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An Assessment of Asymptomatic Bacteriuria During Pregnancy and Antimicrobial Resistance to its Common Bacterial Isolates in the Urine

Sana Noor, Ejaz Mahmood, Noor Shahid, Arooj ul Hassan, Saba Noor

ABSTRACT:

Objective: The objective of this study is to assess asymptomatic bacteriuria during pregnancy and its antimicrobial resistance to the common bacterial isolates in the urine.

Study Design and Setting: The cross-sectional study was carried out in the Antenatal Clinic, Obstetrics and Gynaecology Unit of Avicenna Medical and Dental Hospital, Lahore, Pakistan.

Methodology: This descriptive, cross-sectional study lasted for nine months and information was collected with the help of a self-designed questionnaire using non-probability random sampling. The frequency distribution of socio-economic and demographic factors of 167 pregnant women was observed while the cultural examination was performed on urine samples of diagnosed cases of asymptomatic bacteriuria through microscopy to find out antimicrobial resistance against bacterial isolates.

Results: The prevalence rate of asymptomatic bacteriuria was 13.2%. The most common pathogen was *E. coli* followed by *Klebsiella Pneumoniae* and *Staphylococci*. Resistance of urine pathogens was observed against Ampicillin, Amoxiclav, Norfloxacin, and Piperacillin/Tazobactam.

Conclusion: *E. coli* was identified as the most predominant pathogen that showed higher resistance to Cefotaxime. History of renal stone, trimester, parity, education and low-socio-economic status were the significant factors for ASB

Keywords: Urinary tract infection, Bacteriuria, Bacterial Isolates. Anti-microbial resistance

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INTRODUCTION:

Asymptomatic bacteriuria (ASB) is defined as the occurrence of significant bacteriuria without any clinical findings. There is microbial and hormonal growth in urine during pregnancy.[1] Prevalence of ASB generally ranged from 2.5% to 10% during pregnancy. The change in prevalence rate is due to the variation in geographical region and culture that varies from country to country. Some countries such as Brazil and India showed a higher incidence rate of 12.3% and 13.2%.[2,3] The root cause of the higher incidence rate is still unknown. Pre-term labor is reported as the most common complication with ASB during pregnancy[1,2] while acute pyelonephritis is observed as the most severe complication as it could be life-threatening for foetus and mother.[3]

Early diagnosis and treatment of ASB can minimize the risk of pyelonephritis.[3,4]

Several factors are known to affect the likelihood of ASB in pregnant women. These factors include age, living standard, parity, sexual activity, past history of urinary tract infection (UTI), UTI abnormalities, maternal history, medical history, socio-economic status, and educational status. Such factors have been shown to have an association with the incidence of ASB.[4]

Bacteriuria often develops in the first few months of pregnancy and is frequently associated with a reduction in concentrating ability, suggesting an involvement of the kidney.[5] The smooth muscle relaxation and following urethral dilatation that accompanies pregnancy are thought to facilitate the ascent of bacteria from the bladder to the kidney.[6]

Most of the available research showed that bacteriuria was the only factor associated with pre-term delivery before 36 weeks of pregnancy, preterm premature rupture of membrane,

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and low birth weight. The identification of asymptomatic bacteriuria via urinalysis in the first trimester may be a predictor of adverse perinatal outcomes.[6,7] Studies have been carried out to estimate the development of risk of infection in the patients with asymptomatic bacteriuria after some urologic surgeries, but no association was found between ASB and postoperative complications among these patients. There are also some relevant facts, graded as significant in terms of prevention and screening of asymptomatic bacteriuria among patients going for urologic interventions.[7]

Asymptomatic bacteriuria and symptomatic UTI both are associated with the isolation of a specified quantitative count of bacteria in an appropriately collected urine sample.[5,8] Pregnant women with ASB increased maternal and foetal complications, and have known associated factors like increase in age, sexual activity, history of UTI before pregnancy, lower socio-economic status, several pregnancies, and lack of personal hygiene.[8]

Pathogens and the resistance to antibiotic treatment differ with respect to geographical region. *Escherichia* (*E. coli*) was observed as the most common agent identified during cultural examination.[1,4] *E. coli* has been reported as the most common agent followed by *Klebsiepneumonianiae*.[9] A fast-growing case of ASB over the last decade has shown *Klebsiella pneumonia* as the cause in the US. The prevalence of Streptococcus group B has been observed as a strong prevalent agent in large-scale studies with *E. coli* and *Klebsiella pneumonia*.[9]Antibiotic treatment considerably affects the prevalence of isolate resistance in the case of ASB during pregnancy.[10]

The main aim of this study was to observe the demographic factors that could be the cause and associated risk factors of ASB during pregnancy. With the cultural examination of urine, the major prevalence of pathogens was observed and antibiotic treatment was analysed.

