

## A Case Control study of prevalence of asymptomatic bacteriuria in preterm labour

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### Abstract

**Background & Objectives:** Asymptomatic bacteriuria during pregnancy is one of the risk factor for preterm delivery if untreated. The aim of this study is to find out the prevalence of ASB in pregnant women presenting with preterm labour pain and also to determine the common pathogenic micro-organisms associated and their antibiotic sensitivity.

**Methods:** This is a prospective case- control study carried out in the Jubilee Mission Hospital, Thrissur, Kerala from Oct 2013 to March 2015. Cases (50) are those who came with preterm labour and patients in the control (50) group are those who do not present with preterm labour pain between 24-37 weeks. Patients were selected with specific inclusion and exclusion criteria. They were followed till delivery and treatment was given accordingly. Both maternal and fetal outcomes were noted.

**Results:** Asymptomatic bacteriuria was present in 11 patients whoc presented with preterm labour pain and hence the prevalence of asymptomatic bacteriuria in preterm labour in the study population was 22%. Most common pathogenic organism found was E.coli (20%) followed by Klebsiella (2%). Mixed growth suggestive of contamination was found in both case (14%) and control (12%) group. Sensitivity to nitrofurantoin was seen in 4 cultured samples (36.36%) of the patients with ASB.

**Conclusion:** Asymptomatic bacteriuria is a common infection in pregnancy and they are at an increased risk for adverse maternal and fetal outcomes which could be prevented by antimicrobial therapy. Hence pregnant women should be screened for bacteriuria and treated with appropriate antibiotics according to the sensitivity.

**Keywords:** Asymptomatic bacteriuria, UTI, Pregnant women, Preterm labour, E. Coli.

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### Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections seen during pregnancy<sup>1</sup>. It could be either symptomatic or asymptomatic. Asymptomatic bacteriuria is defined as persistently and actively multiplying bacteria in significant numbers (more than  $10^5$  per ml) within the urinary tract without any obvious symptom<sup>2</sup>. The pregnant women are two times more commonly affected than age matched non-pregnant females<sup>3,4</sup>. Asymptomatic bacteriuria is found in 2-10% of pregnant women<sup>5</sup>.

If asymptomatic bacteriuria is not treated approximately 25% of women will subsequently develop acute symptoms of an infection during pregnancy<sup>6</sup>. Asymptomatic bacteriuria is an entity with serious consequences in the form of maternal and fetal morbidity<sup>7</sup>. It can cause maternal anemia, pyelonephritis, recurrent infection, preterm labour<sup>8</sup>, septicemia and even death of the mother<sup>9</sup>. It can cause Intra Uterine Growth restriction (IUGR)<sup>10</sup>, prematurity, low birth weight of the fetus<sup>11</sup> and the fetal mortality<sup>9</sup>. Out of these preterm labour pain and pyelonephritis are the most common adverse effects<sup>8</sup>.

The association between ASB and preterm delivery (<37 completed weeks) and that between asymptomatic bacteriuria and low birth weight (<2500 gram) were unknown until 1962 when Kass observed an increased risk among untreated bacteriuric women of the delivery of low birth weight<sup>12</sup>. The mean duration of pregnancy among untreated bacteriuric women was found to be reduced by one week on average<sup>13</sup>. Also ASB in pregnant women as a risk factor for preterm birth and antibiotic therapy has been found to significantly reduce the risk.<sup>14,15</sup>

### Aims and Objectives

To find out the prevalence of asymptomatic bacteriuria (ASB) in pregnant women presenting with preterm labour pain. To determine the common pathogenic micro-organisms associated with Asymptomatic Bacteriuria and their antibiotic sensitivity.

### Materials and Methods

This is a prospective case- control study carried out in the Jubilee Mission Hospital, Thrissur, Kerala from Oct 2013 to March 2015. Cases (50) are those who came with preterm labour and patients in the control (50) group are those who do not present with preterm labour pain between 24-37 weeks. Patients were selected with specific inclusion and exclusion criteria. A predesigned proforma was used to record relevant information (patient data, finding, inv report) from individual patients selected with inclusion and

exclusion criteria. Both maternal and fetal outcomes were noted.

