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Detection of Urinary Tract Infection (UTI) and asymptomatic bacteriuria using urinalysis parameters, a review

Abstract

Background: Urinary tract infections (UTIs) are a very common occurrence globally. In order to diagnose a UTI accurately, one must be aware of the variable presentations of a UTI. Given this, UTIs generally have three presentations: Asymptomatic bacteriuria (ASB), acute cystitis, and pyelonephritis. Due to the pathology of UTIs, it is not uncommon to see significant bacteriuria in asymptomatic patients. Since UTIs are common, readily available means of diagnosis which are accurate and cost effective are needed. Therefore, urinalysis is regularly used in the diagnosis of UTI and ASB in pregnancy because they are easy to perform and produce results rapidly. However, there appears to be little evidence of their accuracy and cost–effectiveness as compared with standard culture techniques when quantified for positive and negative likelihood ratios. This is a literature review of the efficacy of urinalysis screening in the diagnosis of asymptomatic bacteriuria or UTI in pregnancy.

Objective: The sensitivity and accuracy of urinanalysis parameters in detecting UTIs and Asymptomatic Bacteriuria during pregnancy was reviewed. This was done in order to evaluate the accuracy of nitrite and Leucocyte Esterase (LE) dipsticks for screening and treating UTIs and ASB in situations where culture results were not available.

Conclusion: Overall, this review demonstrates that the urine dipstick test alone seems to be useful in to exclude the presence of an infection if the results of both nitrites and leukocyte–esterase are negative. Different studies reported broad ranges of sensitivities and specificities for urinalysis parameters. Combination of nitrite and leukocyte esterase when both parameters are positive, seem to have the highest specificity in detecting bacteriuria in asymptomatic pregnant women. Although the combination of positive test results are very sensitive in practice, the usefulness of the dipstick test alone to rule in an infection still remains doubtful, even with high pre–test probabilities. Urine culture remains the gold standard for diagnosis of urinary tract infection and asymptomatic bacteruria.

Keywords: Acute Cystitis, Asymptomatic Bacteriuria (ASB), Cystitis, Pyelonephritis, Sensitivity, Specificity, Urinalysis Parameters, Urinalysis, Urinary Tract Infections (UTIs), Urine Culture

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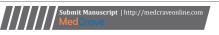**Received:** January 09, 2016 | **Published:** February 11, 2016

Introduction

Urinary tract infections (UTI) are a common occurrence and are a unique pathology as they have a variable presentation.[1] The principal presentations include asymptomatic bacteriuria (ASB), acute cystitis, and pyelonephritis.[2] The focus of this review was on asymptomatic bacteriuria. Asymptomatic bacteriuria is defined as the presence of bacteria in urine without any symptoms of a urinary tract infection. Quantitative criteria for identifying significant bacteriuria in an asymptomatic person are: (1) at least 100,000 colony–forming units (CFUs) per mL of urine in a voided midstream clean–catch specimen and (2) at least 100 CFUs per mL of urine from a catheterized specimen.[3–5]

Epidemiologically, asymptomatic bacteriuria occurs in 5% to 10% of all pregnancies, with the prevalence highest in women of low socioeconomic status (SES) and those with diabetes.[1,6] In females, the urethra is shorter distance to the bladder than males which increases the chances of getting a UTI.[6] Patients in low SES have less access to health care and have a higher prevalence of morbidities such as diabetes which depresses the immune system, making a UTI more likely.[7,8]

The literature suggests that pregnant women with asymptomatic bacteriuria who do not get treatment are more likely to develop pyelonephritis in the third trimester.[6,7] The number is approximated to be 20% to 30%.[8–10] This increases the risk of complications not only to the mother but to the fetus. The risks of the fetus include intrauterine growth restriction (IUGR) and prematurity. The pathogenesis of IUGR is thought to be from the drastic increase in pro–inflammatory cytokines such as IL–6, IFN and TNF and also from upregulation of Cathepsin Q which is an apoptotic factor found in the placenta that induces necrotic cell death.[11]

