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Asymptomatic bacteriuria of pregnant women in a tertiary care centre

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Abstract:

BACKGROUND: Asymptomatic bacteriuria (ASB) is commonly seen during pregnancy due to the various morphological, hormonal, and physiological changes the body undergoes. If left undiagnosed, it can lead to conditions such as pyelonephritis and preterm delivery which could culminate in causing maternal and fetal morbidity and mortality. Therefore, this study aims to determine the prevalence, risk factors, microbial profile, and antibiotic susceptibility patterns associated with ASB in a tertiary healthcare center.

MATERIALS AND METHODS: A cross-sectional study was carried out where 150 urine samples were obtained from pregnant women within the gestational age of 13–36 weeks. Randomized stratified sampling was the method of sampling used. A questionnaire was also administered to them to determine potential risk factors. The samples were cultured and identified using biochemical tests. Antibiotic susceptibility tests were carried out by Kirby–Bauer disc diffusion method. Statistical analysis was carried out using Chi-square test. The graphs and tables were generated using Microsoft Excel and Word.

RESULTS: Out of the 150 samples that were obtained, 8 samples had significant bacteriuria which is a prevalence of 5.33%. *Escherichia coli* was the most frequently isolated organism accounting to 45% of the isolates. The other organisms that were isolated were *Enterococcus*, *Klebsiella pneumoniae*, *Coagulase negative staphylococcus* (CONS), *Candida albicans*, and Group B *Streptococcus* which measured to 11% of the total distribution each. In the antibiotic sensitivity tests, among the gram-negative isolates, marked resistance to Ampicillin and Amoxycillin along with sensitivity to Cotrimoxazole and Nitrofurantoin. Of the gram-positive isolates, there was sensitivity to Ampicillin and Nitrofurantoin. A positive correlation was seen between the age groups of 23–27 and the prevalence of ASB.

CONCLUSION: The prevalence of ASB in this study shows that ASB is not uncommon in the population. Despite the World Health Organization (WHO) guidelines and National Health Mission recommendations to make urine check-ups a routine, it not carried out, possibly due to cost implications. However, it poses a risk for severe maternal and fetal outcomes and hence, should be screened for on a regular basis. Thus, this study emphasizes the importance of screening pregnant women for ASB for promoting better maternal and fetal health.

Keywords:

Asymptomatic bacteriuria, Group B streptococcus, microbial profile, pregnancy, prevalence, risk factors, screening, urine culture

Introduction

Asymptomatic bacteriuria (ASB) is the presence of a significant level of actively multiplying bacteria in the urinary tract excluding the distal urethra, that is, more than 10^5 colony forming units per milliliter

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of urine in patients with no symptoms suggestive of a urinary tract infection. Pregnant women are more susceptible to ASB because of the various morphological, hormonal, and physiological changes the body undergoes during gestation. The short-sized urethra and the proximity of the urinary tract to the anal canal in females poses an increased risk of contamination by

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fecal flora^[1] which when combined with the apparent reduction in immunity during pregnancy along with the glycosuria that is seen in 70% of the women during gestation promotes a suitable environment for the proliferation of bacteria in the urinary tract.^[2]

Studies have shown that with increasing gestational age, the subsequent increase in the uterine size and increase in serum progesterone levels decreases the tone of the ureteric and bladder muscles causing their dilatation which leads to urinary stasis. The relative obstruction caused by the gravid uterus is also attributed to the retention of urine. In addition to this, reflux phenomenon is seen in which due to vesicourethral reflux, the complete voiding of urine is not possible.^[3] These factors contribute to the development of ASB in pregnancy. Keeping these facts in mind, the gestational age of 13–36 weeks was chosen for this study.

Globally, ASB incidence is reportedly between 2% and 10% of all pregnancies^[3] varying with demography and geography. In India, few studies have shown the incidence of ASB to be ranging from 5% to 17%.

