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RESEARCH ARTICLE

A clinical study on asymptomatic bacteriuria in pregnant women

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ABSTRACT

Background: Asymptomatic bacteriuria (ASB) is very common in pregnancy, the prevalence being around 2-10% of all pregnancies. Pregnant women have a higher risk of urinary tract infection (UTI) compared to the general population due to the multiple structural and functional changes which occur in the renal system during pregnancy. **Objectives:** The present study has been undertaken to see the prevalence of asymptomatic bacteriuria, its causative microorganisms, their sensitivity to antibiotics and overall maternal outcome. **Materials and methods:** This was a cross-sectional observational hospital-based study done at our tertiary care centre from January 2018 to December 2018. The sample size chosen was 800 pregnant women. The infection detected was treated and followed up throughout the pregnancy. Details regarding gestational age at the time of delivery, mode of delivery and any other significant intrapartum events were noted. **Results:** In our study ASB is a common bacterial infection, complicating pregnancy with a high prevalence of 16.5%. The prevalence is more common in multigravida and women with anaemia and low socioeconomic status. ASB was found to be significantly associated with PPROM, preterm, anaemia and IUGR (P value < 0.05). In this study, gram-negative organisms (84%) were the most commonest isolated organism, and E Coli was isolated in 83 cases (63%). Meropenem and nitrofurantoin were found most sensitive antibacterial drugs. **Conclusion:** Early recognition and prompt antimicrobial treatment can reduce adverse maternal outcomes. Hence screening with urine culture and treatment with an antimicrobial agent according to sensitivity test should be incorporated as a routine in antenatal care.

Keywords: Asymptomatic bacteriuria, urine culture, antibiotic sensitivity, adverse maternal outcome.

Asymptomatic bacteriuria (ASB) is a condition where bacteriuria exits even when there are no symptoms or signs suggestive of acute urinary tract infection (UTI). Asymptomatic bacteriuria is alternatively defined as the growth of more than 1 lakh colonies of a single bacterial species per millilitre in a clean catch midstream urine sample obtained from a patient who has no urinary symptoms. In general, pregnant women have a higher risk of UTI compared to the general population due to the multiple structural and functional changes which occur in the renal system during pregnancy. The increase in asymptomatic bacteriuria also shows an increasing trend due to similar reasons. This can be explained by the elevation of hormones in the first trimester, mainly progesterone. Dilatation of the ureter, decrease in ureteric peristalsis and decrease in bladder tone are some significant changes which occur during pregnancy. Plasma volume elevation, glycosuria and aminoaciduria have a net result of a reduction in urine osmolality, which results in the reduction in the ability of the lower urinary tract resistance against pathogenic organisms, and resultant bacterial proliferation [1 - 4].

The prevalence of ASB has been reported to be 2-10% in various studies [1, 5]. The factors associated with ASB are extremes of age, multiparity, low socioeconomic state,

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illiteracy, previous history of UTI, and medical disorders like diabetes mellitus. PPROM (Premature preterm rupture of membrane), IUGR (Intrauterine growth restriction), preterm labour, anaemia, preeclampsia and pyelonephritis are all associated with ASB. However, it is a commonly overlooked condition, even though the ministry of health and family welfare mandates that urine examinations be done for all pregnancies. In this context, the present study has been undertaken to add information on the prevalence of asymptomatic bacteriuria, its causative microorganisms, their sensitivity to antibiotics, overall maternal outcome and associated clinical features.

Materials and methods

This prospective comparative observational hospital-based study was conducted at our tertiary care centre from January 2018 to December 2018 after obtaining approval from the institute ethics committee (IEC). Pregnant women presenting without any symptoms of UTI like dysuria, burning micturition, increased frequency of micturition, suprapubic discomfort, and fever was included. Those with pre-existing congenital acquired renal disorders and other chronic debilitating illnesses, documented intake of antibiotic therapy for the last 72hrs and frequent urethral catheterizations were excluded. Pregnant women satisfying the inclusion and exclusion criteria were recruited after obtaining their informed consent.

Detailed history including demographic, obstetric and medical history was noted. Complete general physical, systemic and obstetrical examinations were carried out, as per usual practice. Apart from routine antenatal investigations, urine culture was done (as mentioned below). Women with ASB were treated and followed up throughout the pregnancy. Details regarding gestational age at the time of delivery, mode of delivery and any other significant intrapartum events were noted.

Laboratory evaluation: Urine samples of about 20 ml were collected by standard clean catch mid-stream method in a sterile universal container after appropriate instructions. With labia held apart, midstream urine was collected in a sterile container and transported to the microbiology laboratory within one hour. In case of delay, the sample was refrigerated at 4^0 C for up to 24 hours.