The organism most commonly associated with urinary tract infection is E. Coli.[1,12] Other causes include Staphylococcus Saprophyticus, Klebsiella, Proteus, Pseudomonas, and Enterobacter. Within the subpopulation of pregnant women, Group B Streptococcus (GBS) has also been identified as a cause of UTIs.[12–14] Urinalysis is used in the diagnosis of UTI and asymptomatic bacteriuria in pregnancy as it poses little risk to the patient and produces results in a timely fashion.[6,15] The accuracy and cost–effectiveness when compared with standard culture techniques appears to be a drawback to urinalysis, when it is quantified for positive and negative likelihood ratios.[1,16,17] As a result, urine culture remains the gold standard in diagnosis.[17]

Objective

As this is a literature review of the efficacy of urinalysis screening in the diagnosis of asymptomatic bacteriuria or UTI in pregnancy, the objective was to determine whether urine dipstick or urine microscopy results reliably predicted the presence of a urine pathogen. We reviewed the sensitivity and accuracy of urinalysis parameters in detecting UTIs and Asymptomatic Bacteriuria (ASB) during pregnancy. Furthermore, the accuracy of nitrite and/or Leucocyte Esterase (LE) dipsticks for screening and treating UTIs and asymptomatic bacteriuria was also reviewed.

Methods

A literature review was conducted in order to find out the accuracy and sensitivity of urinalysis parameters in the diagnosis of urinary tract infection in pregnancy. Literature from 1984 through 2014 was searched using search engines Google scholar, Elsevier, Science Direct, and PubMed. The search was limited to the English language with search terms of asymptomatic bacteriuria, pyelonephritis pregnancy, dipstick and urinalysis. Each article was reviewed to determine its relevance the studies objectives. We used articles that had the following criteria: Study was done for diagnosis of asymptomatic bacteriuria in pregnancy or urinary tract infections infection in pregnancy, investigate the use and effectiveness of dipstick tests for nitrites and/or leukocyte esterase, and present empirical data, compared with an appropriate gold standard.

Results

13 studies met the criteria of our search (See Table 1). Data was then separated based on analysis of asymptomatic bacteriuria via Nitrite, Leukocyte Esterase (LE), Nitrite or LE, Nitrite and LE, urinalysis, and urine culture. Nine studies included characteristics and results of Nitrite for detection of asymptomatic bacteriuria in pregnancy. Sensitivity ranged from 18.8 to 66.7% while specificity ranged from 31 to 100% (See Table 2).

Table 1 Performance characteristics of Reagent Strips (LE and NIT) (%) and urinalysis test in screening for bacteria.