### Exclusion Criteria

Women with present history of UTI or any clinical presentation of UTI in the present pregnancy. Women known to be diabetic, chronic hypertensive, multiple pregnancy and women who are immune compromised, as in long-term corticosteroid therapy and antibiotic therapy. Women initially asymptomatic and became symptomatic during the course of pregnancy.

### Methodology

Patients and labour room staff were instructed to take clean catch mid stream urine sample for urine culture and also for quantitative and microscopic examination. The samples were immediately transported to the laboratory and were processed within one hour and maximum within 2 hours. The unspun urine was examined directly under the microscope and pus cells per high power field were calculated.

Calibrated loop direct streak method was used urine culture examination. In this method one biconvex loop full of well mixed uncentrifuged urine specimen was deposited on blood agar plate and Mac conkeys agar plate. Both plates were incubated overnight at 35°C and red next morning. Colonies were examined and counted on both plates. 10<sup>5</sup> colonies per ml were taken as significant bacteriuria.

After determining the plate count, organisms were identified and susceptibility to antibiotics was determined by Disc-Diffusion method. Mixed growth of two or more organisms was considered as contamination and the sample was repeated. If there is no growth, the specimens were held in incubator for another 1 day and if still negative reported as no growth after 48 hours.

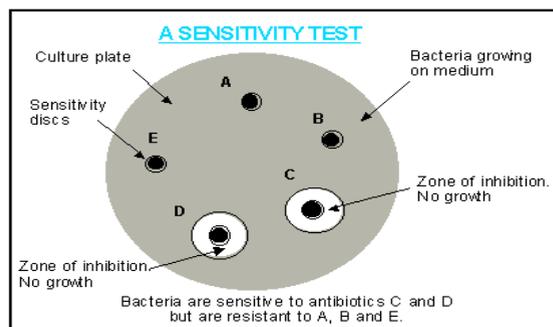
### Identification of Organisms

A smear was prepared from the culture, selecting a single colony and stained by gram staining method. In case if gram positive cocci were found in clusters, a coagulase test was performed by tube method to differentiate between pathogenic and non-pathogenic staphylococci. When gram positive cocci in pairs were isolated from Mac conkeys agar plate, bile solubility heat resistance and mannitol fermentation tests were carried out to confirm enterococci. When pink coloured or pale colonies on Mac conkeys agar plate were seen, Gram staining was done. Similarly a set of biological investigations were carried out to identify various Gram negative bacteria.



### Antibiotic sensitivity

This is done by Disc-Diffusion method of Kirby Bauer. The organisms were grown on nutrient broth for 18 hours. Mueller Hinton Agar plates were then inoculated uniformly by flooding the surface with 2 ml of broth cultures. The excess removed and the discs were then placed at suitable distance from each other and incubated overnight at 37°C. Antibiotic sensitivity zones were read in the zone reader and compared to a standard chart with specified zone diameters for each antimicrobial disc to determine either sensitivity or resistance of the bacterium in question.



(Fig.4-3a)

### Treatment and follow-up

After screening, women with bacteriuria were treated with 14 days course of antimicrobial drugs as per the sensitivity of the organisms. Repeat cultures were obtained 2 weeks after completion of the therapy. If culture was sterile, periodic repeat cultures were done at 4 weeks interval till culture was sterile. All the patients in both groups were followed up till delivery for any evidence of complications like preeclampsia, anemia, preterm labour, fetal growth restriction. Mode of delivery and period of gestation at the time of delivery were assessed. Newborns were assessed for maturity, birth weight and APGAR scores.

