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Research Article

A study of risk factors and consequences of asymptomatic bacteriuria in pregnant women and feto-maternal outcome

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ABSTRACT

Background: The present study is undertaken to know the risk factors and consequences of asymptomatic bacteriuria in pregnant women attending Narayana Medical College Hospital, Nellore.
Methods: 500 pregnant women were recruited for the study after their consent for participation. 85 women with culture positive for ASB were paired with 85 healthy pregnant women without bacteriuria to compare feto maternal outcome.
Results: Antenatal complications like anemia (35%), PROM (14%), preterm labour (18%), IUGR (14%), preeclampsia (5%) and pyelonephritis (3.5%) were higher in culture positive group when compared to control group. There was an increased incidence of mid trimester abortions (4%) and increased rate of caesarean section (48%) in culture positive women cases when compared to controls. Puerperal complications like maternal wound infections (5%), puerperal fever (14%) and UTI (10%), were more in culture positive cases when compared to controls. In the present study, fetal complications like low APGAR (19%), low birth weight (20%) and neonatal infections (8%) were higher in culture positive group compared to control group proving a significant association with ASB.
Conclusions: ASB is commonly encountered in pregnant women especially in women with anaemia. Untreated ASB is a risk factor for pyelonephritis, anaemia, PROM, preterm labour in mother. IUGR and neonatal infections are more common in fetus. Routine screening for ASB as a part of antenatal care reduces the maternal and fetal complications.

Keywords: Asymptomatic bacteriuria, Feto-meternal outcome**,** Urinary tract infections

INTRODUCTION

ASB accounts for 2-10% pregnancies in affluent countries (Whalley and Cunningham, 2000), incidence is much more in developing and under-developed countries. Asymptomatic bacteriuria (ASB) is a major risk factor for the development of Urinary Tract Infections (UTIs) during pregnancy results in adverse feto-maternal outcome. Bacterial products initiate a complex immunological, endocrinological and biochemical processes, culminating in adverse maternofetal outcome.[1] In patients with ASB, bacterial endotoxins and lipopolysaccharides are chronically released. This leads to a continuous and sustained damage to the red cell membranes, causing early cell destruction and anemia with ASB which is refractory to hematinics and responds promptly with anti-microbials.[2] IL-1 directly decreases erythropoietin secretion. IL-1 and TNF-α act through interferon-γ, to suppress the response of the erythroid marrow to erythropoietin. Hepticidin is a protein synthesized by the liver in chronic infection and

inflammation. It suppresses iron absorption from the gut and release of iron from its storage sites.[3]

Escherichia coli is the most prevalent causative microorganism in asymptomatic bacteriuria, accounting for more than 80% of uncomplicated UTIs. Patients with renal scarring due to pyelonephritis are at increased risk for the development of hypertension.[4] Asymptomatic bacteriuria carries an increased risk of pyelonephritis in pregnant women. The anatomic and physiologic urinary tract changes in pregnancy, mainly due to the relative obstruction of urine outflow by the gravid uterus and the smooth muscle relaxation caused by progesterone results ascending infection of bacteria to the kidneys rather than being washed out of the system. This risk is about 30% in the absence of antibiotic therapy but it is reduced to less than 5% with the eradication of bacteriuria by adequate treatment.[5] Acute severe infection of the kidneys cause transient renal dysfunction which ultimately leads to acute renal failure.[6]

Urinary tract infections trigger premature rupture of membranes by release of Bacterial endotoxin which provoke PROM either directly or through a prostaglandin-mediated cascade. PROM with secondary chorioamnionitis and endometritis leads to inability of inflamed uterus to contract effectively thus causing subinvolution.[6]

