# **Original Research Article**

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# Prevalence of asymptomatic bacteriuria among antenatal women and its effects on maternal and perinatal outcome in northern Andhra Pradesh population

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#### **ABSTRACT**

**Background:** The pregnant women are more commonly affected with asymptomatic bacteriuria (ASB) than non-pregnant women and its progression could lead to adverse maternal and perinatal outcomes. The study was designed with an aim to know the prevalence of ASB and its effects on maternal and perinatal outcome.

**Methods:** In this prospective study, 300 antenatal women attending Anil Neerukonda Hospital were screened for ASB. Urine culture was performed using standardized Kirby-Bauer disc diffusion method on blood agar, Mac Conkey's agar for antibiotic sensitivity testing. The screened antenatal women were divided into two subgroups viz. asymptomatic bacteriuria positive (Group I) and asymptomatic bacteriuria negative (Group II) depending on the culture study and were followed till delivery for maternal and perinatal outcomes.

**Results:** The prevalence of ASB was 11.33%. Out of 34 cases of ASB positive, 8 cases (23.5%) were delivered with birth weight <2500 grams as compared to 11 cases (4.1%) in unexposed cases (RR 5.68, 95% CI; 2.46-13.15; p<0.05). Preterm low birth was noticed in 5 (14.7%) cases of ASB positive pregnant women with compared to unexposed cases (RR 1.5, 95% CI; 0.61-3.65, p=0.36). Regarding maternal outcomes, premature labour was observed in 8 cases (23.5%) of ASB exposed women whereas 22 (8.3%) in non-exposed cases (RR 2.84, 95% CI; 1.37-5.88, p=0.004). A significant number of women have developed hypertension (17.6%) and preeclampsia (8.8%) in ASB positive cases as compared to ASB negative cases (4.9% and 2.3% respectively).

**Conclusions:** The prevalence of ASB was 11.33% in the present study. As one third of the cases were identified in early and late trimesters, regular and trimester wise screening need to be incorporated in routine antenatal screening for safe motherhood and new born health.

Keywords: ASB, LBW, Pregnancy, Perinatal outcome, PTL, Preeclampsia

#### INTRODUCTION

Asymptomatic bacteriuria (ASB) is a condition in which urine culture reveals a significant growth of pathogenic bacteria i.e. greater than 105 bacteria/mL without the presence of symptoms related to urinary tract infection (UTI).<sup>1</sup> The pregnant women are more commonly

affected than non-pregnant women due to various morphological, physiological changes and urinary stasis that occur during pregnancy due to the effect of progesterone.<sup>2</sup> The prevalence of ASB in pregnant women varies from 4% to 23.9% globally and the higher prevalence is attributed to lack of personal and environmental hygiene, socio-economic status, parity and

race.<sup>3</sup> During antenatal period, the risk of UTI begins in the 6<sup>th</sup> week and reaches its peak during the 22-24weeks and became the most recurrent causes of admission in obstetrical wards resulting in hospitalization.<sup>4,5</sup>

Usually patients over 20 years of age were more often bacteriuric. It has been identified that, Escherichia coli was the most common organism isolated in most of the studies. However, Proteus mirabilis formed 21.6% of isolates in a study of pregnant women by Ezechi et al.<sup>6</sup> In another study, it has been observed that Staphylococcus aureus was isolated from 72%, and Proteus species from 14%, where 40% of prevalence was reported in pregnant women.<sup>7</sup>

Bacteriuria in individuals with selected interferon regulatory factor 3 (IRF3) and toll-like receptor 4 (TLR4) promoter polymorphisms was characterized by low urinary neutrophil numbers, low interleukin (IL)-6, and low mast cell proteinase-1. The host-specific immune response to asymptomatic bacteriuria is mostly determined through innate immune mediators, and the magnitude of this response is influenced by host genetic variability.<sup>8</sup>

The hypoglycemic effect of newly introduced sodium glucose cotransporter 2 (SGLT2) inhibitors was mediated through blocking the renal receptor in the proximal tubule where the glucose is reabsorbed. As a result, the high levels of glucosuria exists which encourages bacterial growth in the urine. But on the contrary, no occurrence of bacteriuria associated with the use of canagliflozin therapy was observed in a 12-week, phase 2 study.<sup>9</sup>

