A STUDY ON THE PREVALENCE OF ASYMPTOMATIC BACTERIURIA AND THEIR ANTIBIOTGRAM PATTERN AMONG PREGNANT WOMEN IN A TERTIARY CARE HOSPITAL
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ABSTRACT: BACKGROUND: Asymptomatic bacteriuria (ASB) is common in pregnancy, if left untreated it may lead to adverse maternal and fetal complications like abortion, premature delivery and low birth weight. Early diagnosis and treatment have reduced the risk of pyelonephritis in pregnant women with ASB from 20-30% to 2-4% Increasing Resistance trends of uropathogens to commonly prescribed first line antibiotics has posed a great threat with limited therapeutic options. AIMS & OBJECTIVES: The present study was carried out to determine the prevalence of asymptomatic bacteriuria in pregnant women attending antenatal clinic of our tertiary care hospital and also to study the bacteriological profile and determine antimicrobial susceptibility pattern of the pathogens responsible for Asymptomatic Bacteriuria. SETTINGS & DESIGN: A Cross sectional study. METHODS & MATERIALS: Midstream urine samples from 281 pregnant women without urinary symptoms who attended antenatal clinic during March 2012 and March 2013 were included in this study. Samples were processed and isolates were identified as per the CLSI guidelines. Antibiotic susceptibility was done by Kirby bauer disk diffusion method. RESULTS: The overall prevalence of ASB was 13.87%. There was no significant association of ASB occurrence with respect to age [P>0.05]. A significant association with gravid status and trimester [P<0.001] was observed. Escherichia coli was the most predominant with total 26 [66.66%] followed by Staphylococcus aureus 6[15.38%], Klebsiella pneumoniae 5[12.82%] and CONS 2[5.13%]. Amoxicillin [96%], Norfloxacin [84%], ceftriaxone [89%] and Augmentin [94%] were found to be the most effective antibiotics against the uropathogens isolated. CONCLUSIONS: Our study revealed that Asymptomatic bacteriuria is not uncommon in our population studied. Keeping in view that screening, often prevents severe complications, we emphasize the need to include urine culture as a part of antenatal care in order to identify any unsuspecting infection. Increasing antibiotic resistance trends of ASB uropathogens indicate that it is imperative to rationalize the use of antibiotics. KEYWORDS: Asymptomatic bacteriuria, uropathogens.
ASB occurs in 2 - 10% of pregnancy, a similar prevalence as seen in non-pregnant women.[5]

However, pregnancy enhances the progression of asymptomatic to symptomatic bacteriuria, which could lead to symptomatic cystitis [30%] and pyelonephritis (up to 40 percent) in pregnant women. The smooth muscle relaxation and subsequent ureteral dilatation that accompany pregnancy are thought to facilitate the ascent of bacteria from the bladder to the kidney.

Successful treatment reduces the rate of subsequent UTI by 80-90 percent. Studies have also reported consistently a decrease in acute pyelonephritis later in pregnancy from 20-40% to 2-4% [6] of women who have been identified with asymptomatic bacteriuria in early pregnancy and treated. Pyelonephritis could lead to maternal and fetal complications like Low birth weight, preterm labour, pre-eclamptic toxemia and anemia of pregnancy.[7,5]

In view of close association of ASB with adverse maternal and fetal complications, plus the ability to avoid the significant consequences with effective treatment, the screening of pregnant women for bacteriuria have been recommended by various studies.

Prevalence rates show high degree of variations between studies depending on the ethnic and socioeconomic mix.[8] Data on the current distribution and antimicrobial drug susceptibility patterns among urinary bacterial isolates from pregnant women in India is limited. In view of this fact and very few studies have been reported from India, as ASB screening is not carried out routinely probably due to cost implication, this study was undertaken to determine the prevalence of ASB and their antimicrobial susceptibility pattern among pregnant women attending our tertiary care hospital serving the suburban areas of Chennai.

**MATERIALS AND METHODS:** Study area: This study was carried out in our tertiary level referral and teaching hospital, which is serving the suburban population of Chennai. In this cross sectional study, clean catch midstream urine samples [MSU] from 281 pregnant women who attended routine antenatal check- up without symptoms of urinary tract infections during March 2012 to March 2013 were included. This was an analysis of data generated from the records of urine samples received in the laboratory during study period.

Samples received in a leak proof sterile container were processed within one hour. All samples were inoculated onto blood agar, nutrient agar and Mac conkey agar plates using a calibrated loop [0.001ml] and were incubated overnight at 37°C and examined next day. Colony counts yielding bacterial growth of $10^5$ cfu/ml were considered significant as per recommendations. All isolates were identified by standard laboratory techniques.[9]

Antibiotic susceptibility was done by Kirby Bauer disk diffusion method as per CLSI guidelines. Drugs that were tested include Ampicillin, Amoxicillin, Ciprofloxacin, Norfloxacin, Nitrofurantoin, Ceftriaxone, Gentamicin, Cotrimoxazole and Augmentin. Two antibiotics tested only against gram-positive isolates were Oxacillin and Vancomycin.[10]