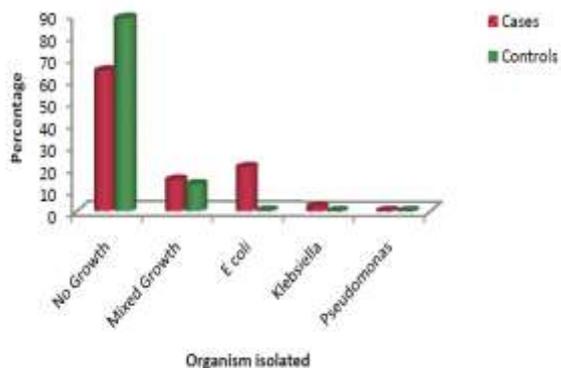
**Statistical methods:** Chi-square and student t test were used.

### Results

Out of 50 patients presented with preterm labour (PTL) pain, 11 patients had asymptomatic bacteriuria

and hence the prevalence of asymptomatic bacteriuria in preterm labour is 22% in the current study. The most common organism isolated was E. Coli which was present in 10 cases (20%) followed by Klebsiella in 1 case (2%).

ASB	PTL	%
No	39	78.0
Yes	11	22.0
Total	50	100.0



This study also found that out of 11 cases with asymptomatic bacteriuria, 7 patients (63.64%) were not sensitive to nitrofurantoin and 4 patients (36.36%) were sensitive to nitrofurantoin. This result is different from other studies done on nitrofurantoin sensitivity.

Other significant associations are ASB was present more in primigravida than multigravida, PPRM was present in 15 patients (30%) in the case group. Fetal complications including Fetal growth restriction was present in 10% of patients with preterm labour pain in Ultrasonogram which is statistically significant when compared with none in the control group. The mean birth weight of the babies in the case group was 2.05 +/- 0.68 kg which comes under low birth weight category.

### Discussion

Asymptomatic bacteriuria (ASB) occurs in 2-10% of all pregnancies. The majority of the most recent studies, including observational studies from developing countries found the prevalence of asymptomatic bacteriuria in pregnant women ranged between 4-10%. Different studies have shown different indices. This variation in studies can be attributed to several factors such as the geographical variation, socio-economic status, ethnicity of the subjects, setting of the study (primary care, community based or hospitals) and the variation in the screening tests (urine dipstick, microscopy, and culture).

Delzell JE et al<sup>16</sup> defined Asymptomatic bacteriuria (ASB) as persistent and actively multiplying bacteria of more than or equal to 1,00,000 colony forming units per ml of urine without any urinary tract symptoms including lower abdominal pain, burning micturition,

fever, frequency, urgency, dysuria, supra pubic discomfort, offensive smelling urine, urge incontinence and nocturia. The ASB diagnosed using urine culture examination was 22% in the cases group with p value <0.001\*\* which is statistically significant. As Delzell et al stated that the Gold standard for detection of bacteriuria is urine culture. Faster screening methods like leukocytes esterase dipstick, nitrite dipstick, urinalysis and gram staining are not useful in the screening for ASB.

Gayathree et al<sup>17</sup> studied 900 pregnant women who attended the Hassan District hospital, Hassan to study the prevalence of asymptomatic bacteriuria. They found that ASB was prevalent in 6.2% in 900. There was a higher prevalence in 3<sup>rd</sup> trimester (61.77%) than in the 2<sup>nd</sup> trimester (32.35%) and the 1<sup>st</sup> trimester (5.88%) and concluded that screening for ASB in all the three trimesters is necessary to prevent the dangerous complications which are associated with ASB in pregnancy. In the current study, the prevalence was 22% and associated with significant maternal and fetal morbidities. Hence screening is recommended.