The progression of ASB to symptomatic bacteriuria could lead to pyelonephritis and adverse outcomes such as intrauterine growth restriction (IUGR), low birth weight (LBW), prematurity and pre-term labor (PTL). 10,11 Untreated ASB results in symptomatic cystitis in approximately 30% of patients, in which 50% later develop pyelonephritis.<sup>12</sup> In a randomized controlled trial, the incidence of PTL and LBW infants decreased in pregnant women who underwent treatment for ASB. However, routine urine culture is not carried out in antenatal women may be due to cost implication and time factor. In addition, no studies were done on pregnant women of northern Andhra Pradesh population. Hence, the present study was aimed to know the prevalence of ASB, the impact of ASB on perinatal as well as maternal outcomes and the need of universal screening for ASB in antenatal women in our population.

#### **METHODS**

This prospective follow up study was carried out in the department of Obstetrics and Gynaecology, NRI Institute of Medical Sciences, Sangivalasa during period from June 2016 to June 2017. A total of 300 antenatal women irrespective of their period of pregnancy, attending antenatal outpatient clinic and those admitted in antenatal

wards were recruited for this prospective study. All the recruited 300 pregnant women were screened for ASB. The written informed consent was obtained from all the subjects. All the subjects were informed to collect "clean catch" mid-stream urine sample in a sterile container. Urine culture was performed using standardized Kirby-Bauer disc diffusion method on blood agar, MacConkey's agar for antibiotic sensitivity testing. The following antibiotics were observed for their antibacterial susceptibility: Gentamycin, amikacin, nalidixic acid, cefuroxime, ceftizoxime, ceftriaxone, cotrimoxazole, cefixime, amoxicillin + clavulanic acid, ampicillin, sulbactam, ciprofloxacin, levofloxacin, azithromycin, piperacillin/tazobactam, meropenem and nitrofurantoin.

The screened antenatal women were divided into two subgroups viz. asymptomatic bacteriuria positive (Group I) and asymptomatic bacteriuria negative (Group II) depending on the culture study. The antenatal women with >10<sup>5</sup> colony counts were named as ASB positive and the rest were regarded as negative. The positive cases were treated with appropriate antibiotic therapy as per their sensitivity and safety during pregnancy. Later, all the antenatal women in both group I and group II were followed till delivery and perinatal outcomes such as birth weight, gestational age and preterm low birth weight were examined. In addition, maternal outcomes including pyelonephritis, anaemia, premature labor, hypertension and preeclampsia were also evaluated.

The information on demographic features such as socioeconomic status, maternal age, gestational age, parity, gravida along with past obstetric, medical, treatment history, personal/family history of hypertension, diabetes mellitus was collected from all the subjects in a specially designed proforma.

Outcome variables: All women were followed till delivery. A special note was made for the presence of maternal complications such as pyelonephritis (high grade fever, chills, costovertebral angle tenderness), anaemia (Hb <11g/dl in 1st and 3rd trimester, <10.5g/dl in 2<sup>nd</sup> trimester), preeclampsia (blood pressure >140/90 mm of Hg, proteinuria >300mg/24h or >1+ dipstick), preterm labour (contractions 2 in 10min, cervical dilatation >1cm, cervical effacement >80% before 37wks of gestation), preterm premature rupture of membranes (PPROM) (on per speculum clear draining of liquor before 37wks of gestation), gestational hypertension (BP >140/90 mm of Hg with or without proteinuria) and perinatal outcomes such as low birth weight (birth weight <2500g), preterm low birth weight (birth weight <10<sup>th</sup> percentile) were also noted. Gestational age at delivery and mode of delivery were recorded for all patients.

### Exclusion criteria

- Any history of UTI symptoms such as dysuria, frequency and urgency etc,
- H/o fever,

- Pregnancy induced hypertension (PIH),
- Pregnancy with diabetes mellitus (DM) and gestational diabetes mellitus (GDM),
- H/o recurrent antibiotic therapy,
- H/o renal stones, urinary tract anomalies,
- Known maternal risk factors for IUGR such as low BMI, heart disease, smoking, alcohol, drugs (anticancer agents, narcotics), multiple gestation etc,
- Previous H/o IUGR,
- Anaemia, APH, fetal anomalies.

#### Statistical analysis

Statistical Package for Social Sciences (SPSS) version 15.0 was used to analyze the data. We used relative risks with their 95% confidence intervals (CIs) to present the comparison between the two groups and the p-value of <0.05 was considered to be significant.