Bacteremia occurs in 15% to 20% of cases of pyelonephritis; the most common pathogen is E coli. Gram-negative bacteria possess endotoxin within their cell wall. Endotoxin-mediated damage includes that of capillary endothelium, diminished vascular resistance, and changes in cardiovascular output. When the active component of endotoxin i.e., lipid A when released into the maternal circulation, it precipitates a cascade response of pro-inflammatory cytokines, histamine, and bradykinins that may lead to the more serious complications like septic shocks, disseminated intravascular coagulation, respiratory insufficiency and Adult Respiratory Distress Syndrome (ARDS).[7]

Systemic infections like pylonephritis caused by ascending and bacterial infections, caused by ascending infections from the lower urinary tract reach the decidua, chorion and the fetus. Bacterial endotoxins initiates a cascade of toxic inflammatory mediators cause local circulatory disturbances in placenta. This placental insufficiency leads to abortions, still births, IUGR and low birth weight.[8]

Bacterial products like mucinases and pro-inflammatory factors promote break down of the cervical plug and spread of infection to the fetus.[9] ASB causes PROM and spread of infection to the fetus.[9] As the fetal-neonatal immunological system is less developed, the fetus is readily prone to infections and acts as a 'culture media' for organisms.[8] Thus, organisms of low virulence, commensals and otherwise non-pathogenic organisms readily colonize and multiply in the fetus causing septicemia. Adinolfi was among the first to propose that, cytokines produced in relation to maternal infections were harmful to the developing fetal brain.[10] Increase in IL-6 is associated with long term neurological consequences and bronco-pulmonary complications in the fetus.[9] Amniotic fluid infection leads to peri-ventricular leukomalacia and bronco-pulmonary dysplasia in the neonate.[9]

METHODS

500 pregnant women were recruited for the study after their consent for participation. 85 women with culture positive for ASB were paired with 85 healthy pregnant women without bacteriuria to compare feto maternal outcome.

Inclusion criteria: Pregnant women with varying gestational periods attending the antenatal clinic for their first visit.

Exclusion criteria

1. Pregnant women with symptoms of urinary tract infections like lower abdominal pain, fever, burning micturition, frequency of micturition and dysuria.
2. Patients with history of UTI in the past one year or during this pregnancy.
3. Patients with diabetes, chronic hypertension and other preexisting medical disorders.
4. Patients who had taken antibiotics in last 6 months.

A detailed history including the demography, complaints (symptoms of UTI), period of gestation of these patients were taken. Emphasis was made on previous obstetric history and medical history. Complete general physical examination was carried out. Obstetrical examination was carried out. Apart from routine antenatal profile, urine culture was done. Women with significant bacteriuria were treated and followed up throughout the pregnancy and outcome was noted.

Laboratory evaluation: Urine samples were collected by standard mid-stream "clean catch" method from all the pregnant women and immediately transported to the laboratory. Microscopic examination of urine was done for pus cells. All samples were cultured on blood agar, nutrient agar and Mac Conkey agar plates. A colony count of 10^5 or more pure isolates were processed further for identification. The isolates were identified by standard biochemical tests. Antimicrobial susceptibility test were performed using Kirby-Bauer disc diffusion test.

Descriptive statistical analysis has been carried out in the present study. Chi-square test ($\chi 2$) has been used to find the significance of study parameters between two groups

(contingency table Chi square statistic). P value <0.05 was considered statistically significant. The statistical software namely graph pad was used for the analysis of the data. Microsoft word and excel have also been used to generate graphs, tables, etc.

RESULTS

In the present study age distribution varied from 18-38 years and highest number of culture positive cases were in the age group of 26-35 years (54%) followed by 37% in age group below 26 years and 9% above 35 years (Figure 1). In our study majority of women (71%) with culture positive belonged to low socio economic status and multigravidae (62%) (Figure 2). In the present study, with respect to trimester majority of the culture positive cases were found in 3rd trimester (49%) followed by 29% and 22% in second trimester and first trimester respectively (Table 1). Antenatal complications like anemia (35%), PROM (14%), preterm labour (18%), IUGR (14%), preeclampsia (5%) and pyelonephritis (3.5%) was higher in culture positive group when compared to control group. A significant association of anemia, PROM, preterm labour and IUGR with ASB was proved in our study while preeclampsia showed no statistical significance (Table 2). There was an increased incidence of mid trimester abortions (4%) and increased rate of caesarean section (48%) in culture positive cases when compared to controls (Figure 3). Puerperal complications like maternal wound infections (5%), puerperal fever (14%) and UTI (10%), were more in culture positive group when compared to control group. Association of UTI and puerperal fever with ASB was found statistically significant (Table 3).

