European Journal of Molecular & Clinical Medicine

ISSN2515-8260 Volume 10, Issue 02, 2023

Original Research Article

ASYMPTOMATIC BACTERIURIA DURING PREGNANCY IN SOUTH INDIAN POPULATION

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Abstract:

Background and Objectives: Asymptomatic bacteriuria (ASB) is common during pregnancy and must be identified and treated to prevent poor maternal and obstetric outcomes. This study aims to determine the prevalence of asymptomatic bacteriuria among pregnant women in our antenatal clinic. The study also looks at any associated factors predisposing to the development of ASB, to identify the causative pathogens and their antibiotic susceptibility profile. **Methods:** It is a hospital based observational study involving 100 pregnant women with no symptoms of UTI at various gestational age. ASB was identified by urine culture and sensitivity studies. **Results:** 15% of the participants were found to have ASB. There was no significant difference in the prevalence of ASB based on age groups, number of pregnancies, gestational age or presence of anemia. Gram negative organisms were the cause of ASB in two thirds of cases. Escherichia coli is the most common isolate followed by Staphylococci. Gentamycin, cefotaxime and nitrofurantoin were the most efficacious of the antibiotics studied. **Conclusion:** ASB is quite prevalent in the pregnant population. E.coli continues to be the leading cause of ASB over the decades but Gram positive organisms are increasingly being recognized as pathogens responsible for ASB during pregnancy. Antibiotic susceptibility pattern differ widely among different study populations and antibiotic stewardship is a must for appropriate treatment and to prevent resistance development.

Keywords: Escherichia coli, Maternal, antibiotic, obstetric outcomes, ASB.

ISSN2515-8260 Volume 10, Issue 02, 2023

Introduction:

Urinary tract infections (UTI) are among the most prevalent bacterial infections. It is probably second only to bacterial vaginosis. Urinary tract infections may be asymptomatic or symptomatic. Asymptomatic bacteriuria is the presence of 10^5 CFU/ml of clean catch midstream urine in a woman who have no symptoms of UTI.(1,2) It is as prevalent during pregnancy as in general population but carries a higher risk of developing complications. It can be harmful to both mother (anemia, cystitis, pyelonephritis, sepsis) and to the fetus (prematurity, intrauterine growth retardation and low birth weight).(3,4) Asymptomatic bacteriuria is not generally treated except in pregnant woman and those undergoing some specific urinary tract manipulation. Routine screening and treatment of asymptomatic bacteriuria reduces the development of complications like pyelonephritis (0.3-0.57% vs 1-2%).(5) In females, short urethral length is the predisposing factor, while anatomical & hormonal changes and sexual activity are the precipitating factors for development of urinary tract infections. Low socio-economic status, multi-parity, diabetes, previous UTI and altered anatomy are risk factors.(6)ACOG recommends screening urine cultures during first ante-natal visit and again in the third trimester of pregnancy.(7) Screening urine cultures are cost effective also. Alternative faster and cheaper methods of detecting UTI like urine microscopy, urine Gram staining, dipsticks for leucocyte esterase/nitrites have high false negativity and poor positive predictive value.(8)The current study was conducted to find how common asymptomatic bacteriuria was among pregnant woman in antenatal clinics, to identify the associated risk factors, causative pathogens and their antibiotic susceptibility pattern in our region.

Material and Methods:

This was a hospital based observational study carried out in the Department of Obstetrics and Gynaecology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India, between November 2021 and October 2022.

Sample size calculated assuming the prevalence of asymptomatic bacteriuria at 7% of pregnant population with precision/absolute error of 5% and type 1 error of 5% was 99. Participants were recruited by non-random sampling method.

Institutional ethics committee approved the study. All participating patients provided written informed consent. Pregnant women attending antenatal clinics and not having any symptoms of UTI (dysuria, increased frequency, fever,loin pain or hematuria) were included. Pregnant women with UTI symptoms, history of any urinary tract abnormalities or manipulation, use of antibiotics in the last one week were excluded. During their initial antenatal appointment they were assessed with a detailed medical history, clinical examination and routine biomedical tests including complete urine examination and urine culture. Patients gently cleansed the genital region and a clean catch midstream urine sample was collected in a sterile wide mouthed container taking care not to contaminate the inner aspect of container. Urine samples were plated using traditional loop (0.002ml) onto MacConkey agar and Blood agar plates by surface streak method for semi-quantitative cultures. Culture plates were incubated at 37^oC. They were inspected for growth overnight. In the presence of growth, the number of colonies were manually counted and the colony forming units (CFUs) were multiplied by 500 to determine the number of CFUs per milliliter of urine. A count more than 10^5 organisms per milliliter was considered to be significant.

Cultures were reported negative if there was no growth or if the number of colonies were less than 10^5 CFUs per milliliter or less than 10^2 CFUs for Staphylococcus aureus. Growth of two or more different types of organisms was considered contamination. The isolates were assessed for their anti-microbial susceptibility using Kirby-Bauer method. Antibiotic sensitivity or resistance was determined in accordance with the Clinical Laboratory Standard Institute guidelines. Women with positive cultures received therapy and followed up for cure. Statistical analysis was done using SPSS version 25. Chi square test was used for statistical analysis. P value less than 0.05 was considered significant.