#### RESULTS

The demographic features such as age, gestational age, parity, and socio-economic status were depicted in table 1. Of the screened 300 pregnant women, 160 (53.3%), 122 (40.7%) and 18 (6%) were in the age groups of 18-25, 26-35 and >36 respectively (Table 1).

Table 1: Demographic features of screened pregnant women.

Variable	Screened (n=300)
Age	
18-25yrs	160 (53.3%)
26-35yrs	122 (40.7%)
>36yrs	18 (6%)
Gestational age	
I trimester	32 (10.6%)
II trimester	146 (48.6%)
III trimester	122 (40.6%)
Parity	
Nulliparous	88 (29.3%)
Multiparous	212 (70.7%)

Out of 300 pregnant women screened, 34 cases were found to have ASB with a prevalence of 11.33% (Table 2). A significant difference in the prevalence of ASB was observed in 26-35yrs age group women and in second trimester (p <0.001 and 0.04 respectively) (Table 2). However, no significance was noticed with regard to parity. The frequency of isolated organisms in the present study was *E. coli* in 24 cases (70.6%), *S. aureus* in 4 (11.8%), *Proteus mirabilis* in 3 (8.8%), *K. Pneumoniae* in 1 (2.9%), *Acinetobacter* species in 1 (2.9%) and *Pseudomonas* in 1 case (2.9%) (Table 3). The comparison of perinatal outcomes in ASB positive group and ASB negative group has been presented in table 4. Out of 34 cases of ASB positive, 8 cases (23.5%) were delivered with birth weight <2500 grams as compared to 11 cases

(4.1%) in unexposed cases (RR 5.68, 95% CI 2.46-13.15; p<0.05). Most of the cases (67.4%) with ASB positive delivered after 37weeks of gestation whereas 32.4% of cases were delivered before 37weeks of gestation. Similarly, in unexposed cases 89.1% of cases were delivered after 37weeks and 10.9% before 37weeks of gestation. Preterm low birth was noticed in 5 (14.7%) cases of ASB positive pregnant women as compared to unexposed cases (RR 1.5, 95% CI 0.61-3.65, p=0.36) (Table 4).

Table 2: Age and trimester wise distribution of culture positive cases.

	Number of Culture positive (n=34)	Number of Culture negative (n=266)	p-value	
Age				
18-25yrs	6 (17.6%)	150 (56.4%)		
26-36yrs	20 (58.8%)	102 (38.3%)	<0.001*	
>36yrs	8 (23.5%)	14 (5.3%)	<0.001**	
Gestational age				
I trimester	5 (14.7%)	27 (10.2%)		
II trimester	22 (64.7%)	124 (46.6%)	0.04*	
III trimester	7 (20.6%)	115 (43.2%)	_	
Parity				
Nulliparous	12 (35.29%)	70 (26.3%)	0.27	
Multiparous	22 (64.71%)	196 (73.7%)	0.27	

Note: p<0.05\* significant

Table 3: Frequency of culture positive cases according to bacterial isolates.

Name of isolate	Number of cases (n=34)	(%)
E. Coli	24	20.58
S. Aureus	4	11.76
Proteus mirabilis	3	8.82
K. Pneumoniae	1	2.94
Acinetobacter species	1	2.94
Pseudomonas	1	2.94

Regarding maternal outcomes, premature labour was observed in 8 cases (23.5%) of ASB exposed women whereas 22 (8.3%) women had premature labour in non-exposed cases (RR 2.84, 95%CI 1.37-5.88, p=0.004). Pyelonephritis was not seen in ASB exposed women whereas 1 case (0.4%) was found in non-exposed women. Out of 34 cases of ASB positive, a significant number of women (17.6%) has developed hypertension and preeclampsia (8.8%) as compared to 4.9%, 2.3% of hypertension (RR 3.6, 95% CI 1.46-8.87, p=0.005) and preeclampsia (RR 3.91, 95% CI 1.03-14.92, p=0.04) in ASB negative cases respectively.

Anaemia was found in 5/34 cases of ASB positive group as compared to 12/266 cases of ASB negative group (RR 3.6, 95% CI 1.22-8.68, p=0.01) (Table 5).

Table 4: Comparison of perinatal outcome in ASB positive and negative pregnant women.