METHODOLOGY:

A cross-sectional study was conducted at Antenatal Clinic, Avicenna Medical & Dental Hospital was collected. The data was collected from 167 pregnant females using a non-probability sampling technique. The study lasted for nine months (from February 2020 till October 2020). The sample size was calculated taking a confidence interval of 95% with 5% as absolute precision by using the following formula:

Sample size (n) = Z^2 1-(α)/2 (P(1-P))/d2

^{Z} 1-α/2 ^{Z} 1-α/2 = 1.96

P is the prevalence of asymptomatic bacteriuria in pregnant women in Pakistan; that is 12.4 %.[1]

$1\text{-}p$ = 1 – 0.124

d^2 = 0.05 margin of error

Substituting values for the symbols:

n = 0.41755/0.0025

n =167

The calculated sample size was observed to be 176 with nine people lost in follow-up during the nine-months study. A self-designed questionnaire based on two sections was used to gather information. The first section was based on demographic information such as age, parity, maternal history, educational status, socio-economic status, history of renal stone, and trimester. The second section listed the information collected through cultural examination. The prevalence rate of common pathogens and antibiotic-resistant was documented. In the urine sample examination, each sample was divided into two portions. One was used for microscopy and the other was kept in a cool and dry place and was used for cultural examination if the results of microscopy were found positive. The reliability of the questionnaire was tested as 70% using Cronbach alpha.

Before the data collection process, a brief explanation of the study was given and written consent was obtained from each participant. Females of age more than 35 years and with any past history of acute pyelonephritis were excluded from the study. The inclusion criteria of the participants were the females of the age group 18-35 years and who visited the antenatal clinic at Avicenna Medical & Dental Hospital during pregnancy.

The ethical approval of the study was taken from the Institutional Review Board (IRB) of the University of Lahore (Ref. No. IRB-UOL-FAHS/716/2020) before the start of the study. The descriptive of the socio-economic and demographic variables were calculated. The categorical variables were presented in the form of frequency distribution. The prevalence of ASB was observed and the chi-square test of association was applied to assess the statistically significant association of socio-economic and demographic variables with ASB at a 5% level of significance. The associated significant factors from the chi-square test of association were further assessed as to whether those were independent risk factors for ASB or not. The binary logistic regression was performed with significant associated independent factors. Results were given in the form of significant values and odd ratios. The percentage of pregnant women with various urinary pathogens isolated from their urine samples was given. Graphically and theoretically, the resistance of each antibiotic to all the pathogens was presented. Statistical Package 21.0 was used for the analysis purpose.

RESULTS:

Data collected showed that the majority of the pregnant women were 20-30 years old. The overall prevalence rate was 13.2%. Most of the pregnant women belonged to a low socioeconomic status. The results of the frequency distribution of pregnant women have been given in Table 1. Approximately 90% of pregnant women visited during the second and third trimesters of pregnancy. Nearly 9% of the women had a history of renal stone but no one was diagnosed

with ASB. The significant associated factors were taken as independent variables. The value of the estimate, standard error, significance level, and odds ratio are given in Table 2. Educational level was found as an insignificant risk factor for ASB. The illiterate group was used as the reference group. The results indicated that illiterate people were at more risk for ASB. The estimate of the coefficient was negative for parity. Multipara was used as a reference group for the factor parity. Since the coefficient is negative with an odds ratio of 0.274, pregnant women with primigravida had more chances of parity. The significance level was greater than 0.05 so parity was found to be insignificant. The coefficient of low socioeconomic status was negative with a significance level of less than 0.05. Low socioeconomic status was found to be a significant risk factor for the development of ASB. The reference group was pregnant women without low socio-economic status. The odd ratio of 0.753 showed that women with low socioeconomic status were at high risk of developing asymptomatic bacteriuria. The number of children also showed a negative coefficient with an odds ratio of 0.778. The significance level showed that the number of children was an insignificant risk factor for ASB. An increase in the number of children by 1 cause (1-0.778) % chances of developing ASB. The ASB was traced to 22 pregnant women in the total sample. Urine culture of these pregnant women was performed after the microscopy. The prevalence of ASB among pregnant women was 13.2%. E. coli accounted for 45.45% was the most dominant agent found in the urine sample. *Klebsiella pneumonia* and *Staphylococcus aureus* were observed as subsequent predominant bacteria that accounted for 18.18% as given in Table 3 Antibiotics were tested for isolated urinary pathogens to find out the resistance level if any (Figure 1). Antibiotics such as Ampicillin, Amoxiclav, Norfloxacin, and Piperacillin/Tazobactam resistance were tested for urinary pathogens. *E.coli* resistance to ampicillin was found in 62% of cases, followed by *Staphylococcus aureus* resistance in 68% of cases. *Klebsiella pneumoniae's* resistance to ampicillin was found in 78%. High resistant E.coli (80%) was found against "Cefotaxime" while Cefotaxime showed the minimum resistance (49%) against *Staphylococcus aureus*. Norfloxacin showed the highest resistance (72%) against *E. coli* and the lowest (60%) against *Staphylococcus aureus* while piperacillin showed the highest (62%) against *Staphylococcus aureus* and lowest (56%) against *Candida albicans.*

