 were invited to participate in the study. Women who had symptomatic UTI, received antibiotics during the past 7 days, pregnancy-induced hypertension, bleeding and history of urinary tract diseases were excluded. Written informed consent was obtained from each eligible woman. Eligible women were advised how to correctly collect clean mid stream urine into 2 sterile containers. One container was sent to the laboratory for urine culture within 30 minutes after collection. Urine culture was performed using blood and Mac Conkey agar incubating at 35°-37°C for 24 to 48 hours. The presence of $\geq 10^5$ colony forming units of a single type of bacteria per milliliter of urine indicated bacteriuria. If a urine culture revealed more than one type of organism the urine culture was repeated. The urine in the other container was tested for leucocyte-esterase, nitrite, blood or protein by a reagent strip (Ames Multistix 10 SG, Bayer Bangkok Ltd, Thailand) and then sent to the laboratory for simple urinalysis. The urine reagent strip test was interpreted as positive if the color on the dipstick was positive for leucocyte esterase, nitrite, blood and more than a trace positive for protein. Simple urinalysis was performed by centrifuge of 10 milliliters of urine at 3,000 round per minute for 5 minutes. It was interpreted as positive if there were ≥5 white blood cells per high power field (WBC/HPF). The diagnostic performance of each test was analysed by using the STATA 6 software program. The Ethics Committee of Khon Kaen University approved this study.

RESULTS

Two hundred and four women were recruited. There were 43 women with positive urine culture. The prevalence of ASB in this study was therefore 21.1 per cent. Using urine culture as a gold standard, the urine reagent strip test had a 13.9 per cent sensitivity, 95.6 per cent specificity, 46.1 per cent positive predictive value, 80.6 per cent negative predictive value, 78.4 per cent accuracy with likelihood ratio positive (LR+) of 3.21 and likelihood ratio nega-

Table 1. Diagnostic performance of reagent strip test as a screening test for asymptomatic bacteriuria in pregnant women.

Reagent strip test	Urine culture		Total
	Positive	Negative	
Positive	6	7	13
Negative	37	154	191
Total	43	161	204

Sensitivity	= 6/43	= 13.9% (95% CI 9.2, 18.7)
Specificity	= 154/161	= 95.6% (95% CI 92.9, 98.5)
Positive predictive value	= 6/13	= 46.1% (95% CI 39.3, 53.0)
Negative predictive value	= 154/191	= 80.6% (95% CI 75.2, 86.1)
Prevalence	= 43/204	= 21.1% (95% CI 15.5, 26.7)
Likelihood ratio positive	= 3.21	
Likelihood ratio negative	= 0.90	

tive (LR-) of 0.90 in detecting asymptomatic bacteriuria in pregnant women, Table 1. Similarly, simple urinalysis had a 7.0 per cent sensitivity, 98.0 per cent specificity, 50.0 per cent positive predictive value, 79.8 per cent negative predictive value, 78.9 per cent accuracy with LR+ of 3.75 and LR- of 0.95 in detecting asymptomatic bacteriuria in pregnant women, Table 2. If considering either the positive reagent strip test or positive simple urinalysis as a positive test, it had a 18.6 per cent sensitivity, a 94.4 per cent specificity, a 47.1 per cent positive predictive value, a 81.3 per cent negative predictive value, 78.4 per cent accuracy with LR+ of 3.33 and LR- of 0.86 in detecting asymptomatic bacteriuria, Table 3. *Staphylococcus epidermidis* was the most common organism responsible for 69.8 per cent of ASB, followed by *Escherichia coli* and *Enterococcus species* and gamma-hemolytic streptococci not group D, Table 4. There was no case of ASB with more than one organism.