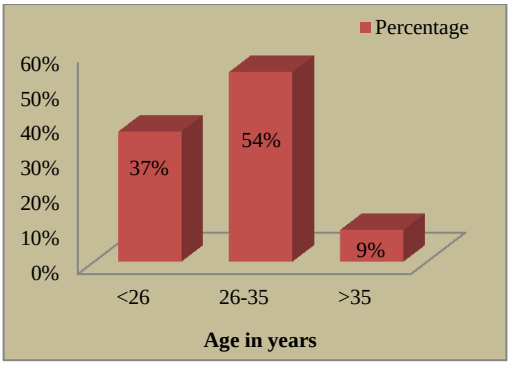

Figure 1: Age distribution.

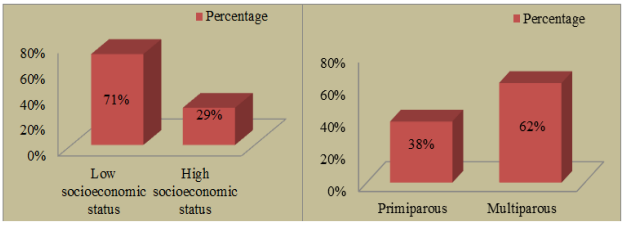

Figure 2: Socioeconomic status.

Table 1: Gestation age.

Trimester	n/t	%
1st trimester	19/85	22%
2nd trimester	24/85	29%
3rd trimester	42/85	49%

Table 2: Complications.

Antenatal complications	Cases (t=85)		Controls (t=85)		P value
	n/t	%	n/t	%	
Anemia	30/85	35%	17/85	20%	0.02 (significant)
PROM	12/85	14%	4/85	5%	0.03 (significant)
Preterm labour	15/85	18%	6/85	7%	0.03 (significant)
IUGR	12/85	14%	4/85	5%	0.03 (significant)
Preeclampsia	4/85	5%	3/85	3.5%	0.69 (insignificant)
Pyelonephritis	3/85	3.5%	-	-	0.08 (insignificant)

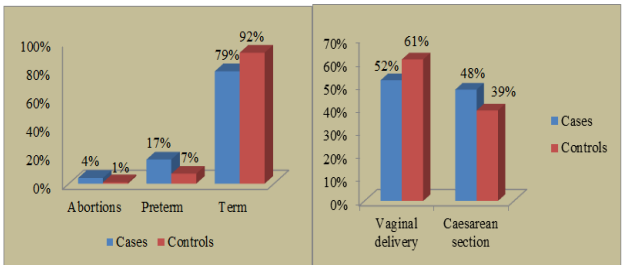

Figure 3: prenatal complications.

Table 3: Puerperal complications.

Puerperal complications	Cases (t=85)		Controls (t=85)		P value
	n/t	%	n/t	%	
Wound infections	4/85	5%	1/85	1%	0.17 (insignificant)
Fever	12/85	14%	3/85	3.5%	0.01 (significant)
UTI	7/85	8%	1/85	1%	0.02 (significant)

In the present study, fetal complications like low APGAR (19%), low birth weight (20%) and neonatal infections (8%) were higher in culture positive group compared to control group proving a significant association with ASB (Table 4).

Table 4: Fetal complications.

