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Original Research Article

# Maternal and Fetal Outcome in Early Versus Late Detected Asymptomatic Bacteriuria During Pregnancy in Tertiary Care Hospital

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**Abstract**

**Introduction:** Untreated asymptomatic bacteriuria (ASB) during pregnancy may lead to acute pyelonephritis, Pregnancy induced hypertension, preterm labour, low birth weight foetus, etc. These obstetric problems are less common when they receive adequate and prompt treatment. The aim of the current study was to compare the obstetric outcomes following therapy in early versus late detected ASB.

**Materials & Methods:** A prospective cohort study was conducted among 250 pregnant women at a tertiary care hospital of Gujarat. They were screened for asymptomatic bacteriuria by urine culture and sensitivity. They were grouped into asymptomatic bacteriuria negative and early detected culture positive (<20 week) and late detected culture positive groups (32 to 34 week). They were followed for obstetric outcome.

**Results:** Prevalence rate of ASB is 16.9%. As compared to ASB negative groups, the likelihood of Urinary tract infection, pregnancy induced hypertension, preterm labour, Low birth weight, intra uterine growth retardation was considerably greater in the LD and ED group.

**Conclusion:** Early detection and treatment of ASB during pregnancy at less than 20 weeks prevents complications like PIH, IUGR, PTL, PPROM and LBW. Therefore, screening and treatment of ASB may be incorporated as routine antenatal care for safe motherhood and healthy new-born.

**Keywords:** Asymptomatic Bacteriuria, early detected, intra uterine growth retardation, late detected, low birth weight, pyelonephritis.



## Introduction

The urinary system undergoes significant physiologic and anatomical changes during pregnancy, which increases the risk of urinary tract infections (UTI).[1] By the 6th week of pregnancy, 90% of pregnant women have urethral dilatation, an increase in bladder volume, a decrease in urinary bladder tone, a decrease in ureter

peristalsis, and a decrease in urethral tone, all of which lead to urine stasis and vesicoureteral reflux. The risk is greatly increased in pregnancy by glycouria and aminoaciduria. Uropathogen colonisation of the urinary system is facilitated by increased bicarbonate excretion, which results in enhanced alkalinization of urine. These modifications make pregnant women more susceptible to urinary tract infections. Although both men and women have asymptomatic bacteriuria, women are significantly more affected than men.[2]

Asymptomatic bacteriuria (ASB) is defined as a pure culture of at least 105 organisms/ml of urine in the absence of symptoms.[3] E coli is the most often colonised organism. Others include Klebsiella, proteus, coagulase negative staphylococci and pseudomonas. Preeclamptic toxaemia (PET), anaemia, low birth weight (LBW), intrauterine growth restriction (IUGR), preterm labour (PTL), preterm premature rupture of membranes (PPROM), and post-partum endometritis are more likely to develop in pregnant women with asymptomatic bacteriuria.[4,5] If left untreated, acute pyelonephritis and symptomatic cystitis can occur in 20–40% and up to 30% of pregnant women with bacteriuria, respectively.[6]

The prevalence of ASB has been found to be substantially greater in India, ranging from 8.1% to 21.1%[1,7,8]. The most cost-effective intervention at the primary level of healthcare to accomplish the millennium development target for health is the screening and treatment of ASB in pregnancy.[9] However, developing nations like India do not practise it. Dipstick analysis and the presence of pyuria are two screening procedures that are frequently employed in the primary healthcare sector, however they have a poor positive predictive value for detecting bacteriuria.[10] The gold standard for identifying ASB is urine culture.[11] The facilities for urine culture and sensitivity may not be accessible at the location of antenatal care, or poor rural women in our nation may not have their first antenatal appointment before 20 weeks. Some of these women might have late-pregnancy visits or late-pregnancy urine cultures. This study was conducted in order to compare the maternal and foetal outcomes of ASB positive and ASB negative women as well as those of early and late detection and treatment in women with ASB.

## Material & Methods

This prospective observational study conducted in the Department of Obstetrics and Gynaecology, in association with Department of Microbiology, Medicine, and Paediatrics of tertiary care hospital of Gujarat, India over a one year period after obtaining institutional ethics committee approval. Calculation of sample size-Size of the sample was calculated by using the formula:

$n = \frac{z^2pq}{L^2}$ where Z=1.96, P is the prevalence of ASB, L is the tolerance error of 5%. The minimum sample size was calculated as 202 taking prevalence rate as 13.9%.[2] and attrition rate of 10%. We enrolled 250 antenatal women.

