Screening for Asymptomatic Bacteriuria during Pregnancy-Dipstick Urine Analysis versus Simple Microscopic Urine analysis

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Abstract: Background: During pregnancy the incidence of asymptomatic bacteriuria (ASB) and symptomatic UTI may be as high as 8% with potentially harmful maternal and fetal results .Nearly 1-2% of women may develop acute pyelonephritis secondary to bacteriuria during pregnancy.Detection of asymptomatic bacteriurea is essential in pregnancy .The gold standard test for detection of ASB is urine culture. **Objective**: To assess whether or not dipstick and simple microscopic urine analysis are helpful for detection of asymptomatic bacteriuria in pregnant patients. Accuracy is evaluated by using urine culture as a gold standard. **Material and Methods:** Midstream voided urine samples obtained from 1st trimesteric 200 pregnant women attending the OPC of Ain Shams University Maternity Hospital then tested using dipstick urine analysis (to detect nitrite and leukocyte esterase enzyme) and simple microscopic urine analysis (to detect pyuria (≥10 WBC/hpf) and bacteriuria (any Bactria/hpf)). Urine cultures were performed using CLED (cysteine, lactose, electrolyte deficient agar) and, and more than 100,000 colony forming units per ml indicating asymptomatic bacteriuria. Each result was compared with urine culture. Validity of dipstick and simple microscopic urine analysis were investigated, using sensitivity, specificity, positive and negative predictive values for each parameter and in combination. **Results:** Nitrite test was found to be the most accurate (85%) for detection of asymptomatic bacteriuria, and showed the best agreement with the urine culture (κ=0.264, P <0.01), Nitrite test showed high specificity (92.75%), low sensitivity (32%), high NPV (90.5%), low PPV (38.1%). Sensitivity of leukocyte esterase test was 84%, specificity was 92.75%, PPV was 18.1% and NPV was 90.5%, it has the highest NPV (95.24%), good negative test. leukocyte esterase test showed low degree of agreement with culture bacteriuria (κ = 0.116, P =0.005). Combining nitrite test with leukocyte esterase makes no difference, sensitivity becomes 84%, specificity becomes 44%, PPV 17.65% and NPV 95.06%, combining the two tests showed little agreement with culture bacteriuria(κ = 0.107, P =0.008). Microscopic examination of bacteriuria showed a little degree of agreement with culture bacteriuria (kappa value= 0.197%), by calculating its sensitivity, specificity, PPV and NPV, it showed low sensitivity (52%), specificity (72%), low PPV (20.97%), high NPV (91.3%). Microscopic examination of pyuria showed little degree of agreement with culture bacteriuria (kappa value= 0.147%). Using either microscopic bacteriuria or pyuria parameter increases its sensitivity (60%), deceases its specificity (62.29%), decreases PPV (18.52%), made no difference with NPV (91.6%). **Conclusion:** Dipsticks or microscopic urine analysis, are not optimal methods for screening of asymptomatic bacteriuria.
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Key words: Asymptomatic bacteriuria, Nitrite test, Leucocyte Esterse test, Microscopic urine examination, Urinary tract infection.

1. Introduction

Urinary tract infections (UTI) occur more frequently in women as compared to men. Approximately 15% of women will have urinary tract infections at some time during their life. During pregnancy the incidence of asymptomatic bacteriuria (AB) and symptomatic UTI may be as high as 8% with potentially devastating results for both the mother and the baby [1, 2]. Nearly 1-2% of women may develop acute pyelonephritis secondary to bacteriuria during pregnancy that can be attributable to the remarkable ureteral dilatation, urinary stasis, vesico-ureteral reflux, and glucosuria leading to bacterial growth. The risk of premature labor and low birth weight infants is also increased in patients with asymptomatic bacteriuria [3]. On the other hand, inappropriate empirical antibiotic therapy increases the cost and the bacterial resistance. Therefore an easy, fast, non-invasive and cost-effective test that will accurately allow early diagnosis of asymptomatic bacteriuria during prenatal visits, is highly desired. Urine culture is the definitive standard test for the screening of asymptomatic bacteriuria, it is time consuming and expensive. Dipstick and microscopic urine analysis are widely available, rapid and relatively inexpensive tests. The aim of this study was to evaluate the accuracy of Dipstick and microscopic urine analysis compared to standard urine culture.

