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Original Research Article

Prevalence and associate risk factors of asymptomatic bacteriuria in pregnancy with bacterial pathogens and their antimicrobial susceptibility in a tertiary care hospital

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ABSTRACT

Background: Asymptomatic bacteriuria (ASB) is defined as the presence of actively multiplying bacteria, which is greater than 105/ ml of urine within the urinary tract excluding the distal urethra, at a time when the patient has no symptoms of UTI. Untreated and undiagnosed ASB is associated with adverse maternal and perinatal outcomes. The objective was to determine the profile, prevalence, microbiological isolates with susceptibility, and risk factors of ASB among pregnant women attending an antenatal clinic at a tertiary care hospital, Andhra Pradesh, India.
Methods: A prospective cross sectional study with 200 pregnant women was conducted for a period of 3 months from January to March 2016. The mid- stream urine specimen was collected and processed from all the cases and social and baseline obstetric data was collected. The isolates from all the cases of ASB were identified by standard biochemical tests. Antimicrobial susceptibility was performed by Kirby- Bauer disc diffusion method and interpreted as per CLSI guidelines.
Results: Prevalence of ASB in our study was 30.5%, mean age of the cases was 27.3± 2.9 years. ASB was most common in 25- 30 year's age group, during 3rd trimester and among multiparous and multigravidae. Previous history of UTI, pre-eclampsia was having significant association among cases with ASB. Escherichia coli was the predominant isolate in the study followed by *K. pneumoniae*, *CONS (Coagulase-Negative Staphylococci)*, *Staphylococcus aureus*, *citrobacter* and *Enterococci*.
Conclusions: Undiagnosed and untreated asymptomatic bacteriuria is associated with complications during pregnancy. Hence routine screening of antenatal women during all trimesters must be considered in preventing the complications and adverse foetal outcomes particularly with known risk factors like increasing age, multiparity and previous history of UTI.

Keywords: ASB, *CONS*, *Escherichia coli*, UTI

INTRODUCTION

Urinary tract infections (UTI) are a relatively common problem that occurs in all age groups and observed most commonly among women than men. Among women they are quite common during pregnancy, because of profound physiological, hormonal, and anatomical changes during pregnancy. These UTI during pregnancy could be either symptomatic or asymptomatic. Symptomatic infections during pregnancy are treated and managed, however, asympto-matic bacteriuria (ASB) during pregnancy is associated with diverse maternal and foetal outcomes if left untreated. Asymptomatic bacteriuria is defined as the presence of actively multiplying bacteria, which is greater

than 105/ml of urine within the urinary tract excluding the distal urethra, at a time when the patient has no symptoms of UTI.[1] Globally asymptomatic bacteriuria affects 2-10% of pregnant women.[2] Untreated and undiagnosed ASB is associated with adverse maternal and perinatal outcomes. Maternal outcomes include anemia, postpartum hypertensive disease, symptomatic cystitis, and acute pyelonephritis (30%), which may lead to preterm labour and delivery. Acute pyelonephritis in pregnancy leads to septicemia in 10-20% of cases and acute respiratory distress syndrome in 2%. Adverse foetal outcomes include prematurity, low birth weight, and increased perinatal mortality.[3] Evidence from various studies suggests that untreated ASB may progress to symptomatic UTI which in turn increases the risk for pre-eclampsia, chorioamnionitis, and postpartum endometritis. Symptomatic UTI also leads to foetal risks like foetal growth retardation, stillbirth, mental retardation and developmental delay. This is due to direct effect of the bacterial toxin on the foetus. Asymptomatic bacteriuria is a microbial diagnosis which depends on the isolation of specified count of bacteria in properly collected urine specimen from pregnant women. Thus, semi-quantitative urine culture is the gold standard in screening and diagnosis of ASB.[4] But a routine culture of urine in pregnant women is not feasible in many developing countries. Hence it is advisable to select pregnant women with risk factors for ASB. Evidence from many of the studies globally indicate gestational diabetes mellitus, past history of UTI, multiparity, advanced maternal age, and low socioeconomic status as some of the risk factors and conflicting results have been observed in different studies. The predominant organism causing UTI in women is Escherichia coli, accounting for 90% of infections. However, the frequencies of isolated pathogens and their antimicrobial sensitivity are variable in different geographical regions. Hence investigating the common causative agents and creating awareness among the physicians is of prime importance in managing the cases of ASB. The objective of the present study was to estimate the prevalence of ASB and its associated risk factors among pregnant women attending an antenatal set up in a tertiary care hospital. In addition, the bacterial pathogens implicated in causing ASB and their antimicrobial susceptibility is also evaluated.