Table 1: Frequency Distribution of Socio-Economic & Demographic Factors

Variables	Categories	ASB		Total	Chi-square	p-value
		ASB	No ASB			
Age	< 20	0	12	12	2.539	0.468
	20-30	19	108	127		
	30-40	3	23	26		
	> 40	0	2	2		
	Total	22	145	**167**		
Parity	Primi-gravida	7	106	113	13.054	0.000
	Multipara	15	39	54		
	Total	22	145	**167**		
Educational Status	Literate	6	83	89	5.741	0.017
	Illiterate	16	62	78		
	Total	22	145	**167**		
Low-Socio Economic Status	Yes	13	126	139	8.684	0.003
	No	9	19	28		
	Total	22	145	**167**		
No. of Children	0	9	59	68	2.203	0.698
	1	2	16	18		
	2	7	29	36		
	3	4	41	45		
	Total	22	145	**167**		
History of Renal Stone	Yes	8	7	15	19.540	0.000
	No	14	138	152		
	Total	22	145	**167**		
Trimester	1	1	9	10	8.865	0.012
	2	3	66	69		
	3	18	70	88		
	Total	22	145	**167**		

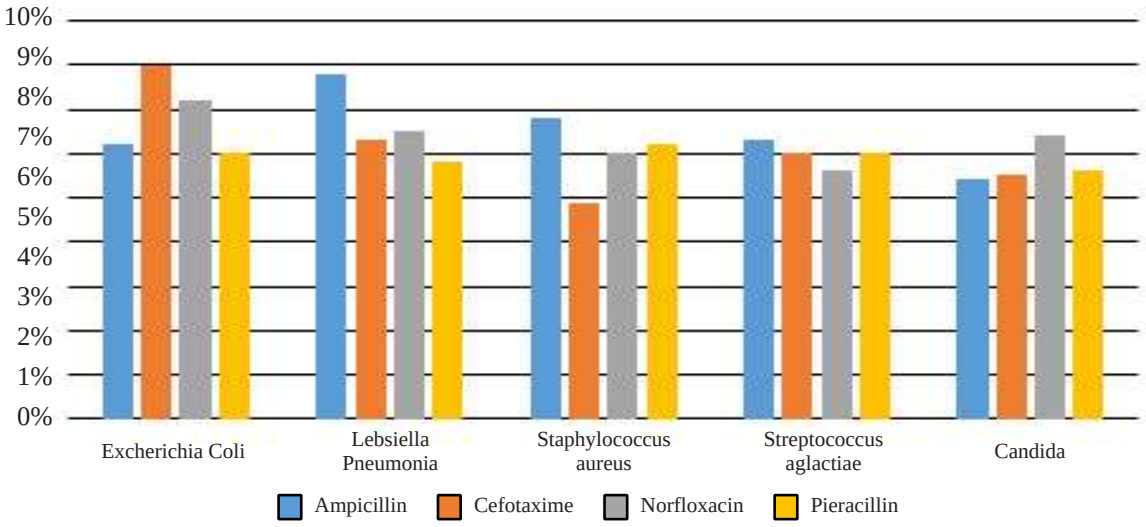
Table 2: Binary Logistic Regression for the Associated Risk Factors

Variables	B	S.E	Significance	Odd ratio
Educational Level	0.095	0.823	0.908	1.099
Parity	-1.293	0.830	0.119	0.274
Low-Socio Economic Status	-0.283	0.712	0.069	0.753
No. of Children	-0.251	0.400	0.530	0.778
History of Renal Stone	-2.636	0.694	0.000	0.072
Trimester	-1.285	0.440	0.003	0.277

Table 3: Spectrum of Urinary Pathogens isolated from urine sample of Pregnant Women with ASB