Results:

A total of 100 asymptomatic pregnant women participated in the study. The mean age of the study population was 24.53 years (SD ±3.38). 84% of them were between 21-30 years. Most of them were primigravida (45%). Of the remaining 55, 31 were in their second pregnancy. 17 were in the first trimester of pregnancy (upto 12weeks), 49 were in second trimester (12-28 weeks) and 34 in the final trimester (>28 weeks).(Table 1)

15 of the 100 women had asymptomatic bacteriuria. Most cases of asymptomatic bacteriuria (13) occurred in the age group of 21 to 30 years. The prevalence of ASB was 7.7%, 15.5% and 33.3% in the <20y, 21-30y and >30y age groups respectively.However this difference was not statistically significant (Chi square test 1.35; P-value 0.509). Culture positivity rate was 8.9%, 16.1%, 29.4% and 14.3% in first, second, third and fourth gravida women respectively and there was no significant difference in the ASB prevalence in different gravida (Chi square test 4.121; P-value 0.249). The prevalence of ASB was similar in all trimesters of pregnancy (5.9%, 22.4% and 8.8% in 1^{st}, 2^{nd} and 3^{rd} trimesters respectively; Chi square test 4.258 & P value 0.119).The mean hemoglobin levels were 10.2g/dl(±1.4) and 10.8g/dl(1.6) among women with ASB and those without (P=0.19). (Table 2)

Table 1

Age	**Frequency**
≤ 20	13
21-30	84
≥ 30	3
Gravida	
1	45
2	31
3	17
4	7
Trimester	
1	17
2	49
3	34

Table 2

	Culture			
	Positive	Negative	Chi square	P-value
Age				
≤ 20	1 (7.7%)	12 (92.3%)	2.148	0.709
21-30	13 (15.5%)	71 (84.5%)		
≥ 30	1 (33.3%)	2 (66.7%)		
Gravida				
1	4 (8.9%)	41 (91.1%)	4.121	0.249
2	5 (16.1%)	26 (83.9%)		
3	5 (29.4%)	12 (70.6%)		
4	1 (14.3%)	6 (85.7%)		
Trimester				
1	1 (5.9%)	16 (94.1%)	4.258	0.119
2	11 (22.4%)	38 (77.6%)		
3	3 (8.8%)	31 (91.2%)		
Hemoglobin				
	10.2(±1.4)	10.8(±1.6)		0.19

Of the 15 positive cultures, 10 were Gram negative bacilli and 5 were Gram positive cocci. E.coli was the most common isolate in the urine cultures (5;33.3%). Klebsiella pneumonia and Staphylococcus saprophyticus were isolated in 3 (20%) samples each and Pseudomonas aeruginosa & Staphylococcus aureus in 2 (13.3%) samples each (Table 3). There was no predominance of any type of pathogens with respect to age, gravidity, trimester of pregnancy, socioeconomic status or anemia.

Table 3: Organisms cultured

Organisms	**Frequency**	**Percentage**
Gram positive	5	33.3
Gram negative	10	66.6
Escherichia coli	5	33.3
Klebsiella pneumonia	3	20
Pseudomonas aeruginosa	2	13.3
Staphylococcus aureus	2	13.3
Staphylococcus saprophyticus	3	20

All the culture isolates were sensitive to gentamycin. Cefotaxime was the next most effective antibiotic with 80% of E.coli, 66.7% of K.pneumoniae and S.saprophyticus and 100% of P.aeruginosa and S.aureus being sensitive. Sensitivity to Cotrimoxazole was as follows: E.coli 80%, K.pnuemoniae 66.7%, P.aeruginosa 50%, S.aureus 50% and S.saprophyticus 66.7%. Cephalexin sensitivity was 40%, 33.3%, 0%, 50% and 33.3% among E.coli , K.pnuemoniae, P.aeruginosa, S.aureus and S.saprophyticus respectively. 40% of E.coli, 33.3% of K.pneumoniae and S.saprophyticus, 50% of S.aureus and none of the isolates of P.aeruginosa were susceptible to ceftriaxone. For nitrofurantoin, sensitivity was observed in 20% e.coli, 33.3% K.pneumoniae, 50% P.aeruginosa and none of S.aureus and S.saprophyticus isolates (Table 4).