METHODS

A prospective cross-sectional study was conducted at Department of obstetrics and gynecology, an outpatient clinic at Narayana Medical college, Nellore a tertiary care hospital in association with Department of Microbiology over a period of 3 months from January to march 2016. A total of 200 pregnant women who attended the antenatal clinic were included in the study.

Inclusion criteria

Patients with no symptoms of UTI, Fever, no history of antibiotic usage for past 2 weeks, no pregnancy induced diabetes mellitus, no history of hypertension, no history of congenital anomalies of urinary tract were included in the study. The participants were clearly informed about the study and informed consent was obtained. The study was started after obtaining ethical clearance from the ethical committee of the institute. All the baseline obstetric data required like age, gravida, parity, trimester, past history of urinary tract infection, diabetes mellitus, hypertension, sexual activity during pregnancy were enquired and data was entered in a separate questionnaire sheet.

Sample collection

Clean catched mid-stream urine was collected from all the pregnant women into a sterile wide mouthed leak proof container.

Sample processing

The specimen was centrifuged and microscopy by wet mount and gram stain performed from the sediment for the presence of pus cells, casts, RBC, and microorganisms. The specimen was processed further as per standard microbiological procedures. The samples were processed by using standard microbiological procedures. The specimens were cultured on dried plates of MacConkey's agar, sheep blood agar (in 5-10% CO_2 atmosphere) and cystine lactose electrolyte deficient agar, by standard loop method and the plates were incubated at 37°C overnight. Culture was interpreted as significant and insignificant as per standard criteria. The samples with significant bacteriuria were processed further and organisms identified by standard biochemical tests. The standardized Kirby-Bauer disc diffusion test was used for testing antimicrobial susceptibility and results interpreted based on CLSI guidelines.[5] The antibiotics which were tested were ampicillin (10mcg), amoxiclav (20/10mcg), amikacin (30mcg), clindamycin (2mcg), cefepime (30mcg), ceftriaxone (30mcg), cefuroxime (30mcg), ciprofloxacin (5mcg), cotrimoxazole (25mcg), erythromycin (15mcg), fosfomycin (200mcg), penicillin G (10units), imipenem (10mcg) and meropenem (10mcg) (Himedia laboratories, Mumbai).

Statistical analysis

All the data was entered in Microsoft excel and mean, medians were calculated.

RESULTS

Out of 200 pregnant women participated in the study, ASB was observed in 61 cases (30.5%), 120 were sterile, 11 showed insignificant bacteriuria and contaminants were grown in 8 specimens. Obstetric data revealed that the mean age of participants in the study was 27.3±2.9 years. The most common age group in the study was between 25-30 years (52%) followed by 31-35 years (25%) and 18-24 years (23%). Out of 200 cases, 39.5%

were in 1st trimester, 38% in 2nd and 22.5% in the 3rd trimester. 43.5% of cases were primigravida, 39.5% were second and 17% belonging to multigravida (>3 was considered multigravida). In the study 76% were primiparous and 23% having second and only 2 cases were having a third pregnancy. Out of total 61 cases of ASB identified in the study, maximum number (32/61) were seen in age group of 25- 30 years (52.46%), 42.62% (26/61) were 2nd gravida, 75.41% (46/61) of cases were primipara and 40.98% (25/61) were in 3rd trimester (Table 1).

Table 1: Demographic variables.