Pregnant women with a gestational age up to 37 weeks were screened for ASB during their first visit. Pregnant women with ASB detected and treated at less than 20 weeks were grouped as early detected (ED) group and women with a gestational age of 28-37 weeks were grouped as late detected (LD) group. —Pregnant women with UTI, diabetes, sickle cell anaemia, prenterm delivery, hypertension, taking antibiotic in the preceding 2 weeks were excluded. After written informed consent, information regarding age, socioeconomic status according to Kuppusamy classification, parity, gestational age, past medical and obstetric history, previous antibiotic intake were collected through pre designed performa. Deliveries before 37 completed weeks were taken as preterm and birth weight less than 2.5kgs at term was regarded as low birth weight. NICU admissions were noted. Baseline

investigations such as hemoglobin levels, urine-albumin and sugar, random blood sugar, blood urea, were done.

A midstream specimen of urine was obtained in the clinic from the women and was sent for culture and sensitivity within two hours of collection. The samples were cultured on dried plates of Mac conkey's agar and blood agar by standard loop method. The plates were read after 24 h of aerobic incubation at 37o C. They were incubated for another 24 h if report was negative. A sample with bacterial count > $10^5$ colony forming units per ml (cfu/ml) was considered as ASB positive case. In case of *Staphylococcus aureus,* a count of $10^2$ cfu/ml was taken as significant. The sensitivity testing was done for antibiotics such as Ampicillin, Amoxicillin with Clavulanic acid, Nitrofurantoin, Cefotaxime, Ceftazidime, Cefuroxime, Amikacin and Imipenem was tested by the standard Kirby Bauer disc diffusion test.

All the pregnant women who were ASB positive were treated with appropriate antibiotics for 7 days. A repeat culture was done after 2 weeks of completion of the treatment to confirm the clearance of bacteriuria. If any woman had persistence of bacteriuria, another course of appropriate antibiotics was given. All the women were followed up till delivery and up to 1 week postpartum.

Details of maternal morbidity such as the development of symptomatic UTI (associated with dysuria, frequency of micturition, fever), acute pyelonephritis (high grade fever with chills and costovertebral tenderness), anaemia (haemoglobin Hb<11 g/dl in 1st and 3rd trimester, <10.5 g/dl in 2nd trimester), gestational hypertension (Blood pressure > 140/90 mmHg with the absence of proteinuria), preeclampsia (blood pressure >140/90 mmHg, proteinuria >300 mg/24 h or >1+ dipstick), preterm labour (uterine contractions of 4 in 20 minutes, cervical dilatation of > 1 cm and cervical effacement > 80% before 37 weeks of gestation), preterm premature rupture of membrane (clear fluid coming out of cervical os on speculum examination before onset of labour and before 37 weeks), PROM ( fluid coming out of cervical os on speculum examination before onset of labour due to rupture of membranes), puerperal pyrexia (oral temperature of ≥38°C after 24 hours and up to 1 week postpartum ) and foetal morbidity in the form of LBW (birth weight <2500 grams ), IUGR (foetal weight < 10th percentile for its gestational age), NICU admission (due to low Apgar /prematurity/LBW/neonatal septicaemia/meconium aspiration syndrome) were noted during the follow up of these patients.

**Statistical analysis**: The data was collected with predesigned proforma and entered in Microsoft Excel 2016. The data was analyzed with Epi info version 7.1.4.0 Continuous data was presented with mean and standard deviation (SD) while categorial data was presented with frequency and percentage. Proportional differences were compared using Fisher's exact test. Comparison of Continuous data was analysed with ANOVA test. P value less than 0.05 was considered as significant.

## Results

A total 250 antenatal women were included in the study. Total 8 women were lost to follow up so 242 women were included in data analysis. Total 130 pregnant women were screened at or less than 20 weeks and they were grouped as early detected group (ED). In this group 18 women were culture positive with a prevalence of 13.84%. Total 112 women were screened at 28-37 weeks of pregnancy and were considered as the late detected group (LD) out of which 23 women showed significant growth giving a prevalence of 20.53%. Overall, 41 pregnant women had significant bacteriuria giving a prevalence rate of 16.94%. (Table 1).

**Table 1: Prevalence of ASB positive**

| | ED group | LD group | Total |
|---|---|---|---|
| **Total** | 130 | 112 | 242 |
| **ASB positive** | 18 | 23 | 41 |
| **Prevalence of ASB positive** | 13.84% | 20.53% | 16.94 |

Table 2 shows basic socio demographic characteristics of the pregnant women. About 80.6% pregnant women belonged to the younger age of 18-24 years and 64.5% were primigravidae. 78.5% of the pregnant women belonged to lower and lower middle socioeconomic class.