2. Material and Methods

The study group includes 1st trimesteric 200 pregnant women attending the OPC of Ain Shams University Maternity Hospital. All subjects were informed about the aim of the study and gave consent. Patients who complained of urinary tract infection symptoms or those currently on antibiotic therapy were excluded from the study.

Urine analysis: clean voided midstream urine specimen collected after proper verbal instructions and provision of a sterile specimen bottle. Then each sample was refrigerated in 4ºc and transported to the lab within 4hrs. Then each sample was investigated for:

1. Culture sensitivity test, each sample was cultured using CLED agar and incubated for 24hrs at 37°C. Asymptomatic bacteriuria is diagnosed by presence of ≥100,000 CFU/ml urine.
2. Microscopic urine analysis: For urinary sediment microscopy, specimens centrifuged in 15ml amount at 2,000 rpm for 5 minutes and urine sediment examined by microscopy under high power magnification. Asymptomatic bacteriuria is diagnosed either by bacteriuria (presence of bacteria/hpf) or pyuria (≥10 WBC/hpf).
3. Combur10® Test (Roche Company): The kit is put in urine sample for (30-60 seconds). A positive test was defined when the strip showed any of the following: any positive result for nitrite, any positive result for leukocyte esterase. LE was recorded as negative, trace (10:25 leukocyte/µl), small (75 leukocyte/µl), moderate (100 leukocyte/µl) or large (500 leukocyte/µl). For the purposes of the study, LE was recorded as positive if the reading was small or more. Nitrite was recorded as positive (if it turns purple) or negative.

3. Results

The age of the patients ranged from 16 to 38 years (25.7±5.01 years), and gestational ages between 6 weeks and 12 weeks' (9.95±1.71 weeks) gestation

Urine culture was positive for asymptomatic bacteriurea in 25 women patients out of 200(12.5%). nitrite test disagreed in 30 cases ,17 (false negative) and 13 (false positive). Nitrite test showed high specificity (92.75%), low sensitivity (32%), high NPV (90.5%), low PPV (38.1%) as shown in table (1). Nitrite test showed high degree of agreement with culture results (κ=0.264 , P <0.01).Tables(1,5)

Leukocyte esterase test disagreed in 99 cases, 4 (false negative) and 95 (false positive). Sensitivity of leukocyte esterase test was 84%, specificity was 92.75%, PPV was 18.1% and NPV was 90.5%. LE test showed low degree of agreement with culture results (κ = 0.116, P =0.005). Tables(2,5).

Table (1): Nitrite test results compared to culture bacteriuria

	Culture positive	Culture negative
Nitrite positive	13	8
Nitrite negatve	17	162

Table (2): LE test results in comparison to culture bacteriuria

	Culture negative	Culture positive
LE positive	95	21
LE negative	80	4

Combined leukocyte esterase and nitrite tests disagreed in 102 cases, 4 (false negative) and 98 (false positive) ,Combining nitrite test with leukocyte esterase adds no benefit, sensitivity becomes 84%, specificity becomes 44%, PPV 17.65% and NPV 95.06% .Combining the two tests showed little agreement with culture bacteriuria(κ = 0.107, P =0.008).Table (3)

Table (3): Combined LE test and nitrite test, compared to culture results, their kappa value

	Lesn*positive	Lesn*negateive	Total
Culture.positive	21(10.5%)	4(2%)	25(12.5%)
Cultureegative	98(49%)	77(38.5%)	175(87.5%)
Total	119(59.5%)	81(40.5%)	200
	κ= 0.107%	P<0.008	

*Lesn: combined LE test with nitrite test

Microscopic examination finding either pyuria or bacteriuria disagreed in 76 cases, 10 (false negative) and 66 (false positive). Microscopic examination had sensitivity (60%), specificity (62.29%), PPV (18.52%) and NPV (91.6%). (κ = 0.114, *P*= 0.034) .Tables(4,5)

Table (4): Microscopic examination pyuria or bacteriuria, compared to the results and culture results, its kappa value