Study #	Authors/Article	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
1	Archbald[29,37]	324	9.3%				
	Nitrites			37	100	0.4 (0.2-0.8)	0.4 (0.2-0.8)
2	Bachman[17,29]	1,047	2.3%				
	Leukocyte Esterase (LE)			16.7	97.2	5.9 (2.2-15.4)	0.9 (0.7-1.0)
	Nitrites			45.8	99.7	156.3 (46.6-524.5)	0.5 (0.4-0.8)
	LE or Nitrites			50	96.9	16 (9.4-27.0)	0.5 (0.4-0.8)
	LE and Nitrites			12.5	100		
3	McNeeley[26,29]	694	8.1%				
	LE or Nitrites			69.6	83.4	PPV%: 26.9	NPV%: 96.9
4	Robertson[19,29]	750	8.3%				
	Leukocyte Esterase (LE)			77.4	96.1	18.9 (12.8-28.1)	0.2 (0.2-0.4)
	Nitrites			43.4	98.9	42.8 (19.4-94.3)	0.6 (0.5-0.7)
	LE or Nitrites			92.0	95.0	18.6 (13.3-26.0)	0.1 (0.02-2.0)
	LE and Nitrites			32.2	94.2		
5	Tincello[20,29]	893	5.4%				
	Nitrites			18.8	99.5	39.6 (12.6-124)	0.8 (0.7-0.9)
	LE and Nitrites			33.3	91.1	PPV%: 69	NPV%: 99
6	Millar[27]	383	11.4%				
	Leukocyte Esterase (LE)			69	69	PPV%: 22 (+/-6)	NPV%: 95 (+/-2.5)
	Nitrites			45	97	PPV%: 63 (+/- 17.5)	NPV%: 93 (+/- 2.5)
	LE and Nitrites			81	97	PPV%: 24 (+/- 7)	NPV%: (+/- 2.2)
7	McNair[36]	528	6.8%				
	Urinalysis			80.6 (63.4- 91.2)	71.5 (67.3-75.4)	PPV%: 17.2 (12-23.0)	NPV%: 98.1 (95.8-99.1)
	Reagent Strips / Urine Dipstick			47.2 (30.8- 64.3)	80.3 (76.4-83.7)	PPV%: 14.2 (9.2-23.1)	NPV%: 95.9 (92.8-97.1)
	Urine culture/Gram Stain			100%	7.7%	PPV%: 7.3 (5.3-10.1)	NPV%: 100 (88.5-100)
8	Mignini[1]	3,048	15%				
	LE or Nitrites			53 (48–58)	92 (91–93)	6.95 (5.8–8.33)	0.51 (0.45–0.57)
9	Kutlay[25]	406	15.3%				
	Urinalysis			71.0%	73.6%	Not Reported	Not Reported
	Reagent Strips / Urine Dipstick			38.7	35.8	Not Reported	Not Reported

Table continued...

Study #	Authors/Article	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
10	Semeniuk[34] (at colony count of > 105)	479	18.9%				
	Leukocyte Esterase (LE)			84.4	59.4	PPV%: 19.4	NPV%: 97.1
	Nitrites			43.6	96.6	PPV%: 75	NPV%: 88.2
	LE and Nitrites			84	98.3	PPV%: 84	NPV%: 98.3
11	Nayak[18]	60	73%				
	Leukocyte Esterase (LE)			61	25	PPV%: 69	NPV%: 19
	Nitrites			50	31	PPV%: 66	NPV%: 18.5
	Reagent Strips / Urine Dipstick (LE or Nitrites)			68	25	PPV%:71.4	NPV%: 22
12	Abbasi[30]	65	4.6%				
	Leukocyte Esterase (LE)			100	100	15.5 (6.0-40.0)	0.1 (0.01-1.8)
	Nitrites			66.7	NA	78.8 (4.5-1379.6)	0.3 (0.1-1.7)
13	Campos-Outcalt[33]	299	4.7%				
	Nitrites			57.1	NA	18.1 (8.2-39.6)	0.4 (0.2-0.8)

Table 2 Characteristics and results of nitrite reagent strip tests performed in pregnant women asymptomatic for bacteriuria to assess the prediction of bacteriuria.[29]

Study #	Parameter(s)	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
1	Nitrites	324	9.3%	37	100	191.4 (11.6-3169.4)	0.6 (0.5-0.8)
2	Nitrites	1,047	2.3%	45.8	99.7	156.3 (46.6-524.5)	0.5 (0.4-0.8)
4	Nitrites	750	8.3%	43.4	98.9	42.8 (19.4-94.3)	0.6 (0.5-0.7)
5	Nitrites	893	5.4%	18.8	99.5	39.6 (12.6-124)	0.8 (0.7-0.9)
6	Nitrites	383	11.4%	45	97	PPV%: 63 (+/- 17.5)	NPV%:93 (+/- 2.5)
10	Nitrites	479	18.9%	43.6	96.6	PPV%:75	NPV%: 88.2
11	Nitrites	60	73%	50	31	PPV%:66	NPV%: 18.5
12	Nitrites	65	4.6%	66.7	NA	78.8 (4.5-1379.6)	0.3 (0.1-1.7)
13	Nitrites	299	4.7%	57.1	NA	18.1 (8.2-39.6)	0.4 (0.2-0.8
Summary	Nitrites	Total: 4300	Range of the Results for Prevalence of Bacteriuria: 2.3% to 18.9%	Range of the Results for Sensitivity: 18.8% to 66.7%	Range of the Results for Specificity: 31% to 100%		

Six studies included characteristics and results of Leukocyte Esterase (LE) for detection of asymptomatic bacteriuria in pregnancy. Sensitivity ranged from 16.7 to 100% while specificity ranged from 25 to 100% (See Table 3).