DISCUSSION

The sensitivity of the reagent strip test as a screening test for ASB in pregnant women was only 13.9 per cent. Even used with simple urinalysis, the combination test still had only 18.6 per cent sensitivity. This sensitivity is too low to be used as a screening test for ASB because more than 80 per cent of patients with ASB would be missed. The prevalence of ASB in this study was 21.1 per cent, which was rather high, compared to previous studies (4-7). The most common causative organism was

Table 2. Diagnostic performance of simple urinalysis as a screening test for asymptomatic bacteriuria in pregnant women.

Simple urinalysis	Urine culture		Total
	Positive	Negative	
Positive	3	3	6
Negative	40	158	198
Total	43	161	204

Sensitivity	= 3/43	= 7.0% (95% CI 3.5, 10.5)
Specificity	= 158/161	= 98.0% (95% CI 96.3, 100.0)
Positive predictive value	= 3/6	= 50.0% (95% CI 43.1, 56.9)
Negative predictive value	= 158/198	= 79.8% (95% CI 74.3, 85.3)
Prevalence	= 43/204	= 21.1% (95% CI 15.5, 26.7)
Likelihood ratio positive	= 3.75	
Likelihood ratio negative	= 0.95	

Table 3. Diagnostic performance of reagent strip combined with simpleurinalysis as a screening test for asymptomatic bacteriuria in pregnant women.

Reagent strip or Simple urinalysis	Urine culture		Total
	Positive	Negative	
Positive	8	9	17
Negative	35	152	187
Total	43	161	204

Sensitivity	= 8/43	= 18.6% (95% CI 13.3, 24.0)
Specificity	= 152/161	= 94.4% (95% CI 91.3, 97.6)
Positive predictive value	= 8/17	= 47.1% (95% CI 40.2, 53.9)
Negative predictive value	= 152/187	= 81.3% (95% CI 75.9, 86.6)
Prevalence	= 43/204	= 21.1% (95% CI 15.5, 26.7)
Likelihood ratio positive	= 3.33	
Likelihood ratio negative	= 0.86	

Table 4. Frequency of causative agents for asymptomatic bacteriuria.

Organisms	Number	%
Staphylococcus epidermidis	30	69.8
Escherichia coli	4	9.3
Enterococcus species	3	7.0
γ-hemolytic Streptococcus not group D	3	7.0
Non-hemolytic Streptococcus not group D	1	2.3
β-hemolytic Streptococcus group A	1	2.3
Klebsiella pneumoniae	1	2.3
Total	43	100

staphylococcus epidermidis that accounted for 69.8 per cent of all ASB. This finding is similar to a previous study by the authors[7].

Although Staphylococcus epidermidis was the most common causative organism in this study, it is unlikely to be due to contamination. The research nurse carefully explained to each recruited woman (in local dialect if necessary) how to correctly collect clean mid stream urine. Moreover, if a urine culture revealed more than one type of organisms which is more likely to be because of contamination, the urine culture was repeated. Staphylococcus epidermidis was also the most common organism (31.8%) found in the other ASB study from the southern part of Thailand[13]. It is quite possible that Staphylococcus epidermidis is really the most common causative organism for ASB in Thai pregnant women. If all specimens with Staphylococcus epidermidis were excluded from the analysis the sensitivity and specificity would be 30.8 per cent and 95.6 per cent respectively. The sensitivity of 30.8 per cent is still too low to be clinically useful.

Concerning the sensitivity of the reagent strip test, the other study conducted in the southern part of Thailand revealed a sensitivity of 39.0 per cent[13]. The most common organism in this study was also *Staphylococcus species* (31.8%). On the other hand, a study from the UK indicated that the leucocyte-nitrite dipstick had an 81.8 per cent sensitivity in detecting bacteriuria in both asymptomatic and symptomatic UTI. A major difference of this study from the 2 Thai studies was that in this study *Escherichia coli* was the most common causative agent and accounted for 62.9 per cent of all infection [12]. There was a report indicating that the nitrite test is more sensitive for ASB caused by gram negative bacteria than that caused by gram positive bacteria [14]. The authors' earlier report showed that the presence of ≥5 WBC/HPF was not sensitive in detecting ASB[7]. This indicated indirectly that there were not many WBC in urine of pregnant women with ASB. This might also help in explaining why a reagent strip test which detects leukocyte esterase was also not sensitive in detecting ASB. It might also be possible that women with ASB caused by gram-positive bacteria do not have as many WBC in their urine as those who have ASB caused by gram negative bacteria.