**Data Management and Analysis:** Data were entered into a database designed using MS Excel spreadsheet and analyzed using SPSS statistical software package [version 20]. Proportions for categorical variables were compared using chi-square test. P value less than 0.05 was considered statistically significant.
RESULTS:

| TOTAL NO OF SAMPLES SCREENED | NO OF SAMPLES POSITIVE BY CULTURE | % OF ASB PREVALENCE |
|-----------------------------|-----------------------------------|---------------------|
| 281                         | 39                                | 13.87               |

Table 1: Prevalence of ASB among pregnant women

A total of 281 MSU samples received during March 2012 and March 2013 were included in this study. Of these, 235 [83.62%] were sterile, 39 [13.87%] showed significant and 7 [2.49%] showed insignificant growth. None of the samples have yielded more than one isolate.

| AGE GROUP | NO. OF CASES SCREENED | NO. OF CASES POSITIVE BY CULTURE[n=39] | % OF CASES POSITIVE FOR ASB |
|-----------|-----------------------|---------------------------------------|----------------------------|
| 20-24     | 73                    | 12                                    | 30.76                      |
| 25-29     | 98                    | 15                                    | 38.46                      |
| 30-34     | 105                   | 11                                    | 28.20                      |
| >35       | 5                     | 1                                     | 2.56                       |

Table 2: Prevalence of ASB among pregnant women with respect to age group

Majority of ASB positive subjects were in the age group of 25-29 yrs [38.46%]. Statistical analysis of ASB with respect to age group did not reveal any significance. About 30.76% were in the age group of 20-24 yrs, 28.2% in 30-34 yrs and 2.56% were more than 35 yrs of age.

| Trimester | No. of cases screened | No. of cases positive for ASB | % of case positive of ASB |
|-----------|-----------------------|-------------------------------|---------------------------|
| 1st       | 132                   | 28                            | 21.2                      |
| 2nd       | 65                    | 5                             | 7.69                      |
| 3rd       | 84                    | 6                             | 7.14                      |

Table 3: Prevalence of ASB according to trimester

Based on the trimester, 132, 65 and 84 subjects were in 1, 2 and 3 trimester of pregnancy. Of this, 28[21.2%], 5[7.69%] and 6[7.12%] of ASB positive subjects were in first, second and third trimester. This study showed high prevalence of ASB in pregnant women of first trimester.

| Gravida  | No. of cases screened | No. of cases positive for ASB | % of case positive of ASB |
|----------|-----------------------|-------------------------------|---------------------------|
| 1[primi] | 96                    | 10                            | 25.64                     |
| 2        | 140                   | 13                            | 33.33                     |
| >2[multi]| 45                    | 16                            | 41.02                     |

Table 4: Prevalence of ASB according to Gravida

According to gravid status, 96 pertained to primi, 140 to second and 45 to multigravida. occurrence of ASB was observed more among multigravid women [41.02%].
**Organism Isolated** | **No. of Isolates [n=39]** | **% of Isolates**
---|---|---
*E. coli* | 26 | 66.66
*Klebsiella* | 5 | 12.82
*Staph. aureus* | 6 | 15.38
CONS | 2 | 5.13

Table 5: Distribution of uropathogens isolated from ASB among pregnant women

*E. coli* was the most common organism isolated with the total of 26 [66.66%] followed by Methicillin sensitive *staphylococcus aureus* 6 [15.38%], *klebsiella pneumoniae* 5 [12.82%] and CONS 2 [5.13%].

| SL. NO. | ANTIMICROBIAL AGENT TESTED | RESISTANCE %[n] |
|---|---|---|
| 1 | Ampicillin | 69.23[28] |
| 2 | Amoxillin | 23.07[9] |
| 3 | Augmentin | 5.12[2] |
| 4 | Ciprofloxacin | 38.46[15] |
| 5 | Nitrofurontoin | 20.51[8] |
| 6 | Norfloxacin | 15.38[6] |
| 7 | Amikacin | 5.12[2] |
| 8 | Gentamicin | 74.35[29] |
| 9 | Vancomycin | 0[0] |
| 10 | Cotrimoxazole | 74.35[29] |
| 11 | Ceftriaxone | 10.25[4] |
| 12 | Oxacillin | 0[0] |

Table 6: Resistance rates of uropathogens isolated

High percentage of resistance has been observed for the antibiotics Gentamicin [74.35] and cotrimoxazole [74.35]. The percentage of isolates resistant to ampicillin was also found to be as much as 69.23 percent. The susceptibility pattern of the isolates showed that most of them were highly sensitive to Augmentin [5.12%], Amikacin [5.12%], Ceftriaxone [10.25] and Nitrofurontoin [20.51]. 100% of all gram positive organisms were sensitive to oxacillin and vancomycin tested.

**DISCUSSION:** In our study, the prevalence rate of ASB among pregnant women screened was found to be 13.87%. This was in accordance with the findings reported by T. Jeyaselan et al[5] and Balamurgan et al[8] in a south Indian population and comparable to the prevalence quoted from Tanzania and Sudan (14%).[11] Other Indian studies have reported 10% from Tumkur,[12] 8.4% in Vishakpatnam,[13] 9 and 11% from Raichur and Kolkata,[14,15] this is slightly lesser than our findings.

