ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Asymptomatic Bacteriuria in pregnant women attending a tertiary hospital in northern India: prevalence, risk factors, causative organisms and antimicrobial sensitivity pattern

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Submission: 11-05-2021 Revision: 11-08-2021 Publication: 01-09-2021

ABSTRACT

Background: Asymptomatic bacteriuria is common and can lead to adverse foetal and maternal outcomes. **Aims and Objective:** The current study aimed to estimate the prevalence of asymptomatic bacteriuria (ABU), its associated risk factors, bacterial isolates and antimicrobial sensitivity pattern in pregnant women attending Outpatient department (services in a tertiary hospital in India. **Materials and Methods:** This was a hospital-based cross-sectional study among asymptomatic women coming for routine antenatal check-ups to obstetrics OPD of a teaching hospital in Northern India. Samples were collected, processed and antimicrobial sensitivity done as per Clinical and Laboratory Standards Institute (CLSI) guidelines. Data was analysed and p value below 0.05 was considered as statistically significant. **Results:** Overall 247 pregnant women were included in the study with a mean age of 25.9 ± 3.1. The overall prevalence of asymptomatic bacteriuria was 18.6%. The most common isolates responsible for ABU were E. Coli (48%), S Aureus (23%), K. pneumonia (12%), Pseudomonas (6%), Enterococcus (6%), Proteus (5%). Gram-negative isolates were mostly sensitive to Fosfomycin, Meropenem, Piperacillin + Tazobactum whereas gram-positive isolates were usually sensitive to Fosfomycin, Vancomycin and Linezolid Most isolates were resistant to Co-amoxiclav, Ciprofloxacin, and Nitrofurantoin. **Conclusion:** Considering the high prevalence of ABU and its association with adverse maternal and foetal outcomes, urine culture should be included in routine investigations being offered to pregnant women. Gram-negative bacteria were the primary causative agents with Fosfomycin, Meropenem and Ceftazidime showing high level of efficacy against the pathogens.

Key words: Antibiotics; Bacteriuria; Culture; Fosfomycin; Sensitivity

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v12i9.37039

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Asymptomatic bacteriuria (ABU) is defined as the presence of bacteria in the urine of a person without signs or symptoms of a urinary tract infection.[1] As the person is asymptomatic, asymptomatic bacteriuria can only be diagnosed by urine cultures. Laboratory criteria for its diagnosis are colony forming units (CFU) of 100,000 per ml of a midstream clean catch urine sample.[2,3] Current guidelines do not recommend routine screening for asymptomatic bacteriuria as it has not been associated with an increase in morbidity or mortality in general population. Pregnant women form an important exception in which untreated asymptomatic bacteriuria can cause adverse maternal and foetal outcomes.[4] ABU has been associated with acute pyelonephritis in pregnant women with a number of studies finding increased risk of premature births, low birth weight or both. Higher prevalence, as well as higher risk of morbidity due to ABU in pregnancy can be related to the hormonal, anatomical, mechanical and immunological changes associated with the pregnancy.[5] In view of these dangers screening for ABU and prompt

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treatment of pregnant women with ABU is a standard practice in antenatal care.

The current study was planned to estimate the prevalence of ABU, its risk factors, microbiological profile and antibiotic sensitivity profile of bacteria associated with ABU. The results from this study can guide in decision making related to screening for ABU and also guide in the selection of proper antibiotics.

The objectives of this study were to estimate the prevalence of ABU, its associated risk factors, microbiological profile and antibiotic sensitivity profile in pregnant women attending ante-natal OPD in a tertiary care hospital.

MATERIALS AND METHODS

Study design, setting and area

The current study was a cross-sectional study conducted among ante-natal women attending an obstetric clinic at a teaching hospital in Haryana state of northern India. The hospital has a high footfall for OPD services with a large number of patients visiting the hospital for routine antenatal services. The routine antenatal services are provided by residents and faculty from the department of gynecology and obstetrics.

Study participants

All pregnant women who came for an antenatal check-up between January 2016 to April 2016 were approached and explained about the purpose of the study and their consent sought for participation in the study. Women with symptoms of UTI, fever and women with history of urolithiasis, urological surgery urogenital fistula were excluded from the study. In addition women who were currently taking antimicrobials or had taken antimicrobials in last two weeks were excluded from the study. Only women who provided informed consent were included in the study. A pretested, self-administered schedule was used to collect socio-demographic information, risk factors, h/o gestational diabetes, h/o hypertension, previous and current obstetric history and previous medical/surgical history. Following the completion of the questionnaire, each subject was explained about the process for collection of a urine sample. The subjects were directed towards a female washroom with the provision for handwashing to avoid contamination of samples.

Collection of urine samples

Each pregnant woman was provided with a sterile and labelled screw capped collection vial. Process of sample collection was explained to reduce chances of contamination. 10-15 ml of midstream urine sample was collected. The samples were processed within 1-2 hours of collection for analysis. A routine microscopy was not performed and the samples were directly processed for culture and sensitivity.