Pregnancy accelerates the progression of ASB to symptomatic bacteriuria in 40% of the women which can pave way to acute kidney failure.^[4] ASB can also lead to symptomatic cystitis which can progress to pyelonephritis. Pyelonephritis is the most severe complication of ASB and is associated with preterm labor and delivery in 13.3% of the women. According to the World Health Organisation (WHO) census released in November 2016, India holds the first position for the incidence of highest preterm births in the world. Acute pyelonephritis can also lead to septicaemia and respiratory distress syndrome in 10–20% and 2% of the cases, respectively.^[5] Other complications caused by ASB are anemia, hypertensive disease, urolithiasis, pre-eclampsia, chorioamnionitis, postpartum urinary tract infection, and chronic kidney failure.^[6] ASB is the cause of several undesirable obstetric outcomes as well. The ascent of bacteria in pyelonephritis affects the fetus by causing the release of bacterial endotoxins that initiate the release of toxic inflammatory cytokines which causes local circulatory disturbances in the placenta. This leads to mid-term abortions, still births, low birth weight, and intra uterine growth restriction.^[4] Products released by the bacteria such as mucinases and pro inflammatory toxins break down the mucus plug which leads to premature rupture of membranes which is a predisposition to the onset of preterm labor. Additionally, due to the breakdown of the mucus plug and the underdeveloped immunological system of the fetus, bacteria colonize and multiply in the fetus with ease, leading to septicaemia.^[4] Other complications include oligohydramnios, polyhydramnios, perinatal

death of fetus,^[6] and higher incidences of recurrent pregnancy loss.

Pathogens that are commonly implicated in ASB are E coli, Klebsiella pneumonia, Proteus mirabilis, and Group B Streptococcus (GBS). A study concluded that there was a relation between the increasing colony count of GBS and the increased grade of chorioamnionitis.^[7] Additionally, a review of 20 studies showed positive correlation between GBS colonization and the occurrence of preterm delivery.^[8] Thus, GBS is one of the most dangerous pathogens causing fetal and maternal complications.

Many studies globally have shown conflicting results regarding the risk factors for ASB. As per WHO, preterm birth is the leading cause of death in infants. ASB is one of the important predictors of preterm births. Therefore, determining the risk factors associated with ASB will be vital in the prevention of fetal mortality. Additionally, increased antimicrobial drug resistance is a widely rampant phenomenon. Due to this, there has to be persistent monitoring of susceptibility patterns of the pathogens.

The World Health Organisation (WHO) recommends routine testing for ASB using midstream clean catch urine samples in early pregnancy and treatment with antibiotics, if positive cultures are seen. However, due to several reasons, possibly cost implications, routine scanning for ASB is not carried out in developing countries. In view of this fact, this study was conducted to determine the prevalence, microbial profile, antibiotic susceptibility, and risk factors associated with ASB in pregnant women.

Objectives of the Cross-Sectional Study

1. To determine the prevalence of ASB in pregnant women with the gestational age of 13–36 weeks
2. To assess the risk factors associated with ASB in pregnant women with the gestational age of 13–36 weeks
3. To analyze microbial profile related to ASB in pregnant women with the gestational age of 13–36 weeks
4. To analyze drug resistance patterns linked with ASB in pregnant women with the gestational age of 13–36 weeks.

Materials and Methods

Study participants and sampling

The sample size of 150 was calculated from the standard formula of $n = \frac{4 \times p \times (100 - p)}{d^2}$ where p is the prevalence obtained from a study conducted in Nepal,^[9] and d is the precision. The participants of the study were recruited through non-probability consecutive sampling method.

Up to 150 pregnant women with a gestation period ranging from 13 to 36 weeks were included in the study.

Inclusion criteria was healthy pregnant women with a gestational age of 13–36 weeks, who were willing to participate, were included in the study.

Exclusion criteria was pregnant women with a history of urinary tract infection symptoms, urinary tract anomalies, and a history of antibiotic therapy in the past 2 weeks were not included in the study.

Data collection and technique

The study period was for 4 months from June to September 2019. The study was commenced after obtaining approval from the institutional ethics committee. The study was explained to the volunteers and those willing to participate were included in the study after their consent was obtained.