		Culture positive	Culture negative	Total
ME positive	n(%)	15(7.5)	66(33)	81(40.5)
ME negative	n(%)	10(5)	109(54.5)	119(59.5)
Total		25(12.5)	175(87.5)	200
		κ = 0.114%	*P*= 0.034	

Table (5): Comparison between (nitrite test leukocyte esterase test-microscopic examination) using sensitivity, specificity, PPV, NPV, accuracy& kappa value

Test	Sens.	Spec.	PPV	NPV	Accuracy	κ
Either bacteriuria or pyuria by ME	60%	62.29%	18.52%	91.6%	62%	0.114%
Nitrite test	32%	92.75%	38.1%	90,5%	85%	0.264%
Esterase test	84%	45.71%	18,1%	95.24%	50.5%	0.116%
Nitrite and esterase tests	84%	44%	17.65%	95.06%	49%	0.107%

4.Discussion

In this study, urine reagent strips had shown, low sensitivity of nitrite test alone (32%), high specificity (92.75%), PPV (38.1%) , high NPV (90.5%) , highest accuracy (85%) and highest kappa value (0.264), this means that nitrite test is a good negative test as its high specificity and NPV, and also this means that nitrite test has the highest degree of agreement with urine culture, this agrees with a study employing urine reagent strips conducted in USA, nitrite test alone showed high specificity (98.9%) and NPV(95.1%)and low sensitivity (43.4%) [(4)]. In a large study applied in USA included 1047 pregnant patients screened for ASB, nitrite test showed high specificity (99.7%) and low sensitivity (45.8%) [(5)] .In this study leukocyte esterase test has the highest sensitivity (84%), therefore it has high false positive results, but it has low specificity (45.71%), low PPV (18.1%) and high NPV (95.24%). This is parallel to the study of Robertson, in which LE test had high sensitivity (77.4%), low PPV (64%) and high NPV (97.9%) [(6)] .In combination of leukocyte esterase test with nitrite there was no added value, this does not agree with other studies as Bachman's study in which combining the two test made a great difference, specificity (100%) and PPV (100%) [(5)]. In another study by Tincello combined LE and nitrite tests showed no added value, as they had 33.3% sensitivity, 91.1% specificity, 17% PPV and 9.6% NPV [(7)] .

Fiona and colleagues 2007 in a similar study concluded that in pregnant women the accuracy of nitrites was high, and that a negative test for both leukocyte esterase and nitrites could rule out infection in pregnant women [(8)] this is parallel to this study as NPV for combined tests was high (95.06%). The above mentioned studies employed urine reagent strips, all showing low sensitivity, and variable specificity, positive as well as negative predictive values, this variability may be due to variable prevalence and variable causative organisms as not all uropathogens can reduce nitrates and some organisms convert nitrates to ammonia efficiently so that there is not enough nitrites during reduction to permit detection. Different cut-off values were used in studies that evaluated the use of pyuria in screening for asymptomatic bacteriuria, but here in this study cut-off was ≥10 WBC/hpf. This study stated that sensitivity of ME (either pyuria or bacteriuria) is (60%), specificity is (62.29%), PPV is (18.52%) and NPV is (91.6%), this means that there was little value for its use because of its low sensitivity and specificity. In a study done by Archibald sensitivity of ME was (20%), specificity was (89%), PPV was (91%) and NPV was (91%) using 5 WBC/hpf or more as a cut-off [(9)], in another study done by Bachman who used 10 WBCs/hpf as a cut-off, sensitivity was 25%, specificity was 99% and PPV was 37.5% [(5)]. In the previous two studies the accuracy of urine analysis using different cut-offs for pyuria, 5 or more leukocytes/hpf and more than 10 leukocytes/hpf, neither showed pyuria to be of value in screening for asymptomatic bacteriuria in pregnancy because of its low sensitivity. Direct examination of urine is rapid and inexpensive and requires little technical expertise; however, the sensitivity is generally low. About 50% of

asymptomatic bacteriurics can have <3 leukocytes/hpf in spun urine. Conversely, about one third of pregnant non-bacteriuric women can have 5 or more leukocytes/hpf [(8)].

Conclusion

This study proves that rapid and cheap methods, in the form of urinary dipsticks or microscopic urine analysis, are not optimal methods for screening of asymptomatic bacteriuria.

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