



Research Article

## UNRAVELLING THE DIAGNOSTIC CONUNDRUM OF BACTERIURIA IN PREGNANCY

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### ABSTRACT

**Background:** Globally Urinary Tract Infection (UTI) and its associated complications account for nearly 150 million deaths per year. It is one of the most common medical complications during pregnancy, associated with risks to both mother and fetus. This study was done to compare and estimate the effectiveness of the rapid uriscreeen tests and culture in the early diagnosis of UTI, among symptomatic pregnant women to facilitate early treatment approaches. **Materials and methods:** Urine samples were collected from a total of 100 antenatal women and submitted for dip stick test (leukocyte esterase, nitrate reduction), direct gram stain and culture. **Results:** Direct gram stain was positive in 23%, leukocyte esterase (LE) was positive in 60% and nitrate reduction (NIT) was positive in 16%. Culture positive with significant bacteriuria was noted in 17 % cases, *Escherichia coli* (E.coli) was isolated in eight cases (47%). **Conclusion:** Gram stain of unspun urine can be used as a screening test in resource poor settings for early diagnosis and treatment, which will definitely reduce the maternal and neonatal complications of UTI.

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### INTRODUCTION

Urinary tract infections (UTI) are described as a group of diseases of the urogenital system involving the renal cortex, bladder extending up to urethra caused by variety of microorganisms (Najar MS *et al* 2009). Globally UTI and its associated complications account for nearly 150 million deaths per year (Mohiuddin AK *et al* 2019). It is more common in female than male; approximately 40 % of women and 12% of men encounter at least one symptomatic UTI during their life span and are prone for recurrent infections (Christy VR *et al* 2019). Precipitating factors for UTI in women are short urethra, pregnancy, contraceptive methods, close proximity of genitourinary tract with anal opening leading to easy contamination of urinary tract with faecal flora and absence of prostatic secretions (Pardesi P 2018). It is one of the most common medical complications during pregnancy and associated with risks to both mother and fetus which include pyelonephritis in later pregnancy, preeclampsia, postpartum urinary tract infection, maternal anemia, preterm birth, low birth weight, still birth, cerebral palsy, mental retardation and increased perinatal mortality (Jeyalakshmi J *et al* 2008). Hence, accurate, reliable and early diagnosis is imperative. Gold standard test for the diagnosis of UTI is culture which takes about 24-48 hours. Descriptive tests such as dip stick Uriscreeen method which detects LE and NIT, direct gram stain on an uncentrifuged specimen and high powered microscopy with a hemocytometer are used to predict UTI (Zorc JJ *et al* 2005). This study was done to compare and

estimate the effectiveness of the rapid uriscreeen tests and culture in the early diagnosis of UTI, among symptomatic pregnant women to facilitate early treatment approaches.

### MATERIALS AND METHODS

This cross sectional study was carried out in a tertiary care teaching hospital, from June to August 2019. Urine samples were collected from a total of 100 antenatal women in the reproductive age group with clinically suspected urinary tract infection who gave written informed consent to participate in the study. Institutional ethical committee approval was obtained. Socio demographic details such as age, occupation, obstetric history, presenting complaints, clinical examination details were collected using a structured proforma.

**Inclusion criteria:** Antenatal women with clinically suspected UTI

**Exclusion criteria**

- Antenatal women with clinically suspected UTI who were on empirical antibiotics.
- Antenatal women who were not willing to participate

Freshly voided clean catch, mid stream urine sample was collected in a sterile wide mouthed leak proof, screw capped container. Samples were tested for LE and NIT using the dip stick combi stick 10 SL, U.K. in the OPD adhering to standard operative procedure. LE was considered positive, if there was a colour change from off-white towards purple within 2

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minutes indicating 500 leucocytes/cu mm. NIT was considered positive, if there was change in colour from colourless to pink within 60 seconds. Then the samples were transported to the laboratory and processed within one hour. Semi quantitative urine culture was performed as per standard operative procedure. Smears were made from unspun urine and gram stain was done and 20 oil immersion fields were examined for microorganisms. All culture plates were read at 24 and 48 hours. Microbial identification and colony count was performed and the results were analyzed statistically.