The urine samples were observed macroscopically for their colour, turbidity and deposits; and then subjected to urine culture. A microscopic examination of urine was done for pus cells. All samples were cultured on blood agar, nutrient agar and Mac-Conkey agar plates. The culture plates were incubated at 37^0 C for 24-48 hours and colonies were counted on each plate. The number of CFU (colony forming units) was multiplied by 100 to determine the number of microorganisms per millilitre in the original specimen. Urine with more than 10^5 CFU/ml was considered to be significant. On the basis of colonial morphology and cultural characteristics, the isolates were further identified by gram staining. A battery of biochemical reactions using appropriate sugar and special tests were performed. An antimicrobial susceptibility test was performed using the Kirby-Bauer disc diffusion method. Mueller Hinton agar plates were used for antibiotic sensitivity tests. After the plates were dried, both suspensions of the organism were made and adjusted to Mcfarland's opacity factor of 0.5. A lawn culture was made over the surface of the media using a sterile swab, and then appropriate antibiotics discs were placed and incubated at 37 ^{0} C for 24 hours after which readings were taken. The zone of inhibition diameter was measured by the clinical laboratory standard institute (CSLI) sensitivity method.

Sample size calculation and study design: Based on the prevalence rate of asymptomatic bacteriuria in pregnant women from the Indian scientific literature at different gestational ages is around 10 % [5-9, 11]. This yielded a sample size of 757 with a power of 95% and an alpha error of 0.05 [10]. To account for attrition, the final sample size was set at 800. Data collected were tabulated in a Microsoft excel datasheet and SPSS version 22.0 software (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. The descriptive statistics were presented as frequencies and percentages. Comparisons were performed between two groups (those with ASB and those without ASB). The Mann-Whitney U test was used for nonparametric variables. The p-value < 0.05 was considered statistically significant.

Results

During the study period, 800 pregnant women were tested and 132 women were identified to be having ASB, giving rise to a prevalence of 132/800(16.5%). The demographic characteristics of the patients with ASB are shown in table-1. The majority (53%) of women were in the age group of 26-35 years and 72% belonged to low socioeconomic status. 83 women (63%) were multigravida and around half of the cases were included in the 3rd trimester.

In ASB group, 91% (120/132) had > 5 pus cells and only 9% (9/132) had ≤ 5 pus cells. In the control, group79% (94/132) had ≤ 5 pus cells and 21% (28/132) had >5 pus cells. In our study, the presence of pyuria defined as > 5 pus cells/HPF was significantly associated with asymptomatic

bacteriuria. Gram-negative organisms were the most commonly isolated group (84%). Among these, Ecoli was isolated in 63% (83/132), followed by Klebsiella species in 18% (24/132) and Staphylococcus species in 11% (15/132). Further details are shown in table 2. Our study did not show any polymicrobial infection.

Table 1: Demographic profile of women with ASB

Age	Number of cases	Percentage
< 26 years	50	38%
26 – 35 years	70	53%
> 35 years	12	09%
Socio-economic status		
Low	95	72%
High	37	28%
Parity		
Primigravida	49	37%
Multigravida	83	63%
Trimester		
First	29	22%
Second	37	28%
Third	66	50%

91% of samples were sensitive to meropenem, 77% sensitive to nitrofurantoin and 73% to ceftriaxone. Surprisingly, ampicillin and amoxicillin showed a lesser sensitivity of 19% (table 2).

The prevalence of anaemia in the ASB group was much higher than that of the control group (36% vs 20%) and the difference was statistically significant (p-value 0.006). The occurrence of PROM was much higher in the ASB group than in the control group (14% vs 4.5%) and the difference was statistically significant. The occurrence of preterm labour was much higher in the ASB group than in the control group (18% vs 7%) and the difference was statistically significant. The occurrence of IUGR was much higher in the ASB group than in the control group (14% vs 4.5%) and the difference was statistically significant. The occurrence of preeclampsia was similar in both groups (5% vs 3%). Though pyelonephritis was seen only in the ASB group - 4 patients (3%), there was no statistically significant difference between the groups (table 3).