However, there are not many studies in the prevalence of ASB in India. The prevalence rates detected from our study is lesser than the rates quoted in other studies from Lucknow(17%)[16] and Hyderabad (16%).[17]
These variations in rate can be explained by the fact that differences in the environment, social habits of the community and educational standard of the population. Another reason could be as a result of improper genital hygiene practices as pregnant women find it difficult to clean their anus properly.[3,5]

In our study, age group 25-29 years had the highest infection rates (38.46%), followed by 20-24 years (30.76%), 30-34 yrs [28.2%] and those who were more than 35 years (7.69%). The aforementioned age group (26-30 years) was also observed in the previous studies to have the highest incidence. A possible explanation would be due to decreased glycogen deposition and reduced lactobacilli related to aging, bacterial adherence and invasion is enhanced. However, statistical analysis of ASB prevalence with respect to age group did not reveal any significance, this agrees with earlier studies.

Similar study conducted by Marahatta et al.[19] showed high prevalence among pregnant women in first trimester which seems similar to our study. A statistically significant association was observed for the ASB occurrence and first trimester. This may be related to anatomical and physiological changes related to month of pregnancy.

There was a statistically significant difference in the prevalence of ASB with respect to gravid status [P <0.0001]. Our study observed high prevalence in multigravida. This could be explained by the fact that multigravid female might have had many children before the present pregnancy and it has been reported that multiparity is a risk factor for acquiring ASB in pregnancy.[3,18]

The most common uropathogen isolated in our study was E.coli (66.66%), which is similar to other reports. (Table 7)

| Organism     | Present study % [2014] | Kerure SB et al., % [2013] | Alemu et al., % [2012] | Jeyaseelan et al., % [2011] | Danizen et al., % [2010] | Jeyalakshmi et al., % [2008] |
|--------------|------------------------|-----------------------------|------------------------|-----------------------------|--------------------------|-----------------------------|
| E. coli      | 66.6                   | 77.7                        | 47.5                   | 69                          | 57.6                     | 57.4                        |
| Klebsiella   | 12.82                  | 6.66                        | 10                     | Nil                         | 30.6                     | 19.21                       |
| Proteus      | Nil                    | Nil                         | Nil                    | Nil                         | Nil                      | 4.25                        |
| Pseudomonas  | Nil                    | Nil                         | Nil                    | Nil                         | Nil                      | 12.6                        |
| Citrobacter  | Nil                    | 2.22                        | 10                     | 14                          | Nil                      | 4.25                        |
| S. aureus    | 15.38                  | 11.11                       | 22.5                   | Nil                         | 4.8                      | 10                          |
| CONS         | 5.13                   | 5                           | 15                     | Nil                         | Nil                      | Nil                         |

Table 7: Isolated organisms across various studies

Another important observation of this study was the increasing trend in the prevalence of S. aureus infection (15.28%). Very few studies have reported such a high rate.[11,15] This dramatic increase in prevalence rate can be attributed to the emergence and global spread of staphylococcus aureus. Hence, recognizing this change in the spectrum of uropathogens remains important to guide changes in empirical antimicrobial therapy. The other organisms isolated were Klebsiella pneumoniae and CONS. They are less common causes of UTI.

Antimicrobial resistance patterns change over time and found to differ in different geographical locations, 74.34% of total isolates showed resistance to Cotrimoxazole. Our findings are in accordance with various Indian studies.[11,20]
The broad-spectrum activity of fluoroquinolones has made them as one of the best therapeutic options for UTI. Although many studies have reported high sensitivity to this group of drugs,[11] our findings are slightly different. A resistance rate of ciprofloxacin was 38.46% against 15.38% of isolates resistant to Norfloxacin.

This might be due to indiscriminate use of ciprofloxacin as they have been prescribed empirically in the last few years. Low sensitivity to Ampicillin has been observed which seems similar to the finding reported by Imade et al could have been contributed by an increase in Ampicillin prescribing practices in recent years.[20,21] High resistance observed for cotrimoxazole, ciprofloxacin and ampicillin.

In this study, the most useful antibiotics as predicted by their sensitivity rates were amoxicillin [96%], nitrofurantoin [79%], norfloxacin [84%], ceftriaxone [89%] and augmentin [94%]. Sensitivity to Amoxicillin was encouraging and it can be safely prescribed during pregnancy as first line antibiotic.

CONCLUSIONS: Significant bacteriuria was observed in asymptomatic pregnant women in our study population and bacterial spectrum and their resistance pattern was observed. So this study emphasizes the need for screening of pregnant women for ASB and periodic monitoring of uropathogens for antibiotic pattern as this data not only reduces the prevalence but also helps in rationalizing the antibiotic usage to restrict further emergence of resistance. Our study revealed that amoxicillin is the most effective drug that can be recommended for ASB during pregnancy.

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Date of Submission: 30/06/2014.
Date of Peer Review: 01/07/2014.
Date of Acceptance: 07/07/2014.
Date of Publishing: 14/07/2014.