Processing and isolation of samples

Urine samples were inoculated and streaked with the help of heat flamed standard wire loop (delivering 0.001 ml) on the culture plate. The culture media used for isolation were cysteine-Lactose Electrolyte-Deficient, blood and chocolate agar plates. The plates were incubated aerobically at 37c for 24 hrs and then examined. Plates with significant growth (at least 100.000 CFU/ml) were considered to be significant and further analysed for microbial identification and drug sensitivity. After incubation, subcultures and biochemical tests on MacConkey agar, Mannitol salt agar and 5% sheep blood agar were done for identification. Repeat cultures were not performed for samples with significant growth.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using Kirby-Bauer (KB) disk diffusion test and interpreted using CLSI and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.[6,7,8] The inoculated culture plates were left at room temperature and disks impregnated with Nitrofurantoin, Fosfomycin, Co-amoxiclav, Ciprofloxacin, Ceftazidime, Piperacillin + Tazobactum, Meropenem, Amikacin, Vancomycin, Linezolid, Penicillin. The culture plates were then inoculated for 24 hours at 37 degrees. They were classified as susceptible and resistant by measurement of inhibition zones using rulers and as per CLSI guidelines.

Statistical methods

Data was first entered in Microsoft excel and then exported to SPSS for analysis. Data was summarized using frequency tables and cross tabs. p value below 0.05 was considered statistically significant.

RESULTS

Socio-demographic characteristics

A total of 247 pregnant women without signs and symptoms of UTI were included in the study. The age of subjects ranged from 19 years to 34 years with a mean age of 25.9 ± 3.1. Almost 62% of participants belonged to rural areas. Almost 1/3rd of participants worked as farmers and another 1/3rd were home makers. Highest proportion of participants belonged to socio-economic class 1 and 2.[9] Half of the participants were in third trimester of their pregnancy and half of the study participants were anaemic (Hb level less than 11g/dl). The details are depicted in Table 1.

Of the study participants, 46 (18.6%) had significant Bacteriuria. Among these one urine sample (2.1%) showed mixed bacterial growth with the rest demonstrating single bacterial growth.

Gram-negative bacteria were the predominant organism. The most common isolated organism was E. coli which contributed to 48% of isolates. Among gram-negative organisms, it was followed by K. pneumonia, Pseudomonas aeruginosa and Proteus mirabilis which contributed to 12.5%, 6.2% and 4% isolates respectively. Gram positive organisms contributed to 29% of isolates with staphylococcus aureus being the most common organism followed by Enterococcus faecalis.

Antimicrobial sensitivity of Gram-negative isolates

In this study, Gram negative isolates were sensitive to Fosfomycin, Meropenem, Piperacillin + Tazobactum. These were mostly resistant to Co-amoxiclav, Ciprofloxacin. Drug sensitivity profiles of individual bacteria are depicted in Table 2.

Antimicrobial sensitivity of Gram-positive isolates

For Gram positive isolates which were mostly contributed by S. Aureus, the isolates were mostly resistant to Nitrofurantoin, Co-amoxiclav, Ciprofloxacin, and Penicillin. The isolates were mostly sensitive to Fosfomycin, Vancomycin and Linezolid. Drug sensitivity profiles of individual bacteria are depicted in Table 2.

DISCUSSION

Appropriate diagnoses and management of ABU is important as untreated ABU can lead to adverse maternal and foetal outcomes. In this study the prevalence of ABU was estimated at 18.6%. the results are comparable to few studies

Table 1: Depicting relation of various factors with prevalence of ABU

Variables	Positive No	Negative No	Total No	% Positive	P Value
ABU	46	201	247	18.6	
Age					
19-22	8	39	47	17.0	*X*2= 0.162
23-26	17	74	91	18.7	*p* = .098
27-30	15	65	80	18.5	
31-34	6	23	29	21.4	
Hb Level					
Normal	19	97	116	16.4	*X*2= 0.727
Anaemia	27	104	131	20.6	*p* = .394
Parity					
Nulliparous	14	84	98	14.3	*X*2= 2.19
Primiparous	19	74	93	20.4	*p* = .333
Multi	13	43	56	23.2	
Gestational period					
1st	6	39	45	13.3	*X*2= 1.11
2nd	14	61	75	18.7	*p* = .571
3rd	26	101	127	20.5	
Education					
Illiterate	12	52	64	18.8	*X*2= 0.021
Literate	5	21	26	19.2	*p* = .999
Primary	17	75	92	18.5	
Secondary	7	30	37	18.9	
Higher education	5	23	28	17.9	
Residence					
Rural	32	121	153	20.9	*p* = .237
Urban	14	80	94	14.9	
Occupation					
Farmer	21	73	94	22.3	*X*2= 0.727
Home maker	13	67	80	16.3	*p* = .394
Salaried (organized sector)	5	26	31	16.1	
Salaried (un-organized sector)	7	35	42	16.7	
Socioeconomic status					
(low) 1	19	69	88	21.6	*X*2= 1.63
2	16	65	81	19.8	*p* = .651
3	6	36	42	14.3	
4	5	31	36	13.9	
H/O of UTI					
Yes	12	27	39	30.7	*P = 0.04*
No	34	174	208	16.3	
H/O catheterization					
Yes	14	34	48	41.1	*X*2= 4.3
NO	32	167	199	16.0	*p* = .03