Table 2: Bacterial isolate and drug sensitivity

Organisms (N =132)	No of isolates (%)	AM (%)	NF (%)	CT (%)	PT (%)	MR (%)
Escherichia coli	83	7	71	58	46	72
Klebsiella pneumonia	24	1	16	18	13	24
Saphylococcus aureus	15	12	8	9	14	14
Enterococci	5	5	3	3	3	5
Pseudomonas	2	0	0	2	2	2
Streptococcus sp	1	1	1	1	1	1
Proteus mirabilis	1	0	1	1	1	1
Acinetobacter	1	0	1	1	0	1

AM-Amoxycillin, NF-Nitrofurantoin, CT- Ceftriaxone, PT - Piperacillin + Tazobactam, MR - Meropenem

Table 3: Comparison of antenatal problems between patients with ASB and controls

Antenatal complications	Cases (with ASB) = 132 Number	Percentage	Controls = 132 Number	Percentage	P-value
Anaemia	47	36%	27	20%	0.006*
PPROM	19	14%	6	4.5%	0.006*
Preterm labour	23	18%	9	7%	0.008*
IUGR	18	14%	6	4.5%	0.01*
Preeclampsia	7	5%	4	3%	0.355
Pyelonephritis	4	3%	-	-	0.12

* Indicates statistically significant difference - p value <0.05

Discussion

Bacterial products initiate complex immunological, endocrinological and biochemical processes culminating in the adverse materno-fetal outcome. ASB during pregnancy has a high prevalence and if untreated can have serious implications like anaemia, preeclampsia, chorioamnionitis, pyelonephritis, PPROM, preterm labour, low birth weight, prematurity and perinatal death. Due to lack of symptoms ASB is often unrecognised unless screening is done. With early detection and prompt treatment above complications can be reduced.

The prevalence of ASB in the present study (16.5%) correlates with the study by Vaishali et al (17%). However, a slightly lower prevalence was seen in studies done by Prabhavathi V et al (11.33%) and Nkwabong Elie et al (7.8%) [11 - 13]. The differences in prevalence could be attributed to the lack of personal and environmental hygiene, low socioeconomic status and low educational status.

In the present study majority of women was multigravida (63%). This is similar to the previous studies done by Prabhavathi V et al (64.7%) and Aliasghar Farazi et al (92%) [12, 14]. Lakshmipriya et al (40.25%) have also shown similar results, suggesting that increasing gravidity increases the chance of ASB. This is probably due to increased colonization of the urinary tract by pathogens due to repeated catheterization in earlier pregnancies or previous infections [15].

In the present study, the majority of women were in the 3rd trimester (50%) on par with a study done by Saheed Shabat et al whereas a study done by Prabhavati et al showed the majority were in the second trimester (64.7%) [16,12]. This increased incidence of ASB in the third trimester is probably because of the anatomical and physiological changes related to advancing gestational age. This led to stasis of urine and encourage bacterial proliferation[15,17].

The microorganisms commonly isolated in our study were E coli (63%) which is found similar to studies done by Prabhavathi V et al (70.6%) and Nkwabong Elie et al (57.7%) [12, 13]. Uropathogenic E coli possess adherences that

help in adhering to the epithelial cells and hence preventing it from urine washing[19].

The sensitivity and resistance to antibiotics vary from one region to another and from hospital to hospital. This may be a consequence of the emergence of resistant strains as a result of the wide usage of antibiotics. In the present study, 91% of isolates were sensitive to meropenem, 77% were sensitive to nitrofurantoin and 73% to ceftriaxone. Lesser sensitivity of 19% was seen for ampicillin and amoxicillin. The same sensitivity pattern was seen in studies done by Girishbabu et al and Priscilla et al [20,21].

In the present study, anaemia was more common in the ASB group as compared to the control group (36% vs 20%). This is similar to the findings by Prabhavati et al (14.7%vs 4.5%)[12]. But a study done by Vaishali et al has not shown any causal relationship between ASB and anaemia[11]. Though we found a significant association in our study, it could not be established as etiopathogenesis of anaemia in the ASB group. As anaemia in pregnancy is multifactorial it could be due to low socioeconomic group, nutritional deficiency; malaria and hookworm infestation.

Due to the infections, bacterial enzymes such as collagenase may weaken the fetal membranes which can result in preterm premature rupture of membrane (PPROM). In our study, preterm premature rupture of membranes (PPROM) was statistically significant seen in ASB women as compared to the control group (14% vs 4.5%) and which correlated with another study done by Jain et al (26.2% vs 4.4%)[11]. PPROM is an accepted complication of ASB which leads to preterm labour, chorioamnionitis, endometritis, and fetomaternal sepsis ultimately leading to an adverse fetomaternal outcome [22].

In the present study, preterm labour was more common in women with ASB as compared to the control group (18% vs 7%) this was statistically significant. Premature uterine contractions were initiated in response to bacterial infection. There is a release of proinflammatory cytokines and prostaglandins which were secreted by maternal and fetal cells resulting in preterm labour.