Fetal outcome	Cases (t=81)		Controls (t=84)		P value
	n/t	%	n/t	%	
Low APGAR	15/81	19%	5/84	6%	0.01 (significant)
Low birth weight	16/81	20%	7/84	8%	0.03 (significant)
NICU admissions	23/81	28%	10/84	12%	0.01 (significant)
Neonatal infections	7/81	8.5%	1/84	1.19%	0.02 (significant)

In culture positive group, 23% babies required NICU admissions because of preterm, 16% due to IUGR, 22% due to neonatal sepsis and 4% due to birth asphyxia (Table 5). Perinatal mortality in culture positive group was 3.6% while in control group was 1.19% though showing no statistical significance (Table 6).

Table 5: NICU admissions.

Causes of NICU admissions	Cases (t=23)		Controls (t=10)	
	n/t	%	n/t	%
Low birth weight (Preterm + IUGR)	14/23	60%	6/10	60%
Neonatal sepsis	7/23	36%	1/10	20%
Birth asphyxia	1/23	4%	1/10	20%
Others	1/23	4%	2/10	40%

Table 6: Perinatal mortality.

Perinatal mortality	Cases (t=82) (85-3 abortions)		Controls (t=84) (85-1 abortion)	
	n/t	%	n/t	%
Still births	1/82	1.2%	-	-
Neonatal deaths	2/82	2.4%	1/84	1.19%
IUD	-	-	-	-
Total	3/82	3.6%	1/84	1.19%

$\chi 2=1.15$; P value 0.28; insignificant

DISCUSSION

Majority of the women in our study belonged to the age group of 26-35 years (54%) which correlates with other studies done by Nawal et al.[19] (53%) and Sudha et al.[16] (52%). This high incidence of ASB in the young reproductive age group is due to early pregnancy and multiparity in our country, especially in the rural sector. Many studies show advancing age as a risk factor for acquiring ASB in pregnancy. There is decrease in glycogen deposition and reduction in the lactobacillus as a part of ageing process which enhances bacterial adherence and invasion by pathogens and make them more susceptible.[12]

In our study most of the patients belonged to low socioeconomic status i.e., 71%. This correlates to the study done by Lavanya et al.[14] This increased prevalence of ASB those women is due to low socio economic status is due to poor sanitation, lack of general hygienic practice and failure to attend antenatal clinic.

In the present study, majority of the women with ASB were multigravidae (62%). This was close to study done by Okonko et al.[17] The higher incidence of ASB in the multigravida is due to increased colonization of urinary tract by pathogens due to repeated exposure to urinary stasis or previous infections.

Most pregnant women in our area report to antenatal checkups during 2nd and 3rd trimester. In the present study, majority of the women with ASB were in 3rd trimester (49%). This correlates with the study done by Jeyaseelan et al.[12] The incidence of ASB is more pronounced in the third trimester probably because of the anatomical and physiological changes related to advancing gestational age. This leads to stasis of urine and encourage bacterial multiplication.

85 women with culture positive for ASB were paired with 85 healthy pregnant women without bacteriuria to compare fetomaternal outcome. In the present study, anemia was seen in 35% patients with ASB and 20% of patients in control group. A significant association between ASB and anemia (P=0.02) was seen in the present study, correlating to Ansari et al study.[13] This proved a direct relation of anemia with asymptomatic bacteriuria.

In the present study, PROM was seen in 14% patients with ASB and 5% patients in control group. The association between ASB and PROM was statistically significant (P=0.03) and correlates in our study which correlates with other studies by Jain et al.[11] and Sheiner et al.[20] PROM is an accepted complication of ASB which leads to preterm labor, chorioamnionitis, endometritis, feto-maternal sepsis ultimately leading to an adverse feto-maternal outcome.[13]

ASB triggers preterm labour and delivery. Bacterial endotoxins released is believed to provoke labour directly or through a prostaglandin mediated cascade. In the present study, preterm labour was seen in 18% patients with ASB and 7% in control group. Association between ASB and preterm labour was statistically significant (P=0.03) in our study and correlates with the study done by Sheiner et al.[20]

IUGR was seen in 14% patients with ASB and 5% patients in control group. Association between ASB & IUGR was statistically significant (P=0.03) in our study and correlates with the study done by Jain et al.[11] This emphasizes the need for early detection and aggressive treatment of ASB in pregnancy.