Table 2: Table depicting antimicrobial sensitivity of microbial isolates

Bacterial isolates	No. of strains sensitive to antibiotics (%)								
Gram negative	**No**	**NIT**	**F0**	**AMC**	**CIP**	**CTZ**	**PIT**	**MRP**	**AK**
E. coli	23	87	91	52	52	78	87	83	78
K. Pneumoniae	6	67	83	33	33	67	83	67	83
P. Aeruginosa	3	66	100	33	33	100	100	66	66
Proteus	2	0	100	50	0	100	100	100	50
Total	34								
Gram positive	**No.**	**NIT**	**FO**	**AC**	**CF**	**VM**	**LZ**	**PE**	
S. Aureus	11	64	91	54	36	82	100	18	
Enterococcus	3	100	100	100	0	100	100	66	
Total	14								

Nitrofurantoin (NIT), Fosfomycin (FO), Co-amoxiclav (AMC), Ciprofloxacin (CIP), Ceftazidime (CTZ, Piperacillin + Tazobactum (PIT), Meropenem (MRP), Amikacin (AK),), Co-Amoxiclav(AC), Cefoxitin (CF),, Vancomycin (VM), Linezolid (LZ), Penicillin (PE)

done in north India.[10,11] Though the prevalence estimated is higher than few studies conducted in India which may be due to differences in composition of the population being catered to by this hospital.[12,13] In the current study, ABU was not found to have a statistically significant relation with age, haemoglobin level, parity, gestational period, education, residence or socioeconomic status even though different studies have found an association with some of these factors. This could be due to differences in population characteristics in terms of education and hygiene.

Asymptomatic bacteriuria was found to be significantly related with a previous history of urinary tract infection and catheterization. The same finding has been found by multiple other studies.[14,15] This finding reinforces the need for ensuring that all aseptic precautions are followed during catheterization, particularly during childbirth. Though there was no significant association with the parity of women which could be due to small sample size for identifying any relation with parity.

Gram-negative bacteria mostly contributed by E Coli were the predominant organisms which contributed to 70% of isolates. The bacteria responsible for ABU are primarily of faecal origins which colonize the peri-urethral area. This finding is similar to multiple other studies as most studies have found E. Coli to be the most common pathogen responsible for ABU.[12,16,17] The second most common pathogen responsible for ABU in our study was S. Aureus which has also been identified in multiple studies.[14,18] Among gram-negative organisms, it was followed by K. pneumonia, Pseudomonas and Proteus which contributed to 12.5%, 6.2% and 4% isolates respectively. Overall Gram-positive organisms contributed to 29% with Enterococcus contributed to the rest of gram-positive isolates.

Sensitivity to antimicrobials

In this study, gram-negative isolates were mostly sensitive to Fosfomycin, Meropenem, Piperacillin + Tazobactum. These were mostly resistant to Co-amoxiclav, Ciprofloxacin and Nitrofurantoin. Around 2/3rd of gram negative isolated were sensitive to cotrimoxazole. This is similar to what has been found in multiple other studies. This can also be due the fact that these antibiotics are commonly prescribed over the counter drugs in India.

For gram positive isolates which were mostly contributed by S. Aureus, the isolates were mostly resistant to Nitrofurantoin, Co-amoxiclav, Cefoxitin, and Penicillin. The isolates were mostly sensitive to Fosfomycin, Vancomycin and Linezolid. Resistance to cefoxitin was used as a maker for Methicillin Resistant Staphylococcus Aureus (MRSA). Around 2/3rd of isolates were to Cefoxitin resistant. Development of drug resistance for infections related to pregnancy is a grave problem as it further reduces the available options which are already reduced due to pregnancy.

In conclusion, the overall prevalence of ABU in our study was 18.6%, the most common agent for ABU was E. Coli followed by S Aureus. Gram-negative isolates were mostly resistant to Co-Amoxiclav, Ciprofloxacin and Nitrofurantoin whereas Gram-positive isolates were mostly resistant to Nitrofurantoin, Co-Amoxiclav, Ciprofloxacin, and Penicillin. Bost groups were mostly sensitive to Fosfomycin and Piperacillin + Tazobactum.

Recommendations

Considering the high prevalence of ABU and the fact that untreated cases can have adverse maternal and foetal outcomes, urine culture should be included in the routine investigations being offered to pregnant women. Further studies can be conducted to identify the best time for conducting routine urine cultures in pregnant women.

Limitations of the study

The study subjects mostly belonged to rural areas so the findings cannot be extrapolated to urban populations and non-agrarian groups.

Ethics statement

All the subjects who had significant bacteriuria were contacted and explained the result and were advocated to consult their treating doctor.

ACKNOWLEDGMENT

The authors would like to thank the whole staff from the department of microbiology and OBGY for their support in the study.

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Source of Funding: None, **Conflict of interest:** None.