A questionnaire enquiring about the demographic and socioeconomic details was administered to the subjects by the researcher in the local language to determine the risk factors. Clinical information of the patient pertaining to diabetes, anemia, and hypertension was taken from their hospital records. Following this, the participants were counseled on how to obtain a midstream clean catch urine sample. They were directed to gently clean their private parts and separate their labia following which they were to void the midstream urine into the wide mouthed sterile universal container.

Culture methods

A pre made media was prepared as per the manufacturer’s instructions and used for sample culturing. The samples were streaked and cultured in blood agar and Hichrome agar following which they were incubated at 37°C for 24 h. Once isolated, the organisms were identified using standard biochemical tests. Antibiotic resistance tests were performed in suitable media using Kirby–Bauer disc diffusion method to determine the susceptibility patterns.

Statistical analysis

The graphs and tables of the results were generated using Microsoft Excel and Microsoft Word. Chi-square test was performed for the statistical analysis of the data. *P* (Probability value) of <0.05 was considered statistically significant.

Results

Sociodemographic details

A total of 150 pregnant women were recruited for the study. The mean age of pregnant women was 26.6 years with standard deviation of 3.8 years [Figure 1].

Among the recruited participants, 50 women were in the second trimester, that is, between the gestational age of 13–26 weeks. The remaining 100 women were in the third trimester, that is, between 27 and 36 weeks. The distribution is illustrated in Figure 2.

Among the recruited participants, 47.3% women had a history of previous viable pregnancy, while 52.6% were primigravidae [Figure 3].

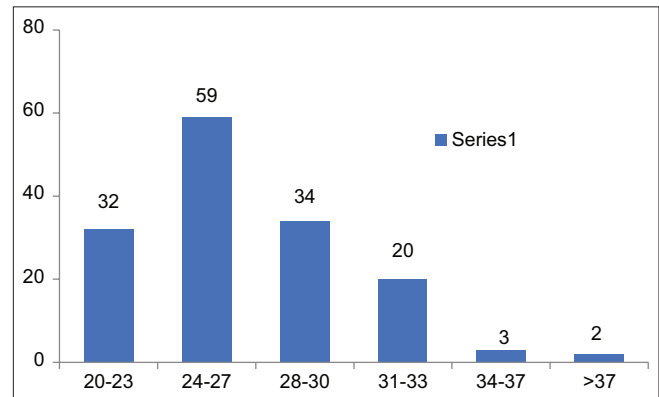


Figure 1: Age distribution of the sample

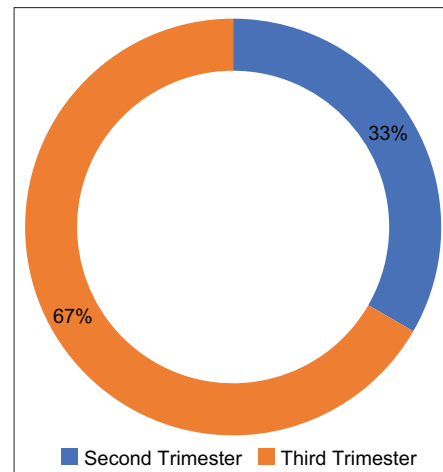


Figure 2: Trimester distribution of the sample

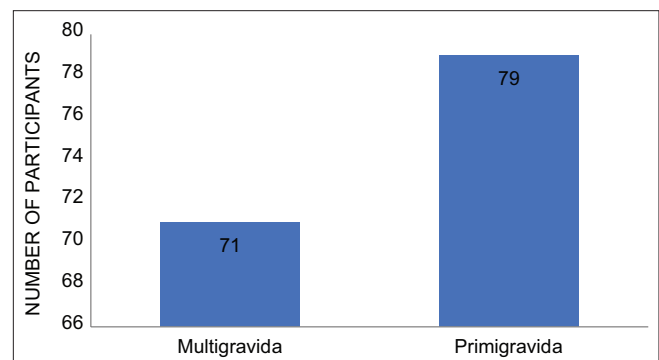


Figure 3: Distribution of parity of the sample

The distribution of the socioeconomic status of the women was determined using the modified Kuppuswamy scale 2018 [Figure 4].