Variable	No.	%	ASB (No.) (%)
Age (Years)			
18-24	46	23	14 (22.95%)
25-30	104	52	32 (52.46%)
31-35	50	25	15 (24.59%)
Gravida			
1	87	43.5	23 (37.7%)
2	79	39.5	26 (42.62%)
>3	34	17	12 (19.67%)
Para			
1	152	76	46 (75.41%)
2	46	23	15 (24.59%)
3	2	1	0
Trimester			
1st	79	39.5	16 (26.23%)
2nd	76	38	20 (32.79%)
3rd	45	22.5	25 (40.98%)

Risk factors and Association

Out of 200 cases in the study, 69 had a history of old UTI and 24 cases were ASB positive and was statistically highly significant (p<0.001) in the study. 57 were anemic and 16 cases were ASB positive which was not a significant risk factor in the study. In total 200 cases, 9 were diagnosed with eclampsia and 5 cases were ASB positive and was statistically significant (P value<0.05). Out of 12 known diabetics, ASB was identified in 5 cases and 113 cases had a sexual activity during pregnancy and 18 cases were identified with ASB and were not statistically significant. A significant association was found with an old history of UTI and eclampsia in our study (Table 2).

Table 2: Risk factors and association.

Risk factor	No.	%	ASB (No.) (%)
Past H/O of UTI	69	34.5	24 (39.34%)
Anaemia	57	28.5	16 (26.23%)
Pre-Eclampsia	9	4.5	5 (8.20%)
Diabetes	12	6	5 (8.20%)
Sexual activity	113	56.5	18 (29.51%)

Isolates and sensitivity

A total of 61 isolates were isolated from cases of ASB. All of them were isolated in pure form and no mixed growth was seen in the study.

Table 3: Pathogens isolated.

Isolate	No.	%
Escherichia coli	27	44.26
Klebsiella pneumoniae	9	14.75
Coagulase Negative *staphylococcus*	11	18.03
Staphylococcus aureus	5	8.20
Enterococci sp	6	9.84
Citrobacter sp	3	4.92
Total	61	

Table 4: Antimicrobial susceptibility pattern of Isolated organisms.

Antibiotic	*Esherichia coli (n) (%)*	*K.pneumoniae (n) (%)*	*Citrobacter (n) (%)*	*Staphylococcus aureus (n) (%)*	*CONS (n) (%)*	*Enterococci (n) (%)*
AMP	12 (44.44%)	3 (33.33%)	1 (33.33%)	3 (60%)	6 (54.55%)	4 (67%)
AMC	23 (85.19%)	7 (77.78%)	2 (66.66%)	ND	ND	ND
AK	21 (77.78%)	7 (77.78%)	3 (100%)	ND	ND	ND
CPM	22 (81.48%)	6 (66.67%)	3 (100%)	ND	ND	ND
CTR	22 (81.48%)	5 (55.56%)	2 (66.66%)	ND	ND	ND
CIP	16 (59.26%)	5 (55.56%)	2 (66.66%)	ND	ND	ND
CD	ND	ND	ND	5 (100%)	10 (90.91%)	ND
COT	ND	ND	ND	5 (100%)	8 (72.73%)	6 (100%)
CXM	24 (88.89%)	6 (66.67%)	3 (100%)	ND	ND	ND
E	ND	ND	ND	3 (60%)	7 (63.64%)	ND
FO	ND	ND	ND	ND	ND	6 (100%)
P-G	ND	ND	ND	ND	ND	3 (50%)
IPM	27 (100%)	9 (100%)	3 (100%)	ND	ND	ND
MPM	27 (100%)	9 (100%)	3 (100%)	ND	ND	ND

Escherichia coli was the commonest isolate (44.26%) followed in order by *CONS* (18.03%), *Klebsiella pneumoniae* (14.75%), *Enterococci sp*. (9.84%), *Staphylococcus aureus* (8.2%) and *Citrobacter sp*. (4.92%). Gram-negative isolates demonstrated 100% sensitivity to imipenem and meropenem and Gram-positive isolates to clindamycin. *Enterococci* documented 100% sensitivity to cotrimoxazole and fosfomycin. (Table 3 and 4) Moderate sensitivities were noted to amikacin, amoxyclav, and cefepime.