Table 4: Antibiotic sensitivity of isolated organisms

Antibiotic / Organism	E.coli	K.pneumoniae	P.aeruginosa	S.aureus	S.saprophyticus
Gentamycin	5 (100%)	3 (100%)	2 (100%)	2 (100%)	3 (100%)
Cefotaxime	4 (80%)	2 (66.7%)	2 (100%)	2 (100%)	2 (66.7%)
Cotrimoxazole	4 (80%)	2 (66.7%)	1 (50%)	1 (50%)	2 (66.7%)
Nitrofurantoin	3 (60%)	2 (66.7%)	1 (50%)	1 (50%)	2 (66.7%)
Cephalexin	2 (40%)	1 (33.3%)	0 (0%)	1 (50%)	1 (33.3%)
Ceftriaxone	1 (20%)	1 (33.3%)	1 (50%)	0 (0%)	0 (0%)

Discussion:

Urinary tract infections are one of the most common infections in female population. It has the potential to cause serious adverse effect on pregnancy outcomes. So it has been recommended that all pregnant women be screened for evidence of urinary tract infection – whether symptomatic or not. Any pregnant woman with asymptomatic bacteriuria also needs to be treated with appropriate antibiotics. The burden of ASB has been reported from a low of 5-7% to as high as 45-68%.(9–11)During the course of the study, ASB was found in 15% of pregnant women attending antenatal care clinics at our center. This prevalence rate is higher than that reported in western studies and many Indian studies but lower than reported from many African countries.The nutritional and hygiene status of the pregnant women probably influence the prevalence of ASB.

The prevalence of ASB was higher with older age groups. Also, the presence of ASB was higher in multiparous women (not statistically significant).Chandel et al also reported higher ASB in older women but others have found ASB to be higher in teenage pregnancies.(11,12) Older women tend to be multiparous and multiparity has been reported to be a risk factor for ASB.(13) Second trimester pregnant women had more ASB (not statistically significant).But otherstudies have found first trimester to be a high risk period.(14,15) Overall it appears that there is no uniform pattern of ASB occurrence and the entire pregnancy period is a high risk period. So it is prudent that pregnant women be screened for ASB at their first visit and again later in the pregnancy.

In this study there was no significant difference in hemoglobin levels between those with ASB and those without. Enayat K et al found anemia to be a significant factor associated with ASB with an odds ratio of 9.4. Anemia here is a surrogate marker of overall nutritional deficiency and susceptibility to infections. It is worth noting that the mean hemoglobin levels in our study population was significantly lower than that reported by Enayat K in their study. The overall poor nutritional status might have masked the association between anemia and ASB in our study.(16) Presence of diabetes is also identified as a risk factor for the development of ASB during pregnancy. However there were no patients with gestational diabetes in the present study population.

Gram negative organisms were the leading cause of ASB accounting for two third of isolates. The major organism isolated in this study was E.coli (a third of all the isolates and half of Gram negative organisms). Staphylococci organisms (saprophyticus and aureus) were the next major pathogens responsible for ASB during pregnancy. K.pneumoniae and P.aeruginosa were the other significant isolates. E.coli has remained the leading cause of ASB over the decades as it is one of the GI commensal and the proximity of anal canal and urethral orifice in the perineum allows its easy access. Gram negative organisms are responsible for 75 to 95% of uncomplicated UTIs in young, sexually active non-pregnant women but Gram positive organisms especially S.saprophyticus are increasingly becoming the reason in pregnant women.(17,18)

The susceptibility of the isolated organisms to antibiotics shows that gentamycin was the most effective agent with all the organisms being susceptible. Aminoglycosides can theoretically cause ototoxicity and nephrotoxicity. A large Hungarian study did not show any association between gentamycin exposure during pregnancy and adverse maternal outcomes or fetal structural abnormalities.(19) Gentamycin has the largest available documented evidence for use during pregnancy and Gentamycin may be used during pregnancy if benefits to mother exceeds the risk. Cefotaxime was the next most effective antibiotic with 80% of organisms being susceptible. It was effective against 80% of Gram negative organisms and 80% of Gram positive organisms. Cotrimoxazole and Nitrofurantoin were the next most effective antibiotics with roughly two thirds of the organisms being susceptible. Ceftriaxone was the least effective with 80% of isolates being resistant. Guidelines suggest that all pregnant women with ASB should be treated with antibiotics to prevent adverse effects to mother and fetus.Antibiotic resistance pattern has to be studied at each locale and appropriate ones should be used. Nitrofurantoin is one of the most commonly used antibiotic for ASB and UTI. Other studies have also shown nitrofurantoin to be very effective against both Gram positive and Gram negative organisms. Given its safety during pregnancy, nitrofurantoin is probably the best first line antibiotic to treat ASB. Resistance pattern to beta lactam antibiotics are variable due to wide spread use and development of betalactamases, drug efflux pumps or alteration in the penicillin binding sites. If susceptible strain is isolated, beta-lactams are another safe group of antibiotics to be used during pregnancy. Cotrimoxazole is an anti-metabolite acting by inhibiting dihydrofolate reductase and dihydropteroate synthetase enzymes. Though it has less affinity to human enzymes, it crosses placental barrier and achieves fetal blood levels comparable to that of mother. Its use in early pregnancy can cause neural tube defects. Hence cotrimoxazole may be used only in exceptional conditions for treatment of ASB in pregnancy.

Conclusion:

ASB is quite prevalent in the pregnant population. E.coli continues to be the leading cause of ASB over the decades but Gram positive organisms are increasingly being recognized as pathogens responsible for ASB during pregnancy. Antibiotic susceptibility pattern differ widely among different study populations and antibiotic stewardship is a must for appropriate treatment and to prevent resistance development.

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