**RESULTS**

A total of 100 mid stream urine samples from antenatal women with clinically suspected UTI were analyzed. Of them, 41% were primi, 73% were anaemic with haemoglobin below 10.4 gms% and high risk pregnancy was recorded in 30% cases. LE was positive in 60% and NIT was positive in 16%. Direct microscopy (gram staining) was positive in 23%. Microscopic pyuria was recorded in 44% cases. Culture positive with significant bacteriuria was noted in 17 % cases. (Table 1 & 2). *Escherichia coli* was isolated in eight cases (47%).The other isolates were *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Enterococci* spp and *Candida albicans*. Urine dipstick test, microscopy and culture were positive in 17 patients.

**Table 1** Distribution of positive uriscreen methods

Gravida	No. studied	LE positive (%)	NIT positive(%)	Microscopic pyuria positive (%)	Gram stain positive (%)	Culture positive (%)
First	41	25(61)	04(9.75)	15(36.9)	08(19.5)	09(21.95)
Second	30	18(60)	06(20)	16(53.3)	07(23.3)	04(13.3)
Third	19	10(52.6)	04(21)	06(31.6)	03(15.8)	02(10.5)
Fourth	10	07(70)	02(20)	07(70)	01(10)	02(20)
Total	100	60(60)	16(16)	44(44)	23(23)	17(17)
Trimester 1	06	03(50)	02(33.3)	02(33.3)	02(33.3)	02(33.3)
Trimester 2	23	13(56.5)	01(4.34)	09(39)	02(8.69)	02(8.69)
Trimester 3	71	44(62)	13(18.3)	33(46.5)	15(21.12)	13(18.3)
Total	100	60(60)	16(16)	44(44)	23(23)	17(17)

**Table 2** Comparative evaluation of uriscreen methods

Parameters	LE test Number(%)	NIT Number(%)	Microscopic pyuria Number(%)	Gram stain Number(%)
True positive	15(25)	07(43.75)	13(29.54)	13(68.42)
False positive	45(75)	09(56.25)	31(70.45)	06(31.57)
False negative	02(5)	10(11.9)	04(7.14)	04(4.93)
True negative	38(95)	74(88.09)	52(92.85)	77(95.06)
Sensitivity (%)	88.23	41.17	76.47	76.5
Specificity (%)	45.78	89.15	62.65	92.77
PPV (%)	25	43.75	29.54	68.42
NPV (%)	95	88.09	92.85	95.06

**DISCUSSION**

During pregnancy UTI is classified into two categories, as symptomatic and asymptomatic bacteriuria (Schnarr J *et al* 2008). Involvement of lower urinary tract leads to asymptomatic bacteriuria which is the most common cause in pregnancy. Involvement of upper urinary tract leads to symptomatic bacteriuria which is characterized by acute pyelonephritis (Yasmin T *et al* 2018).

Increased risk of UTI during pregnancy is due to lower socio economic status, lack of personnel hygiene, sickle cell trait, anaemia, increased parity and age, increased frequency of sexual activity, previous history of UTI, lack of prenatal care, diabetes, immunodeficiency and urinary tract abnormalities

(Yasmin T *et al* 2018). Apart from these factors, physiological, hormonal and mechanical changes during pregnancy increase the risk of urinary stasis and vesicoureteral reflex (Kavitha V *et al* 2015). Moreover increased urinary content of amino acids, vitamins and other nutrients encourage the persistence of infection. Physiological increase in plasma volume decreases the urine concentration and 70% of pregnant women develop glycosuria which encourages urinary infection. Further some maternal defense mechanisms are inefficient during pregnancy (Manjula NG *et al* 2013). Hence precise and early diagnosis is mandatory.

In the present study sensitivity, negative predictive value (NPV) and false positivity of LE test were noted respectively as 88%, 95% and 75%. False positive may occur due to high urine ascorbic acid, phenazopyridine and albumin (Jeyalakshmi J *et al* 2008).