The urinary infection produces sufficient inflammation in the uteroplacental unit leading to intrauterine growth retardation (IUGR). In the present study, IUGR was seen in 14% of patients with ASB and 4.5% of patients in the control group. Association between ASB and IUGR was statistically significant in our study which correlates with the study done by Vaishali Jain et al (23.4% vs 4.8%) [11]. Michael Bolton et al demonstrated in mice that localized cystitis induced robust cellular inflammatory response in uteroplacental tissue and there is a correlation between polymorphonuclear (PMN) infiltration and diminished fetal weight gain suggesting the presence of PMN may contribute to IUGR[23]. This emphasizes the need for early detection and aggressive treatment of ASB in pregnancy.

In our study, preeclampsia was seen in 5% of patients with ASB and 3% of patients in the control group. The association between ASB and preeclampsia was not statistically significant in our study which was in contrast with the studies done by Vaishali Jain et al (23.4 vs 4.8) and Prabhavathi et al (8.8% vs 2.3%)[11,12]. This higher incidence of preeclampsia in ASB women can be attributed to elevated maternal cytokines which cause an imbalance of Th1 and Th2 cells in the uteroplacental bed. This change from Th2 to Th1 will alter placental vascular endothelial function which in turn leads to preeclampsia [24, 25].

In the present study, pyelonephritis was seen in 3% of patients with ASB and none in the control group. Among the 4 patients who developed pyelonephritis, all had hydroureter / hydronephrosis. E coli and Klebsiella were the organisms isolated. The association between ASB and pyelonephritis was not statistically significant in our study which correlates with the study done by Vaishali Jain et al (1.7% vs 0%) [11]. Acute pyelonephritis during pregnancy may have serious complications. If ASB is left untreated then 25-40% of them will develop symptomatic UTI including pyelonephritis [22]. The predisposing factors like immunosuppression during pregnancy may decrease the ability to respond to the infection and physiological changes induced by pregnancy cause mechanical bladder compression and ureteral dilatation favour the proliferation and ascent of bacteria resulting in a 20-fold increased risk of pyelonephritis in pregnant women [25]. Though pyelonephritis is a proven, undebated complication of ASB, prompt treatment of ASB decreases the risk of pyelonephritis by 80-90% [27].

Conclusion

In our study ASB is a common bacterial infection, complicating pregnancy with a high prevalence of 16.5%. The prevalence is more common in multigravida and women with anaemia and low socioeconomic status. E coli is the common organism causing ASB and is sensitive to nitrofurantoin and meropenem. Nitrofurantoin is recommended in the treatment of ASB due to its high sensitivity, safety and ease of administration for use in pregnancy. If unrecognized and untreated, ASB leads to adverse maternal outcomes like anaemia, PROM, preterm delivery, IUGR, pre-eclampsia, pyelonephritis and adverse fetal outcomes like prematurity and low birth weight. All

these complications related to ASB could be reduced by early recognition and prompt antimicrobial treatment in pregnancy. Hence screening and treatment of ASB should be incorporated as a routine in antenatal care. Health education about personal hygiene should be emphasized to all pregnant women during their antenatal visits.

Conflict of interest: None. **Disclaimer:** Nil.