Parameter	Screened women (n=300)		Relative risk	95 % CI	p-value
	Exposed (n=34)	Unexposed(n=266)	(RR)	95 % CI	(<0.05 significant)
Birth weight					
<2500g	8 (23.5)	11 (4.13)	5.68	2.46-13.15	<0.001*
>2500 g	26 (76.5)	255 (95.9)			
Gestational age					
<37weeks	11 (32.4)	29 (10.9)	2.96	1.63-5.38	0.0003*
>37weeks	23 (67.4)	237 (89.1)			
Preterm low birth weight					
Yes	5 (14.7)	26 (9.8)	1.5	0.61-3.65	0.36
No	29 (85.3)	240 (90.2)			

Note: p<0.05\* significant

Table 5: Comparison of maternal outcome in ASB positive and negative pregnant women.

Parameter	Screened		Relative risk	95% CI	p-value (<0.05
	Exposed	Unexposed	(RR)	95% CI	significant)
Premature labour					
Yes	8 (23.5)	22 (8.3)	2.84	1.37-5.88	0.004*
No	26 (76.5)	244 (91.7)	2.04		
Pyelonephritis					
Yes	0	1 (0.4)	<b>7.6</b>	0.48-118.8	0.14
No	34 (100)	265 (99.6)	7.0		
Hypertension					
Yes	6 (17.6%)	13 (4.9%)	3.6	1.46-8.87	0.005*
No	28 (82.4%)	253 (95.1%)	3.0		
Anaemia					
Yes	5 (14.7%)	12 (4.5%)	3.2	1.22-8.68	0.01*
No	29 (85.3%)	254 (95.5%)	3.2		
Preeclampsia					
Yes	3 (8.8%)	6 (2.3%)	3.91	1.03-14.92	0.04*
No	31 (91.2%)	260 (97.7%)			

Note: p<0.05\* significant

## **DISCUSSION**

The urinary tract infection is one of the most common problems in women with pregnancy due to increase in the sex hormones, anatomical changes and physiological changes occur during pregnancy.<sup>13</sup> These changes can take place as early as 6weeks of gestation and reaches peak during 22-24 weeks. The prevalence of ASB in pregnancy varies from 4 to 29% globally. In the present study, the prevalence of ASB was 11.33% and our results were in accordance with the previous study where the prevalence has been observed as 12.27%.14 However, the prevalence of ASB in the present study was significantly low when compared with findings of Imade et al, (45.3%) and Amadi et al, (78.7%). 15,16 The prevalece differences among these studies can be attributed to differences in environmental conditions, socio-economic statuses, level of education and social habits of the community.

In the present study, the highest prevalence of ASB (58.8%) was observed in age group of 26-35 years as compared to other age groups. Similar results were also

claimed by others, where the incidence was 52% and 54% respectively in the similar age group. 17,18 On the contrary, highest incidence of 33.33% was reported in the age group of 20-25 years which is a young reproductive age group. Early marriage and child bearing may be contributing factors for higher incidence in younger reproductive group. But, advancement of age is also a risk factor to acquire ASB in pregnancy as glycogen deposition and reduction in lactobacillus occur in an ageing process which enhances bacterial adherence and invasion and make them more vulnerable. 17

In addition, most women between 26-35years may be multiparous and multiparity is a risk factor for ASB.<sup>15</sup> In the present study, the multigravida women were more susceptible to ASB as compared to nulliparous, 64.7% and 35.3% respectively. Our results were in agreement with a previous study, where the similar incidence has been observed.<sup>19</sup> The increased colonization of urinary tract by pathogenic organisms due to repeated exposure to urinary stasis or previous UTI may be the causative factor for higher incidence in multigravida.

Typically, ASB occurs during early pregnancy however a quarter of cases identified in the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters. <sup>20</sup> In the present study, 64.7% of ASB positive cases were in 2<sup>nd</sup> trimester as compared to 14.7% in first and 20.6% in 3<sup>rd</sup> trimesters. On the contrary, trimester did not show any significant difference in the prevalence of ASB and higher prevalence was observed in 3<sup>rd</sup> trimester. <sup>3,15</sup>

Bacterial isolates have been changing from place to place from time to time. It has been observed in several studies that *E. coli* is the most frequent organism isolated in the urine samples of pregnant women with ASB.<sup>15,21</sup> Urinary stasis which is a very common in pregnancy and poor genital hygiene practices during pregnancy could be the possible causes for higher incidence of *E. coli* isolation as most of the *E. coli* strains prefer that environment. *E. coli* was the most prevalent organisms observed in our present study, followed by *Staphylococcus aureus* (70.6% and 11.8% respectively). Our findings agree with earlier studies where *E. coli* was found to be commonest isolate.<sup>2</sup>