This study strictly followed the principle of good clinical practice in conducting clinical research. The inter observer variation was controlled by using only one person performing the reagent strip test, only one person performing the urine culture and also only one group of people performing the simple urinalysis. The people who performed each test did not know the result of the other tests. The sample size was calculated in advance to ensure adequate sample size and that the target sample size was reached.

The result of the present study indicated that neither reagent strip test nor simple urinalysis looking for the presence of WBC is sensitive enough as a screening test for ASB in pregnant women. Urine culture should still be recommended as a screening test for ASB in pregnant women wherever possible. In the authors' opinion, in a low resource setting urine culture should be considered in high risk women such as low socioeconomic, sickle cell trait, diabetes mellitus, anemia and prior UTIs[15-18].

ACKNOWLEDGEMENTS

The authors wish to thank all nursing and supporting staff at the antenatal care clinic, Srinagarind Hospital, Khon Kaen University for their assistance in giving advice to the patients and collecting the specimens, Associate Professor Kriangkri Kitcharoen for Ames Multistix, Dr. Bandit Thinkhamrop for his help in data analysis, and the Faculty of Medicine, Khon Kaen University for the financial support.

(Received for publication on April 24, 2002)

REFERENCES

1. Stamm WE. Urinary tract infection and pyelonephritis. In: Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL, editors. Harrison's Principles of Internal Medicine. 13th ed. New York: McGraw-Hill, 1994: 548-54.
2. Lorentzon S, Hovelius B. The diagnosis of bacteriuria during pregnancy. Scand J Prim Health Care 1990; 75: 81-3.
3. Platt R. Quantitative definition of bacteriuria. Am J Med 1983; 75: 44-52.
4. Mark G, Martin S. Pyelonephritis. Obstet Gynecol Clin Nor Am 1989; 16: 176-8.
5. Reddy J, Campell A. Bacteriuria in pregnancy. Aust NZ J Obstet Gynecol 1985; 25: 176-8.
6. Olusanya O, Ogunledun A, Fogaya TA. Asymptomatic significant bacteriuria among pregnant and nonpregnant women in Sagamu, Nigeria. West Afr J Med 1993; 12: 27-33.
7. Chongsomchai C, Piansriwatchara E, Lumbiganon P, Pianthaweechai K. Screening for asymptomatic bacteriuria in pregnant women: urinalysis *versus* urine culture. J Med Assoc Thai 1999; 82: 369-73.
8. Romero R, Oyarzun E, Mazor M, Sirtori M, Hobbins JC. Meta-analysis of the relationship between asymptomatic bacteruria and preterm delivery/low birth weight. Obstet Gynecol 1989; 73: 577-82.
9. Cunningham FG, MacDonald PC, Gant NF, et al. Williams Obstetrics. 20th ed. Stamford: Appleton & Lange, 1997: 1125-44.
10. Gruneberg RN, Leigh DA, Brunfitt W. Relationship of bacteriuria in pregnancy to acute pyelonephritis, prematurity and fetal mortality. Lancet 1969; 2: 1-3.
11. Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy (Cochrane Review). In: The Cochrane Library, Issue 4, 2000. Oxford: Update software.
12. Etherington IJ, James DK. Reagent strip testing of antenatal urine specimens for infection. Brit J Obstet Gynaecol 1993; 100: 806-8.
13. Suntharasuj T, Akrawinek S, Manopsilp P. The urine dipstick for screening of asymptomatic bacteriuria in pregnant women. Songklanagarind Med J 1993; 11: 15-20.
14. Ozeki S, Kawamura T, Nishino Y, Ishihara S, Ban Y, Kawada Y. Clinical evaluation of nitrite test for the detection of bacteriuria. Hinyokika-Kiyo 1997; 43: 861-5.
15. Chongsomchai C, Piansriwatchara E, Lumbiganon P, Pianthaweechai K. Risk factors for asymptomatic bacteriuria in pregnant women. Srinagarind Med J 1997; 12: 69-73.
16. Pritchard JA, Scott DE, Whalley PH, Cunningham FG, Mason RA. The effects of maternal sickle hemoglobinopathies and sickle cell trait on reproductive performance. Am J Obstet Gynecol 1973; 117: 662-70.
17. Lye WC, Chan RK, Lee EJ, Kumarasinghe G. Urinary tract infections in patients with diabetes mellitus. J Infect 1992; 14: 169-74.
18. Stamm WE, McKevitt M, Roberts RL, White NJ. Natural history of recurrent urinary tract infections in women. Rev Infect Dis 1991; 13: 77-84.