Cox SM et al<sup>18</sup> in 1987 found that bacterial enzymes such as collagenase may weaken the fetal membranes which can result in preterm premature rupture of membrane. There is evidence that when there is no symptom, untreated bacteriuria in pregnancy may lead to less favourable pregnancy outcomes and complications like preterm delivery, low birth weight, pre-eclampsia and anemia of pregnancy. Prematurity is one of the leading causes of perinatal mortality. Uterine contractions may be induced by cytokines and prostaglandins, which are released by microorganisms<sup>19,20</sup>. In the present study PPRM was present in 15 patients (30%) in cases group and PPRM being the reason for preterm labour pain. Kass<sup>21</sup> reported that severe uterine contractions occur within moments after endotoxin injection in an animal model, thus linking bacteriuria with early delivery. Early delivery results in Low birth weight. Patterson et al<sup>22</sup> in 1987 found that subclinical chorioamnionitis associated with bacteriuria. Phospholipid A2 production by the bacteria may be the proposed cause for initiation of preterm labour. It may be also due to release of pro inflammatory cytokines, secreted by maternal and fetal monocytes in response to bacterial products.

Cardiff Birth Survey<sup>23</sup> in 1995 which prospectively studied 25,844 births, reported that asymptomatic bacteriuria adjusted for demographic and social factors was not associated with preterm delivery. However, when preterm births were categorised into medically indicated or spontaneous preterm births, there was a significant association between bacteriuria and medically indicated preterm births but not for spontaneous preterm births and the authors concluded that if asymptomatic bacteriuria does not progress to pyelonephritis, it is not associated with preterm birth.

Asymptomatic bacteriuria other than pregnancy is said not to require any treatment. **Smail F et al**<sup>24</sup> in 2002 stated in a cochrane systematic review of randomised controlled trials that antibiotic treatment reduced persistent bacteriuria during pregnancy, reduced preterm delivery or low birthweight babies and reduced the development of pyelonephritis.

Nitrofurantoin is the drug of choice in pregnancy<sup>25</sup>. This study also found that out of 11 cases with asymptomatic bacteriuria, 7 patients (63.64%) were not sensitive to nitrofurantoin and 4 patients (36.36%) were sensitive to nitrofurantoin. This result is different from other studies done on nitrofurantoin sensitivity. But it should be avoided after the onset of labour in G6PD deficiency, since it may cause hemolysis in neonates due to immature erythrocyte enzyme systems (Glutathione instability)<sup>26</sup>. It cannot be used in cases of pyelonephritis since it does not achieve adequate tissue penetration<sup>27</sup>.

So it is important to screen and treat asymptomatic bacteriuria so as to prevent the associated maternal and fetal morbidities. The American College of Obstetrics and Gynaecology<sup>28</sup> strongly recommends that the urine culture to be obtained in the first prenatal visit itself. The American Academy of Family Physicians<sup>29</sup> also recommends screening for ASB at 12-16 wks of gestation or at the first visit by culture method. The Infectious Disease Society of America<sup>30</sup> recommends screening with a urine culture 'at least once' in early pregnancy.

## Conclusion

Asymptomatic bacteriuria is a common infection. Pregnant women with asymptomatic bacteriuria are at an increased risk for adverse maternal and fetal outcomes which could be prevented by antimicrobial therapy.

In this study, out of 50 randomly selected women with preterm labour pain, 11 were found to have asymptomatic bacteriuria which gives a prevalence rate of 22%. Organisms isolated were E.coli, Klebsiella pneumonia and mixed growth. E.coli was the most common organism in the cases group (20%). Sensitivity to nitrofurantoin was seen in 36.36% of the patients with ASB.

Maternal morbidities including low haemoglobin levels, PPRM and severe preeclampsia were present in the patients in the cases group. Significant fetal morbidities including preterm birth, IUGR and low birth weight were seen in the patients in the cases group. Hence pregnant women should be screened for bacteriuria and treated with appropriate antibiotics according to the sensitivity if results are positive.

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-Dr. R. K. Vidhyalakshmi

## Conflicts of interest

As with any other study, this study also has limitations. There were mixed growth which is suggestive of contamination found in the urine culture, but this can be ignored as the number of mixed growth was almost equally distributed. Patients in the control group, who became symptomatic during the course of the pregnancy, were excluded from the study and new patients were added to attain the sample size. The patients in the control group had no asymptomatic bacteriuria which may be due to strict following of exclusion criteria.

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