Additional data that was obtained from the questionnaire that was administered to the participants is depicted in Table 1.

Prevalence and microbial profile

Out of the 150 urine samples that were analyzed, 8 samples were positive for significant bacteriuria which is a prevalence of 5.33%. Among these, six different isolates were identified, predominantly gram-negative bacteria. The isolates were E Coli, Klebsiella pneumoniae, Enterococcus, Group B streptococcus, CONS, and Candida albicans. E coli was the most frequently isolated microorganism accounting for 45% while the rest of the pathogens added up to 11% each. The graph in Figure 5 depicts the various microbial isolates. The distribution of ASB among demographic details are shown in Tables 2–6.

Antimicrobial susceptibility

The antibiotic susceptibility profile of the microbial isolates is depicted in Table 7. Among the gram-negative isolates, there was marked resistance to Ampicillin and Amoxycillin. However, sensitivity to Cotrimoxazole and Nitrofurantoin was also seen. Of the gram-positive isolates, there was sensitivity to Ampicillin and Nitrofurantoin.

Risk factors associated with ASB

Chi-square analysis was used to test for association between possible risk factors and the prevalence of ASB. *P* value <0.05 is considered statistically significant. Significant association was discernible between the prevalence of ASB and the age group of 24–27 years. No other statistically significant association was determined with any of the other potential risk factors. This data is shown in Table 8.

Discussion

In the present study, the prevalence of ASB among the pregnant women was found to be 5.33%. These results were similar to the findings from Ghana^[10] and Netherlands. Previous studies conducted in a comparable South Indian population by Cooly *et al.*^[11] and Udawat *et al.*^[11] have also shown similar prevalence rates. Other Indian studies from Kanpur (7.3%),^[12] Shimla (7.34%),^[13] Raichur (9%),^[6] and Kolkata (11%)^[14] has showed prevalence rates that are analogous to the current study. Studies conducted in Nigeria (45.3%),^[15] Ethiopia (21.2%),^[16] and Tanzania (68.4%)^[17] showed significantly higher prevalence rates. This may be due to the differences in the environment, community health infrastructure, social habits of the community, socioeconomic status, personal hygiene practices, and educational standards of the population.

Nearly 75% of the patients with ASB belonged to the age group of 24–27 years. This is comparable to other studies conducted by Rohini *et al.*,^[5] Byna *et al.*,^[4] and Rao *et al.*^[18] where similar age groups have higher frequency of ASB occurrence.

Table 1: Additional details from the questionnaire

Details	Present	Absent
Diabetic	13 (8.6%)	137 (91.3%)
Anemia	8 (5.3%)	142 (94.6%)
Sexual activity	42 (28%)	108 (72%)
Hypertension	2 (1.3%)	148 (98.6%)
Direction of washing of genitals	Front to back 129 (86%)	Back to front 21 (14%)
Quantity of water consumed	<3 L/day 86 (57.3%)	64 (42.6%)
Frequency of micturition	≤3 times/day 10 (6.6%)	>3 times/day 140 (93.3%)