DISCUSSION

Asymptomatic bacteriuria during pregnancy is one of the many prime risk factors responsible for maternal and foetal adverse outcomes. Women who have bacteriuria have 20- 30% higher chance of getting pyelonephritis than those without. The prevalence of ASB in the study group was 30.5% which is significantly high when compared with findings of Annie Rajaratnam et al (13.2%), Sujatha R et al (7.2%) and on par to findings of Neupane et al (26.5%) and less than findings of Imade et al (45.3%) who reported higher prevalence of ASB in their studies.[6-9] Variations among these studies may be due to differences in environmental conditions, socioeconomic statuses, social habits of the community and educational level of the patients in the study. In present study the highest prevalence was noticed in the age group of 25 -30 years with 52.46% which coincides with findings of Alghalibi et al (55.62%), Sujatha R et al., (72.72%) but some studies reported a higher prevalence in the age group of 20-25 years.[10] The age distribution of patients did not have a significant association with ASB in our study which is a similar finding in many studies, whereas some studies have shown significant association with age, stating that ASB is associated with advances in age.[11] In present study, no significant association was seen with period of gestation, 40.98% of cases were ASB positive in 3rd trimester which coincides with the findings of Saeed et al but differs with the findings of Yahodara et al who reported incidence of ASB was higher in 1st trimester, whereas studies done by Roy et al, Nath et al, reported higher incidence of ASB during 2nd trimester.[12] This finding of more cases of ASB in the 3rd trimester, can be explained by the fact that most of the women were referred from primary health centre to tertiary care hospital for their first visit in the 3rd trimester.[13-15] More number of cases of ASB were associated with multiparous and multigravidae than seen in primiparous women. The same findings were observed in studies of Fatima N et al, Kovavisarach E et al.[16,17]

There was a significant association of ASB with the previous history of UTI, in present study (39.34%) and similar association was reported in studies of Nerissa Isabel C Sescon et al and many others.[18] Anemia and ASB had no significant association in present study and 26.23% were ASB positive among 57 cases of anemia in the study, however, some studies reported a high prevalence of UTI among anemic pregnant women and high chances of development of pyelonephritis because of resistance developed by the bacteria to chemotherapy.

In our study 9 cases of pre-eclampsia were diagnosed during the 3rd trimester, and 5 cases (8.2%) were ASB positive and significant statistically. Findings in the study of JA Hill et al also found a similar association with pre-eclampsia and is a significant risk factor for ASB.[19] 12 cases of known diabetics were present among 200 cases and 5 were found to be ASB positive. However, there was no significant association between diabetes and ASB in present study.

Escherichia coli was the commonest isolate in this study, and this coincides with the studies locally and globally. *Escherichia coli* being a commensal of the intestine has common access through the faecal material into the female urinary tract. In this study, it was 44.26% which is on par with findings of Chandel et al, Khattak et al, Jain et al.[20-22] All the gram-negative isolates of this study exhibited 100% sensitivity to Imipenem and meropenem. Moderate sensitivity was noted to amikacin, cefepime, and amoxyclavulanic acid. However, antimicrobial sensitivity and resistance pattern vary from place to place, region to region, which was because of the emergence of resistant strains because of indiscriminate usage of antibiotics. Coagulase-negative *Staphylococcus* was the 2nd most common isolate and exhibited maximum sensitivity to Clindamycin and moderate sensitivity to cotrimoxazole and erythromycin. Enayat et al in his study reported *Enterococci* as the most common isolate.[23] The upsurge in antibiotic resistance patterns could have been caused by antibiotic abuse and self-medication. Also, low costs and availability of drugs on the table could be other factors contributing to antibiotic resistance.

CONCLUSION

To conclude, undiagnosed and untreated asymptomatic bacteriuria is associated with complications during pregnancy. Hence routine screening of antenatal women during all trimesters must be considered in preventing the complications and adverse foetal outcomes particularly with known risk factors like increasing age, multiparity and previous history of UTI. In view of changes observed in antibiotic resistance among the pathogens, physicians should be guided by the empirical management of cases of ASB.

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