การใช้แถบทดสอบไม่ไวพอที่จะใช้คัดกรองภาวะการติดเชื้อแบคทีเรียในปัสสาวะแบบไม่มีอาการของสตรีตั้งครรภ์

ภิเศก ลุมพิกานนท์, พ.บ., M.S., บัณฑิต ชุมวรฐายี, พ.บ.*,*
โฉมพิลาศ จงสมชัย, พ.บ., M.H.S., เจศฎา ถิ่นคำรพ, พ.บ., M.Sc.**

การศึกษานี้เพื่อประเมินความสามารถของแถบทดสอบในการคัดกรองภาวะการติดเชื้อแบคทีเรียในปัสสาวะแบบไม่มีอาการในสตรีตั้งครรภ์ สตรีตั้งครรภ์จำนวน 204 คน ที่มาฝากครรภ์ครั้งแรกที่โรงพยาบาลศรีนครินทร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น ระหว่างวันที่ 1 เมษายน 2542 ถึง 30 มิถุนายน 2542 สตรีตั้งครรภ์ที่มีอาการของการอักเสบในทางเดินปัสสาวะได้รับยาปฏิชีวนะในระยะ 7 วันที่ผ่านมา มีภาวะความดันโลหิตสูง มีเลือดออกทางช่องคลอดหรือมีประวัติโรคทางเดินปัสสาวะถูกคัดออกจากการศึกษา ผู้ตั้งครรภ์ที่เข้าร่วมโครงการเก็บปัสสาวะโดยวิธีเก็บส่วนกลางอย่างสะอาดเพื่อทำการตรวจปัสสาวะแบบธรรมดา ตรวจโดยใช้แถบทดสอบและเพาะเชื้อ วิเคราะห์ความสามารถของแถบทดสอบในการคัดกรองภาวะการติดเชื้อแบคทีเรียในปัสสาวะพบว่ามีความไว 13.9% ความจำเพาะ 95.6% ความถูกต้องเมื่อการตรวจให้ผลบวก 46.1% และความถูกต้องเมื่อการตรวจให้ผลลบ 80.6% เนื่องจากความไวของการทดสอบต่ำมาก จึงไม่ควรใช้สำหรับคัดกรองภาวะการติดเชื้อแบคทีเรียแบบไม่มีอาการในสตรีตั้งครรภ์

คำสำคัญ : แถบทดสอบ, ภาวะการติดเชื้อแบคทีเรียในปัสสาวะแบบไม่มีอาการ, สตรีตั้งครรภ์

ภิเศก ลุมพิกานนท์, บัณฑิต ชุมวรฐายี,
โฉมพิลาศ จงสมชัย, เจศฎา ถิ่นคำรพ
จดหมายเหตุทางแพทย์ ฯ 2545; 85: 922–927

* ภาควิชาสูติศาสตร์-นรีเวชวิทยา, คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น, ขอนแก่น 40002