**Table 2: Basic characteristics of patients**

| Age | ASB negative (n-199) | ED (n-18) | LD (n-25) | Total (n-242) |
|---|---|---|---|---|
| 18-24 | 163 (81.9%) | 15 (83.3%) | 17 (68%) | 195 (80.6%) |
| 25-34 | 36 (18.1%) | 3 (16.7%) | 8 (32%) | 48 (19.5%) |
| Mean ± SD | 23.56 ± 3.98 | 24.00 ± 3.23 | 25.06 ± 4.11 | 24.43 ± 4.34 |
| **Parity** | | | | |
| Gravida 1 | 139 (69.8%) | 9 (50%) | 8 (32%) | 156 (64.5%) |
| Gravida 2 | 43 (21.6%) | 4 (22.2%) | 10 (40%) | 57 (23.5%) |
| Gravida 3 | 14 (7%) | 4 (22.2%) | 2 (8%) | 20 (8.3%) |
| Gravida 4 | 2 (1%) | 0 (0%) | 0 (0%) | 2 (0.8%) |
| Gravida 5 | 0 (0%) | 1 (5.56%) | 3 (12%) | 4 (1.6%) |
| Gravida 6 | 1 (0.5%) | 0 (0%) | 2 (8%) | 3 (1.2%) |
| **Socio economic class** | | | | |
| ≤ Middle class | 41 (20.6%) | 5 (27.78%) | 6 (24%) | 52 (21.5%) |
| ≥ Lower middle class | 158 (79.4%) | 13 (72.22%) | 19 (76%) | 190 (78.5%) |

The incidence of UTI was significantly higher in LD group (20.0%) as compared to ED group (5.6%) and ASB negative group (3.0%, p - 0.001). PIH was observed in 16.0 of LD group, 11.1% in ED group and 3.0% in ASB negatibe group. This difference was statistically significant (p – 0.008). Total 6 (24.0%) woman in the LD group and 2 (11.1%) women in the ED group had preterm labour as against 8 (4.0%) women in the ASB negative group which was statistically significant. ($p < 0.001$). Incidence of anaemia, PPROM, PROM, Puerperal pyrexia, APN were not statistically significant between three groups (Table 3).

**Table 3: Comparison of maternal outcome among three groups**

| Maternal complication | ASB negative (n-199) | ED (n-18) | LD (n-25) | p value |
|---|---|---|---|---|
| Anaemia | 22 (11.1%) | 3 (16.7%) | 7 (28%) | 3.59, 0.16 |
| Symptomatic UTI | 6 (3%) | 1 (5.6%) | 5 (20%) | 13.61, 0.001 |
| Gestational HTN/ preeclampsia | 6 (3%) | 2 (11.1%) | 4 (16%) | 9.50, 0.008 |
| PPROM | 7 (3.5%) | 1 (5.6%) | 2 (8%) | 1.22, 0.54 |
| PTL | 8 (4%) | 2 (11.1%) | 6 (24%) | 25.62, < 0.001 |
| PROM | 4 (2%) | 1 (5.6%) | 2 (8%) | 3.32, 0.18 |
| Puerperal pyrexia | 5 (2.5%) | 1 (5.6%) | 2 (8%) | 2.40, 0.30 |
| APN | 0 (0%) | 1 (5.6%) | NA | NA |

Total 8 (32.0%) babies in LD group had LBW which was significantly higher than ED group (1, 5.6%) and ASB negative group (12, 6.0%, p < 0.001). Total 4 (16.0%) babies in LD group and 8 (4.0%) babies in the ASB negative group had IUGR whereas none of the babies in the ED group had IUGR which was significant (p-0.02). None of the babies in the ASB negative group had neonatal septicaemia. Whereas, 1 (5.6%) babies in ED group and 2 babies (8.0%) in LD group had neonatal septicaemia (p-0.009). (Table 4)

**Table 4: Comparison of Foetal outcome among three groups**

| Foetal morbidity | ASB negative (n-199) | ED (n-18) | LD (n-25) | p value |
|---|---|---|---|---|
| LBW | 12 (6%) | 1 (5.6%) | 8 (32%) | 19.41, < 0.001 |
| IUGR | 8 (4%) | 0 (0%) | 4 (16%) | 7.77, 0.02 |
| NICU admission | 18 (9%) | 2 (11.1%) | 6 (24%) | 5.18, 0.07 |
| Neonatal septicaemia | 0 (0%) | 1 (5.6%) | 2 (8%) | 14.06, 0.009 |

Escherichia coli (41.9%) and Enterococcus sp (23.3%) were the predominant organisms isolated. Three women in ED group and 2 women in LD group needed another course of antibiotic. (Total 5). About 90.7% of the pathogens isolated were sensitive to Imipenem and 74.4% were sensitive to Nitrofurantoin (Table 6).