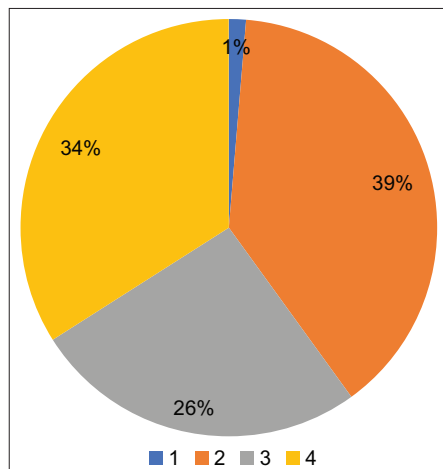


Figure 4: Distribution of socioeconomic status of the sample

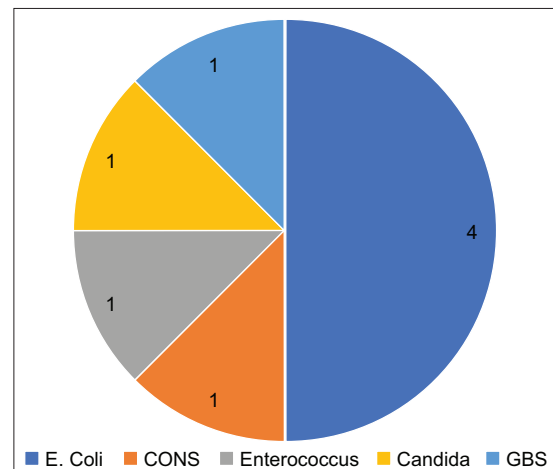


Figure 5: Distribution of microbial isolates

Table 2: Distribution of trimester among ASB positive women

Age distribution	Asb prevalence n (%)
20-23	0
24-27	6 (75%)
27-30	0
31-33	1 (12.5%)
24-37	0
>37	1 (12.5%)

Table 3: Distribution of age among ASB positive women

Trimester	Asb prevalence n (%)
Second trimester	4 (50%)
Third trimester	4 (50%)

Table 4: Distribution of socioeconomic status among ASB positive women

Socioeconomic status	Asb prevalence n (%)
1	0
2	4 (50%)
3	1 (12.5%)
4	3 (37.5%)

Table 5: Distribution of parity among ASB positive women

Parity	Asb prevalence n (%)
Primigravidae	4 (50%)
Multigravida	4 (50%)

Table 6: Details from the questionnaire among the ASB positive women

Details	Present n (%)	Absent n (%)
Diabetes	1 (12.5%)	7 (87.5%)
Anemia	0	8 (100%)
Sexual activity	2 (25%)	6 (75%)
Hypertension	0	8 (100%)
Direction of washing of genitals	Front to back 8 (100%)	Back to front 0
Quantity of water consumed	<3 L/day 6 (75%)	≥3 L/day 2 (25%)
Frequency of micturition	≤3 times/day 1 (12.5%)	>3 times/day 7 (87.5%)

In the present study, no other statistically significant correlation was found between ASB prevalence and potential risk factors. This result could be because of the limited number of positive samples, due to which a viable correlation could not be done. Since the sample size was limited to 150, the number of positive samples that were generated were also less. A possible extension of the study on a larger scale could prove helpful in determining a positive correlation between the prevalence of ASB and factors like socioeconomic status and frequency of micturition. This risk factor findings of this study are in consensus with studies

undertaken by Mohankumar *et al.*^[19] and Mekapogu *et al.*^[20] However, several other studies^[21-23] concluded that there is a statistically significant association between ASB prevalence and the other potential risk factors.

The predominant microbial isolate was found to be E coli. This is in accordance with several studies.^[12,15-17] The other commonly found isolates were *Klebsiella pneumoniae*, *Enterococcus*, GBS, and CONS. The findings of this study is concurrent with the findings of other studies.^[16,22,24-27]

There is a change in pattern in antibiotic resistance due to which susceptibility patterns have to be monitored regularly. Nitrofurantoin was found to be sensitive toward the gram-negative organisms. The gram-positive organisms were found to be sensitive to ampicillin and nitrofurantoin. Nitrofurantoin was found to be the most effective antibiotic to treat ASB in pregnancy. Similar sensitivity patterns have been reported in several studies.^[10,28,29] Ampicillin can also be utilized since it is safer during pregnancy and has lesser side effects.^[30-33] Resistance to drugs like amoxicillin and amoxicillin can be attributed to their irrational usage and empirical prescription of these drugs over the years.^[34-36]

From the data depicted in Table 9, it can be seen that the Population Attributable Risk of the various obstetric complications are very high. The incidence of adverse complications like preterm labor, preeclamptic toxemia, low birth weight, intrauterine growth retardation, and premature preterm rupture of membranes can be reduced drastically by early detection of ASB.^[37-39] Hence, this study advocates that mandatory screening for ASB is necessary so it can be uncovered early and appropriately treated.