In the present study, preeclampsia was seen in 5% patients with ASB and 3.5% patients in control group. The association of ASB and preeclampsia was not statistically significant in our study (P=0.69) which correlates with the studies done by Jain et al.[11]

The chronic subclinical infection causes increased maternal cytokines level sufficient to affect vascular endothelial function which is responsible for development of preeclampsia. The underlying renal impairment accounts for higher risk of preeclampsia rather than ASB. Therefore larger multicentric studies are required to establish, whether the association of ASB & preeclampsia is casual.

In the present study, pyelonephritis was seen in 3.5% patients with ASB and none in control group. Among the 3 patients who developed pyelonephritis, all had hydroureter/hydronephrosis. The association of ASB and pyelonephritis was not statistically significant in our study (P=0.69) which correlates with the studies done by Jain et al.[11] Though pyelonephritis is a proven, un-debated complication of ASB; prompt treatment of ASB decreases the risk of pyelonephritis by 80-90%. E. coli & Klebsiella were the organisms isolated.

In the present study, there was an increased incidence of mid-trimester abortions (4%) and preterm deliveries (15%) in the ASB group when compared to the control group. Many studies showed significant decrease in the incidence of spontaneous abortions and preterm deliveries when ASB was screened and treated with suitable antibiotics early in pregnancy.

In our study, the rate of caesarean section was higher in ASB group (48%) than in control group (39%). This high incidence of caesarean section is explained by increased incidence of PROM, preterm labour and IUGR associated with ASB.

In the present study, wound infection was seen in 5% patients with ASB and 1% patients in control group which is not statistically significant. There were no studies available to compare.

In the present study, puerperal fever was seen 14% patients with ASB and 3.5% patients in control group which showed significant association ASB and puerperal fever. This is explained by increased incidence of PROM and preterm associated with ASB and is responsible for chorioamnionitis and endometritis leading to puerperal fever.

In the present study, symptomatic UTI developed in 8% patients with ASB and 1% patients in control group. The present study shows higher prevalence of ASB in third trimester as the anatomical and physiological changes that occur during this period predisposes to the risk of developing symptomatic UTI.

In the present study, low APGAR scores were seen in 19% babies of ASB group and 6% of control group. These low APGAR scores are explained by higher incidence of PROM and preterm labour in ASB group.

In the present study, low birth weight babies were seen in 20% of ASB group and 8% of control group. A significant relation between ASB and low birth weight (P=0.04) is proved in our study which correlates with the study done by Jain et al.[11] This significant low birth weight in this study is explained by higher incidence of preterm and IUGR in ASB group.

In the present study, 28% babies in ASB group and 10% babies in control group required NICU admissions which showed a statistical significance. The causes for NICU admissions were preterm labour, IUGR, neonatal sepsis and birth asphyxia in our study.

In the present study, 8% babies in the ASB group and 1.1% babies in the control group were affected with infections. This increased neonatal infection in ASB group was statistically significant in our study and correlates with the study Betty Chacko et al.[18] The lower incidence of neonatal infections in our study is explained by effective treatment of ASB. The E. coli, Klebsiella spp. and Staphylococcus were the common organisms isolated.

ASB has potential effects to cause adverse fetal outcome. There is significant decrease in the perinatal mortality when ASB was treated effectively during pregnancy. There were 2 neonatal deaths due to sepsis and 1 still birth in the ASB group. The perinatal mortality in the present study was statistically not significant and correlates with the study done by Sheiner et al.[20]

CONCLUSION

ASB is commonly encountered in pregnant women especially anaemic women are more prone. Untreated ASB is a risk factor for development of pyelonephritis, anaemia, PROM, preterm labour in mother. IUGR and neonatal infections are more common in fetus. Routine screening for ASB as a part of antenatal care reduces the maternal and fetal complications.

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