A number of observational studies have demonstrated the relationship between maternal symptomatic UTI and the risk of PTL and LBW but some of the studies failed to establish the association.<sup>22,23</sup> However, the association of ASB with maternal and foetal complications remains an area of continued debate. The Cochrane Library metaanalysis stated that antibiotic treatment was effective in reducing the incidence of LBW infants but not of PTL.<sup>24</sup> The present study showed an increased risk of LBW (RR=5.68) among group I (pregnant women with ASB) as compared to group II (without ASB) and is statistically significant. Our results were in accordance with other studies where similar results were found.<sup>25</sup> Although, the exact reasons may be unexplainable for this condition, some authors think that the bacteria present in genital organs could be the cause for the subclinical chorioamnionitis which in turn leads to LBW.<sup>24</sup>

In addition, the increased risk of PTL (RR=1.5) among group I pregnant women was observed in the present study as compared to group II, though not statistically significant. The proinflammatory cytokines secreted by maternal or fetal macrophages in response to bacterial endotoxins may trigger the process of preterm labour in ASB pregnant women.<sup>26</sup>

It is well known that both preeclampsia and UTI in pregnancy are closely associated. Minassian et al, observed that the increased odds of preeclampsia in pregnant women with any UTI versus those without UTI.<sup>27</sup> In the present study, the incidence of preeclampsia and hypertension in group I pregnant women and group II women was found to be 8.8%, 17.64% and 2.3%, 4.88% respectively. The risk of preeclampsia (RR 3.6) among pregnant women with ASB was high and is statistically significant. Similar results were claimed by Radha et al, where the incidence of preeclampsia was found to be 6.1%. The higher incidence of preeclampsia in group I women can be attributed to increased maternal cytokines

found in ASB may reflect vascular endothelial function which in turn leads to preeclampsia.<sup>29</sup>

The incidence of anaemia was found to be high (14.7%) in group I pregnant women as compared to group II (4.5%). The results were in agreement with many previous studies where the higher incidence of anaemia has been reported to be associated with ASB.<sup>30</sup> However, the association between ASB and anaemia could not be constituted as the aetiopathogenesis of anaemia during pregnancy is multidimensional.

To date, repeated urine culture tests have been suggested only in high-risk women (with diabetes, sickle cell immunological defects, urinary anemia, abnormalities or a history of recurring infections before pregnancy).31 However, the current studies suggest that performing the urine culture in all three trimesters improve the detection rate of ASB.<sup>32</sup> It was identified from various studies that ASB prevalence varies from trimester to trimester. McIsaac et al, demonstrated that the single urine culture before 20weeks of gestation leaves more than half of the ASB cases undiagnosed since 40.8% ASB positives were made after 1st culture vs 63.3% after second vs 87.9% after the third culture.32 Similarly, the prevalence distribution of ASB in the first, second, and third trimesters was 0.9%, 1.83%, and 5.6%, respectively in another study.<sup>33</sup>

In our study also, the prevalence distribution of culture positive cases differed among trimesters suggesting that several women without bacteriuria in the first trimester may develop bacteriuria during the later stages of gestation. Moreover, in spite of treatment with appropriate antibiotic therapy for ASB positive cases, the present study showed the poor perinatal and maternal outcomes.

Hence, authors suggest that screening of pregnant women for ASB also in the second and third trimesters might reduce the adverse perinatal and maternal outcomes. However, until large, prospective, randomized clinical trials (RCTs) are available and a clear benefit of this routine additional repeated screening is observed, no conclusions can be made for or against it.

#### **CONCLUSION**

In conclusion, the prevalence of ASB was 11.33% in the present study. It also demonstrated that even after treatment for ASB, increased chances of delivering LBW, preterm LBW baby, PTL, anaemia and preeclampsia were 5.68, 1.5, 2.84, 3.2 and 3.91 times respectively.

All the sequelae of ASB during pregnancy could be reduced by early detection and appropriate antimicrobial treatment.

Hence, regular and repeated trimester wise screening need to be incorporated as a routine antenatal care for an integrated approach for safe motherhood and newborn health.

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