Furthermore, implementation of a health care based educational intervention by policy and health care workers will play a vital role in increasing screening for ASB among pregnant women and consequently, will improve the overall maternal and fetal health.^[40-42]

Limitations and recommendations

The sample size in this study is limited to 150 due to which the number of samples which were positive for ASB were also limited. Carrying out this study on a larger scale in determination of risk factors and microbial patterns associated with ASB.

Conclusion

This study has been useful in providing insight into the prevalence, risk factors, microbial profile, and drug susceptibility patterns associated with ASB. A prevalence rate of 5.33% was observed which shows that ASB is not uncommon among our study population.

Table 7: Antimicrobial susceptibility of the microbial isolates

Isolate/drug	Ampicillin	Amoxicillin	Norfloxacin	Cotrimazaxole	Gentamicin	Ciprofloxacin	Nitrofurantoin
Escherichia coli [n=4] n (%)	0	0	2 (50%)	4 (100%)	1 (25%)	2 (50%)	4 (100%)
Klebsiella Pneumonia [n=1] n (%)	0	0	1 (100%)	1 (100%)	1 (100%)	1 (100%)	1 (100%)
Gbs [n=1] n (%)	1 (100%)	1 (100%)	0	0	0	0	1 (100%)
Enterococcus [n=1] n (%)	1 (100%)	Na	1 (100%)	Na	1 (100%)	1 (100%)	1 (100%)
Cons [n=1] n (%)	Na	Na	Na	1 (100%)	Na	Na	Na

Table 8: Chi square analysis of risk factors

Risk Factors	Category	Asb Positive	Asb Negative	Chi Square Value	P
Diabetes	Present	1 (7.6%)	12 (92.3%)	0.156	0.692
	Absent	7 (5.1%)	130 (94.8%)		
Sexual activity	Present	2 (4.7%)	40 (95.2%)	0.042	0.837
	Absent	6 (5.5%)	102 (94.4%)		
Trimester	Second trimester	4 (8%)	46 (92%)	1.110	0.292
	Third trimester	4 (4%)	96 (96%)		
Frequency of hydration	<3 L/day	6 (6.7%)	80 (93.02%)	1.110	0.292
	>3 L/day	2 (3.1%)	62 (96.8%)		
Frequency of micturition	<3 times/day	1 (10%)	9 (90%)	0.130	0.718
	>3 times/day	7 (5%)	133 (95%)		
Maternal age	24-27 years	6 (11.5%)	52 (89.6%)	4.650	0.031
	Other age groups	2 (2.1%)	90 (97.8%)		
Socioeconomic status	Low socioeconomic status	5 (5.05%)	94 (94.9%)	0.036	0.849
	High socioeconomic status	3 (5.8%)	48 (94.1%)		
Parity	Multigravida	4 (5.6%)	67 (94.3%)	0.034	0.853
	Primigravida	4 (5.06%)	75 (94.9%)		

Table 9: Population attributable risk for the complications of ASB

Complication	Relative risk	Population attributable risk
Intrauterine growth retardation	3.27 ^[30]	10.7
Low birth weight	5.68 ^[31]	19.8
Premature preterm rupture of membranes	3.63 ^[30]	12.2
Preterm labor	3.27 ^[30]	10.7
Preeclamptic toxemia	3.79 ^[30]	12.8
Puerperal pyrexia	1.83 ^[30]	4.2

The maternal age of 24-27 years also showed statistically significant association with ASB prevalence. Hence, this study emphasizes the importance of screening pregnant women for ASB keeping in mind the adverse maternal and fetal outcomes that untreated ASB can cause. Making urine check-ups a routine during pregnancy will go a long way in reducing undesirable complications in the mother and infant.

Abbreviations

1. ASB: Asymptomatic bacteriuria
2. GBS: Group B Streptococcus
3. CONS: Coagulase negative staphylococcus.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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