Table 3 Characteristics and results of leukocyte esterase reagent strip test performed in pregnant women asymptomatic for bacteriuria to assess the prediction of bacteriuria.[29]

Study#	Parameter(s)	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
2	Leukocyte Esterase (LE)	1,047	2.3%	16.7	97.2	5.9 (2.2-15.4)	0.9 (0.7-1.0)
4	Leukocyte Esterase (LE)	750	8.3%	77.4	96.1	18.9 (12.8-28.1)	0.2 (0.2-0.4)
6	Leukocyte Esterase (LE)	383	11.4%	69	69	PPV%: 22 (+/-6)	NPV%: 95 (+/-2.5)
10	Leukocyte Esterase (LE)	479	18.9%	84.4	59.4	PPV%: 19.4	NPV%:97.1
11	Leukocyte Esterase (LE)	60	73%	61	25	PPV%: 69	NPV%: 19
12	Leukocyte Esterase (LE)	65	4.6%	100	100	15.5 (6.0-40.0)	0.1 (0.01-1.8)
Summary	Leukocyte Esterase (LE)	Total: 2784	Range of the Results for Prevalence of Bacteriuria: 2.3% to 73%	Range of the Results for Sensitivity: 16.7% to 100%	Range of the Results for Specificity: 25% to 100%		

Seven studies included characteristics and results of Leukocyte Esterase (LE) or Nitrite for detection of asymptomatic bacteriuria in pregnancy. Sensitivity ranged from 38.7 to 92% while specificity ranged from 25 to 96.2% (See Table 4).

Five studies included characteristics and results of Leukocyte Esterase and Nitrite for detection of asymptomatic bacteriuria in pregnancy. Sensitivity ranged from 12.5 to 84% while specificity ranged from 91 to 100% (See Table 5).

Two studies included characteristics and results of urinalysis test for detection of asymptomatic bacteriuria in pregnancy. Sensitivity ranged from 71 to 80.6% while specificity ranged from 71.5 to 73.6% (See Table 6). One study included urine culture and gram stain for detection of asymptomatic bacteriuria in pregnancy. Sensitivity ranged from 100% while specificity ranged from 7.7% (See Table 7).

Table 4 Performance characteristics of Reagent Strips (LE or NIT) (%) test in screening for bacteria.

Study #	Parameter(s)	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
2	LE or Nitrites	1,047	2.3%	50	96.9	16 (9.4-27.0)	0.5 (0.4-0.8)
3	LE or Nitrites	694	8.1%	69.6	83.4	PPV%: 26.9	NPV%: 96.9
4	LE or Nitrites	750	8.3%	92.0	95.0	18.6 (13.3-26.0)	0.1 (0.02-2.0)
8	LE or Nitrites	3,048	15%	53 (48–58)	92 (91–93)	6.95 (5.8–8.33)	0.51 (0.45-0.57)
7	Reagent Strips / Urine Dipstick (LE or Nitrites)	528	6.8%	47.2 (30.8- 64.3)	80.3 (76.4-83.7)	PPV%: 14.2 (9.2-23.1)	NPV%: 95.9 (92.8-97.1)
9	Reagent Strips / Urine Dipstick (LE or Nitrites)	406	15.3%	38.7	35.8	Not Reported	Not Reported
11	Reagent Strips / Urine Dipstick (LE or Nitrites)	60	73%	68	25	PPV%: 71.4	NPV%: 22
Summary	LE or Nitrites	Total: 6533	Range of the Results for Prevalence of Bacteriuria: 2.3% to 73%	Range of the Results for Sensitivity: 38.7% to 92%	Range of the Results for Specificity: 25% to 96.2%		

Table 5 Performance characteristics of Reagent Strips (LE and NIT) (%) test in screening for bacteria.