Bacteria	No. of Pregnant Women with ASB	Percentage among Pregnant Women with ASB
Escherichia coli	10	45.45%
Klebsiella pneumoniae	4	18.18%
Staphylococcus aureus	4	18.18%
Streptococcus aglactiae	3	13.63%
Candida albicans	1	4.54%
Total	22	100%

Figure 1. Resistance of Antibiotics against Urinary Pathogens



DISCUSSION:

The prevalence rate of ASB during pregnancy varied with respect to the change in culture and geographical region. The prevalence rate observed in the present study was 13.2% which was higher compared to many other studies conducted in Pakistan. A study conducted in Pakistan reported an 8.89% prevalence of ASB among pregnant females presented at IYB Headquarters Hospital Attock, Pakistan[11]. This result was slightly lower than our findings. The findings were somehow closer to another study conducted in Ethiopia where the prevalence of ASB among pregnant females was 16.9%[12]. Another study conducted in Bangladesh reported that the prevalence of ASB during pregnancy was 16.5%[13]. The same findings can be observed in another study conducted in Ethiopia where the prevalence of ASB was reported as 16.1%[14]. These studies showed the prevalence rate of ASB was slightly higher than our study. Another study in the literature reported that the prevalence was 11.5%[15]. As opposed to our results, some studies showed a prevalence rate between 4.3% and 4.8% during pregnancy.[16,17] In a study carried out in Turkey, the incidence rate of ASB in pregnant women was reported to be 8.5%[14]while the prevalence rate of ASB in pregnant women ranged from 2.5% to 10%. Similar to our findings research conducted in India has reported the prevalence of ASB as 13.2%.[3] A retrospective randomized study carried out in Israel reported the incidence of ASB as low as 2.5% among the screened 199,093 pregnant women.[18]

Most of the women diagnosed with ASB visited during the 2nd and 3rd trimesters in the present study. Similar was the case in Bulgaria where 65 women were screened with a difference in mean-age i.e., 31.3 years.[19] In our study the common age group was 20-30 years while the mean age group was reported as 28.2 and 25.33 in other studies that supported our findings.[20,21]

E. coli has been observed as the strong pathogen identified from cultural examination of urine in the present study This pathogen had also been reported in many other types of research. In one such study, *E. coli* was identified in 58.9% of cases with an incidence rate of 2.5%[18]. Another screening test isolated *E. coli* in 76.6 of the ASB cases[14]. Another study conducted in India found that *E. coli* was the most dominant and usual isolate[22,23]. In addition to *E. coli*, another dominant pathogen isolated from the urine sample in our study was *Klebsiella pneumonia* and *Streptococci*. Another study conducted in Ethiopia also observed *E. coli* as the predominant among all pathogens followed by *Staphylococcus aureus*[12]. These pathogens were also observed as dominant bacteria in large-scale studies with a low incidence rate of ASB.[14,19] Another study also observed *E. coli* as the dominant pathogen among all followed by *Staphylococcus aureus.* The study observed *E. coli* in 43.75% and the second most prevalent *Staphylococcus aureus* at *31.25%*[11] Study also concluded that there exists a prominent difference in the dominance of pathogens liable for ASB from place to place indicating the importance of urine culture to support in identifying the exact correct causative organism.[11]

Many pathogens isolated in urine have been found to be sensitive to antibiotic treatment in the present study. Screening at early stages would give useful grounds to the antibiotic treatment[1]. Some studies strongly recommended screening at an early stage of pregnancy or at the first prenatal visit at a medical center.[21] A routine screening was also suggested in those regions where the incidence rate was higher than normal.[23]

CONCLUSION:

A cross-sectional study, carried out at Gynaecology and Obstetrics Outpatient Department comprised 0–30-year-old pregnant women, most of whom were literate and belong

to a low socioeconomic class. Most of these women visited the antennal clinic in the 2nd and 3rd trimesters. The prevalence rate of ASB was found to be 13.2%. Maternal and medical history was not a significant factor for ASB. Through urine cultural examination, *E. coli* was found as the most significant pathogen followed by *Klebsiella pneumonia* and *Staphylococci.* Antibiotics such as Ampicillin, Amoxiclav, Norfloxacin, and Piperacillin/Tazobactam resistance were tested for these urinary pathogens. *Klebsiella pneumonia* was highly resistant to Ampicillin while *E. coli* had maximum resistance to Cefotaxime.

Authors Contribution:
Sana Noor: Literature search, questionnaire design, data collection and compilation
Ejaz Mahmood: Conceived the idea, Study design and concept, and Supervision
Noor Shahid: Data analysis and interpretation, manuscript writing
Arooj ul Hassan: Co-supervised the research work
Saba Noor: Data collection and compilation, Research collaboration

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