**Table 5: Bacteria isolated in culture positive women**

| Bacterium isolated | No. of cases (n=43) | Percentage |
|---|---|---|
| Escherichia coli | 18 | 41.9 |
| Enterococcus sp. | 10 | 23.3 |
| Klebsiella pneumoniae | 7 | 16.3 |
| Staphylococcus aureus | 3 | 7.0 |
| Mixed | 5 | 11.6 |

**Table 6: Antibiotic sensitivity pattern of uropathogens.**

| Antibiotic | Sensitivity (%) |
|---|---|
| Imipenem | 90.7 |
| Nitrofurantoin | 74.4 |
| Cefotaxim | 74.4 |
| Amikacin | 48.8 |
| Amoxicillin with clavulanic acid | 39.5 |
| Cefoxitin | 30.2 |
| Ceftazidime | 25.6 |
| Cefuroxime | 25.6 |
| Ceftriaxone | 11.6 |
| Ampicillin | 9.3 |
| Amoxicillin | 4.7 |

## Discussion

In the current study, prevalence rate of ASB is 16.9%. Prevalence was observed in several Indian studies to range from 8.1% to 21.1%[1,7,8] Variations in prevalence may be brought on by the various sociodemographic characteristics of study participants. As compared to ASB negative groups, the probability of having UTI, PIH, preterm labour, LBW, and IUGR was considerably greater in the LD and ED group in the current study.

In the study of Guntoory I et al.[2], UTI was significantly higher in LD groups (16%) as compared to ED group (9%) and ASB negative group (1.4%). Similarly, PIH and preterm labour were higher in LD groups

and ED groups as compared to ASB negative groups. [PIH: LD groups – 16.6%, ED group –9.1%, ASB negative groups- 2.1%; Preterm labour: %, LD groups – 25.0%, ED group – 9.1 ASB negative groups- 4.2%]. Foetal outcome such as low birth weight, IUGR and NICU admission were higher in LD groups and ED groups as compared to ASB negative group. [LBW: LD groups – 33.3%, ED group –9.1%, ASB negative groups- 2.8%; IUGR: LD groups – 16.6%, ED group –16.6%, ASB negative groups- 2.1%; NICU admission: LD groups – 25.0, ED group –9.1%, ASB negative groups- 4.2%].

In a prospective cohort research of Jain V. et al.[1], the prevalence of ASB was 16.0% in the LD group and 17.0% in the ED group. PET (RR 3.79, 95% CI 1.80-7.97), PPROM (RR 3.63, 45% CI 1.63-8.07), PTL (RR 3.27, 95% CI 1.38-7.72), IUGR (RR 3.79, 95% CI 1.80-79), and LBW (RR1.37, 95% CI 0.71-2.61) were all more common in the LD group compared to ASB negative women, whereas there was no statistically significant difference in the ED group compared to ASB negative women.

It is generally known that women with ASB who become pregnant run the risk of experiencing symptomatic UTI and APN. According to Hill et al.[12], 1.4% of pregnant women experience APN. In a systematic analysis, Smaill et al.[13] found that the overall incidence of APN in the untreated ASB group was 21%, with a range of 2.5 to 36%. The incidence of APN was reduced by around 75% as a result of treatment for ASB.[3] Additionally, a successful course of treatment reduces the likelihood of a recurrent symptomatic UTI by 80–90%.[14] In our study, one woman in ED group developed APN even though urine culture was sterile after second course of antibiotics. Incidence of APN was 0.41% (1/242)

Escherichia coli (41.9%) and Enterococcus sp (23.3%) were the most frequently isolated species in the current study. This agrees with findings by Verma A et al.[15] and Guntoory I et al.[2] In the present study, almost 3/4 of uropathogens were Nitrofurantoin sensitive. In the study by Verma A et al.[15] nitrofurantoin was found to be very sensitive (>90%-100%) against all strains except pseudomonas Prescriptions of nitrofurantoin during pregnancy seemed to be safe, and a survey of doctors revealed that the majority of doctors still adhered to this recommendation. About 11.6% of women with positive cultures needed a second round of antibiotics. Recurrence with the same organism or failure to eliminate is indicative of renal parenchymal infection or structural abnormality. Following delivery, these women were instructed to have a urologic exam and get follow-up culture. When prescribing a course of action, local resistance rates should be taken into account.[16] Antimicrobial susceptibility should, if possible, be used to guide the selection of antibiotics for the treatment.[17]

## Conclusion

According to the current study, ASB is very common in pregnant women. Additionally, it showed that even with infection treatment, if a disease was discovered late in pregnancy, it might still result in various maternal and newborn complication like PIH, premature labour, LBW, and IUGR. Therefore, it is more effective to screen for asymptomatic bacteriuria at an early stage of pregnancy at less than 20 weeks and to treat it appropriately with a susceptible antibiotic.

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