Study #	Parameter(s)	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
2	LE and Nitrites	1,047	2.3%	12.5	100		
4	LE and Nitrites	750	8.3%	32.2	94.2		
5	LE and Nitrites	893	5.4%	33.3	91.1	PPV%: 69	NPV%: 99
6	LE and Nitrites	383	11.4%	81	97	PPV%: 24 (+/- 7)	NPV%: (+/- 2.2)
10	LE and Nitrites	479	18.9%	84	98.3	PPV%: 84	NPV%: 98.3
Summary	LE and Nitrites	Total: 3552	Range of the Results for Prevalence of Bacteriuria: 2.3% to 18.9%	Range of the Results for Sensitivity: 12.5% to 84%	Range of the Results for Specificity: 91% to 98.3%		

Table 6 Performance characteristics of urinalysis test in screening for bacteria.

Study #	Parameter(s)	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
7	Urinalysis	528	6.8%	80.6 (63.4- 91.2)	71.5 (67.3-75.4)	PPV%: 17.2 (12-23.0)	NPV%: 98.1 (95.8-99.1)
9	Urinalysis	406	15.3%	71.0%	73.6%	Not Reported	Not Reported
Summary	Urinalysis	Total: 934	Range of the Results for Prevalence of Bacteriuria: 6.8% to 15.3%	Range of the Results for Sensitivity: 71% to 80.6%	Range of the Results for Specificity: 71.5% to 73.6%		

Table 7 Performance characteristics of Urine Culture test in screening for bacteria.

Study #	Parameter(s)	N	Prevalence of Bacteriuria	Sensitivity %	Specificity %	Likelihood ratio for positive Test results[29]	Likelihood ratio for negative Test results[29]
7	Urine culture/ Gram Stain	528	6.8%	100%	7.7%	PPV%: 7.3 (5.3-10.1)	NPV%:100 (88.5-100)
Summary	Urine culture	Total: 528	Range of the Results for Prevalence of Bacteriuria: 6.8%	Range of the Results for Sensitivity: 100%	Range of the Results for Specificity: 7.7%	PPV%: 7.3 (5.3-10.1)	NPV%:100 (88.5-100)

Discussion

Since plate cultures are considered the gold–standard in determining the presence of bacteriuria, other methods are regularly employed due to the time constraints and cost–effectiveness of processing urine cultures. Methods such as urinalysis and urine dipsticks for nitrites or leukocyte esterase (LE) can produce results quickly and cheaply in comparison to plate cultures.[18–20]

The U.S. Preventive Services Task Force (USPSTF) recommends screening for asymptomatic bacteriuria with a clean–catch urine specimen in pregnant women at either the first prenatal visit or at 12–16 weeks gestation.[21,22] The USPSTF also recommends the use of urine culture rather than urine dipstick or urine microscopy due to the fact that both do not have a high enough sensitivity and negative predictive value in pregnant women.[23,24]

From reviewing the literature, it was concluded that the sensitivity and specificity of dipstick testing were not high enough to recommend them as means of detecting ASB/UTI.[25–27] Furthermore, a positive dipstick tests for LE and/or nitrite should not be thought of a specific indicator of a UTI due to the high false–negative.[28–30]

Untreated asymptomatic bacteriuria significantly increased rates of low birth weight and preterm delivery.[22,31] ACOG also recommends treatment of asymptomatic bacteriuria in pregnancy followed by a test of cure.[21] This is recommended due to the fact that the treatment of asymptomatic bacteriuria decreases the incidence of antenatal pyelonephritis as well as reducing the rate of low birth weights.[24]

The literature suggests that urine dipstick testing with both the leukocyte esterase and nitrite tests is inadequate for pregnant women due to its low sensitivity.[22] Although urine microscopy and urinalysis provides better results, it still is not as good when compared to urine culture. There have been literature studies which looked at the efficacy of gram staining, but these studies proved to be inadequate.[33]