NIT test takes about 4 hours for an uropathogen to change dietary nitrates to nitrites in the bladder to give a positive test. False negative results are noted with rapid bladder emptying as in infants and children, especially in inflammatory UTI. Various other reasons for false negative tests include uropathogens that do not reduce nitrate to nitrite, ie *Enterococcus* spp., *Staphylococcus saprophyticus*, *Pseudomonas aeruginosa* and *Candida* spp, antibiotics that inhibit bacterial metabolism and the competitive effect of ascorbic acid in the urine (Doern CD *et al* 2016).

It has been observed that pyuria can occur in the absence of UTI, as in fever from other infections or conditions such as Kawasaki disease and following strenuous exercise. The American Academy of Pediatrics proposed that when pyuria is absent in true UTI, there is usually a fault either in the method (spun versus unspun, number of cells/mm<sup>3</sup> versus number of cells/HPF, centrifuge speed and time) or in the definition of pyuria (Roberts RB 2011). Renal tuberculosis is suspected when there is recurrent pyuria and routine urine culture is negative.

Gram stain of uncentrifuged urine is the most useful single test. However, it requires trained personnel to screen and is subjected to inter observer variation. Further it helps in choosing the antibiotic therapy, but it is not indicated routinely. Because, clean catch specimen from females are frequently contaminated by vaginal flora. Whereas bacteria in a properly collected male urine sample is suggestive of infection and culture should be done (Simerville JA *et al* 2005). In the present study, 32% false positive results were noted which could be due to fastidious bacteria or effect of antibiotics. No false negative result was noted in this study, if found it could be due to less number of bacteria. The minimal threshold for detection by microscopy is 10<sup>5</sup>organisms/mL and for culture is 10<sup>3</sup>organisms/mL (Patil SS *et al* 2011).

Despite the fact that culture is the gold standard test in the diagnosis of UTI, it has some drawbacks too. Because it takes at least 48 hours, requires well equipped laboratory and trained staff for better results. Five bacteria per HPF indicates 10<sup>5</sup> CFU/mL, the diagnostic criteria for asymptomatic bacteriuria and definitely compatible with UTI. Similarly in symptomatic patients with a colony count of as low as 100 CFU/mL, denotes UTI and antibiotics should be advocated (Simerville JA *et al* 2005).

The members of the family Enterobacteriaceae are the most common pathogens isolated, which account for 84% of UTI (Gales AC *et al* 2000). *E.coli* tops the list, it is the endogenous flora of the colon, colonizes the periurethral area and vaginal introitus, ascends bladder upto the renal pelvis through receptor mediated ascending process. This process involves bacterial and host factors such as tissue receptors and expression of bacterial attachment factors. Uropathogenic *E.coli* expresses vacuolating cytotoxin that damages renal epithelium (Guyer DM *et al* 2002). Other gram negative pathogens include *Klebsiella pneumoniae*, *Enterobacter spp.*, *Citrobacter spp.*, *Proteus mirabilis* and *Pseudomonas aeruginosa* (Arjunan M *et al* 2010). Some intestinal organisms such as *Pseudomonas* adhere to the urinary catheter and forms biofilm which acts as a reservoir for bacterial growth (Lebeaux D *et al* 2014). Recurrence is an unavoidable consequence of UTI which is due to frequent and abrupt emergence of drug resistant strains. Most of the isolates show resistance to commonly used antibiotics due to improper treatment and indiscriminate use of antibiotics (Arjunan M *et al* 2010).

Urine dipstick test saves patient's time and money and may aid in the initiation of early treatment. Further it is a rapid, easy to carry out test, does not require expertise and can be done in resource poor settings.

## CONCLUSION

Although each test has high specificity for UTI, as a single test, the sensitivity is low. Gram stain of unspun urine can be used as a screening test in resource poor settings which will definitely reduce the maternal and neonatal complications of UTI.

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