References

1. Kerure RD, Umashanker. Prevalence of asymptomatic bacteriuria among pregnant women in a tertiary care hospital. International Journal of Scientific and Research Publications. 2013; 3(11): 2250-3.
2. Belty A, Daniel FF, Alice SS, Wersfeld. Bailey & Scott's Diagnostic Microbiology. 12th edition. St Louis: Mosby; 1998. pp.556-80.
3. Cunningham FG, Leveno KJ, Bloom SL, Hauth J, Rouse DJ. Williams obstetrics. 24rd edition. New York: McGraw-Hill Companies; 2014. pp.1033
4. Imade PE, Izekor PE, Eghafona NO, Enabulele OI, Ophori E. Asymptomatic bacteriuria among pregnant women. N Am J Med Sci. 2010 Jun; 2(6): 263-6.
5. Sujatha R, Nawani M. Prevalence of asymptomatic bacteriuria and its antibacterial susceptibility pattern among pregnant women attending the antenatal clinic at kanpur, India. J Clin Diagn Res. 2014 Apr; 8(4): DC01-3.
6. Chandel LR, Kanga A, Thakur K, Mokta KK, Sood A, Chauhan S. Prevalance of pregnancy associated asymptomatic bacteriuria: a study done in a tertiary care hospital. J Obstet Gynaecol India. 2012 Oct; 62(5): 511-4.
7. Lavanya SV, Jogalakshmi D. Asymptomatic bacteriuria in antenatal women. Indian J Med Microbiol. 2002 Apr-Jun; 20(2):105-6.
8. Ankur G, Namita S, Sapna G, Anu P, Neha K, Daniya S, et al. Prevalence of asymptomatic urinary tract infections in the three trimesters of pregnancy. International Journal Current Microbiology and Applied Sciences. 2015; 1:110-7.
9. Jain SA, Pandya JM, Mehta SJ, Jain AG, Kikani KM, Pandya MR. Evaluation of asymptomatic bacteriuria in antenatal women at CU Shah Medical College and Hospital, Surendranagar, Gujarat. Int J Med Sci Public Health. 2013; 2:1022-24.
10. Goruntla N, Jampala S, Mallela V, Bandaru V, Thamineni R, Bhupalam P. Epidemiology and antibiotic sensitivity pattern of asymptomatic bacteriuria during pregnancy: A cross-sectional study. J Health Res Rev. 2019; 6: 5-10
11. Jain V, Das V, Agarwal A, Pandey A. Asymptomatic bacteriuria & obstetric outcome following treatment in early versus late pregnancy in north Indian women. Indian J Med Res. 2013 Apr;137(4):753-8.
12. Prabhavathi V, Krishnamma B, Krishna Murthy G, Prasad DKV. Prevalence of asymptomatic bacteriuria among antenatal women and its effects on maternal and perinatal outcome in northern Andhra Pradesh population. Int J Adv Med. 2018; 5:179-85.
13. Nkwabong E, Moustapha E, Fomulu NJ. Outcome of pregnancy complicated by asymptomatic bacteriuria. Gynecol Obstet (Sunnyvale). 2014; 4(259): 2161-0932.
14. Farazia A, Jabbariasl M. Asymptomatic bacteriuria in pregnancy in the central region of Iran: Frequency, risk factors, and causative organisms. Clinical Epidemiology and Global Health. 2019; 7: 309-12.
15. Lakshmipriya R, Raveendran SR, Chitralekha S, Menezes GA. Prevalence of Asymptomatic Bacteriuria during Second Trimester of Pregnancy With Respect To Parity. Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2013; 4(3):1316-21.
16. Saeed S, Tariq P. Symptomatic and asymptomatic urinary tract infections during pregnancy. International journal of microbiological research. 2011; 2(2): 101-4.
17. Pipkin FB. Maternal physiology. In: Edumunds DK (Ed). Dewhursts textbook of Obstetrics and Gynaecology. 7th edition. London: Black well publishing; 2007. pp. 10-18.
18. Luthje P, Brauner A. Virulence Factors of Uropathogenic E. coli and Their Interaction with the Host. Adv Microb Physiol. 2014; 65: 337-72.
19. Sheiner E, Mazor-Drey E, Levy A. Asymptomatic bacteriuria during pregnancy. Journal of Maternal- Fetal and Neonatal Medicine. 2009 May; 22(5): 423-7.
20. Girishbabu RJ, Srikrishna R, Ramesh ST. Asymptomatic bacteriuria in pregnancy. International journal of biological and medical research. 2011; 2(3):740-42.
21. Priscilla R, Latha G, Devaprasanna R, Munasira S. Prevalence and antimicrobial resistance pattern of bacterial strains isolated from patients with urinary tract infection. MOJ Public Health. 2017; 5(1): 32-5.
22. Smaill F. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane data base system review. 2001; 2: CD 000490.

23. Bolton M, Horvath Jr DJ, Li B, Cortado H, Newsom D, White P, et al. Intrauterine Growth Restriction Is a Direct Consequence of Localized Maternal Uro-pathogenic Escherichia coli Cystitis. PLoS ONE. 2012; 7(3): e33897.
24. Toldi G, Rigo J(Jr), Stenczer B, Vasarhelyi B, Molvarec A. Increased Prevalence of IL-17-Producing Peripheral Blood Lymphocytes in Pre-eclampsia. American journal of reproductive immunology. 2011 Sep; 66(3): 223-9.
25. Conde – Agudelo A, Villar J, Lindheimer M. Maternal infection and risk of preeclampsia. American journal of obstetrics and gynaecology. 2008 Jan; 198(1): 7-22.
26. Kim SJ, Parikh P, King AN, Marnach ML. Asymptomatic Bacteriuria in Pregnancy Complicated by Pyelonephritis Requiring Nephrectomy. Hindawi Case Reports in Obstetrics and Gynecology. 2018; Article ID 8924823.
27. Geerlings S. Asymptomatic Bacteriuria (ASB), Renal Function and Hypertension, Chronic Kidney Disease. 2012. Available from: https://www.intechopen. com/ books/chronic-kidney-disease/asymptomatic-bacteriuria-asb-renal-function-and-hypertension.

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