A study performed in 1999 on 479 non–pregnant ambulatory women with symptoms of a UTI indicated that urine dipstick analysis was not effective in determining bacteriuria. Of the 479 women, 19% did not have a positive leukocyte esterase (LE) or positive nitrite tests (NIT). The researchers of this study conclude that in situations where the colony count is < 10^5 CFU/mL, which is the cutoff for significant bacteriuria, urine dipstick analysis via the LE and NIT tests are not effective, even when both values are combined. This is especially important in pregnant women, where the risk of complications increases.[34]

Furthermore, a 2009 WHO–funded study of 3048 eligible pregnant women in Argentina, Philippine, Thailand, and Vietnam also concluded that dipstick testing for the diagnosis of asymptomatic bacteriuria was poor. A positive test increased the likelihood of asymptomatic bacteriuria from 15% pretest probability to 54% post–test probability, and that a negative test would reduce the post–test probability to 8%. The study concludes that if dipstick testing were the primary screening method for asymptomatic bacteriuria, 46% of pregnant women would be missed.[1]

Other studies which compared the urine dipstick test and other parameters of urinalysis against gold standard urine cultures, showed that leukocyte esterase appears to be the most accurate.[35] One study indicated that leukocyte esterase test component of the dipstick test appears to have the highest reliability and validity.[35] It also had the highest accuracy, of 90.25%, concluding that a positive test in a pregnant woman merits empiric antibiotics, and a negative test is an indication for urine culture.[35] However, it was noted that there still remains a poor correlation between urine dipstick testing and urine culture.

A study of 528 pregnant women also concluded that gram staining, in addition to urine dipstick testing and urinalysis was not acceptable in the diagnosis of asymptomatic bacteriuria. The sensitivity and specificity of gram staining was 100% and 7.7%, and urinalysis and dipstick testing yielded a sensitivity of 80.6% and 47.2% and a specificity of 71.5% and 80.3%. Additionally, no combination of tests improved specificity over urinalysis alone.[36]

Additionally, a meta–analysis of 70 publications from 1990–1999 indicated that accuracy of the nitrite test was high in pregnant women (OR = 165), but the predictive value of combinations of positive test results were low. The study concluded that the sensitivity of a combined test ranged from 68–88% across all patient groups, and that positive tests must be confirmed by urine culture.[3]

A study done in Turkey in 2000 indicated that in a clinical unit where urine culture was not available, urine microscopy should be used to determine if empiric antibiotic therapy is needed in asymptomatic bacteriuria. The study noted that dipstick testing, with sensitivity and specificity of 38.7% and 35.8%, were not high enough to be recommended as a screening tool for diagnosing asymptomatic bacteriuria.[25]

Randomized trials have demonstrated that antimicrobial treatment of asymptomatic bacteriuria during pregnancy will decrease the risk of complications. A Cochrane analysis of 14 studies including 2302 pregnant women concluded that antiobiotic treatment reduced the incidence of pyelonephritis and was associated with a reduction in the incidence of Low Birth Weight (LBW) infants, although no difference in preterm delivery was seen.[10,24] These significant improvements in the number of complications associated with asymptomatic bacteriuria underlie need of screening as a standard practice in obstetric care.

Conclusion

Urinalysis is a rapid test for evaluation of urinary tract infection and asymptomatic bacteruria. Overall, this review demonstrates that the urine dipstick test alone seems to be useful to exclude the presence of infection if the results of both nitrites and leukocyte–esterase are negative [35]. Different studies reported broad ranges of sensitivities and specificities for urinalysis parameters. Combination of nitrite and leukocyte esterase when both parameters are positive, seem to have the highest specificity in detecting bacteriuria in asymptomatic pregnant women. Although the combination of positive test results is very sensitive in clinical practice, the usefulness of the dipstick test alone to rule in infection remains doubtful, even with high pre–test probabilities [35]. Urine culture remains the gold standard for diagnosis of urinary tract infection and asymptomatic bacteruria.

Acknowledgments

Conflicts of interest

None.

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