

BACTERIURIA WITH PRETERM LABOUR IN PREGNANT WOMEN: A PROSPECTIVE STUDY

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Abstract

Background: Bacteriuria, both symptomatic and asymptomatic, is shown to be associated with adverse maternal and fetal outcomes, including preterm birth. Preterm labour is a leading cause of neonatal morbidity and mortality worldwide. It is the leading cause of death in the first month of life and preterm neonates are at an increased risk for post-neonatal mortality and a wide range of respiratory, infectious, metabolic, and nervous system morbidities. **Objectives:** To estimate the proportion of pregnant women having bacteriuria (symptomatic and asymptomatic) and to determine the association between it and preterm labor. Also, it was aimed to assess the effect of treating such cases with different appropriate antimicrobials in preventing development of preterm delivery. **Materials and Methods:** A prospective study was carried out in the Department of Obstetrics and Gynaecology, JNIMS, Imphal, Manipur during the period November 2020 to October 2022. A total of 270 pregnant women attending the OPD or admitted in the Ward of the Department of Obstetrics & Gynaecology, JNIMS were the study population. Only those women with gestational age up to 37 weeks of any viable pregnancy, willing to undergo required investigations and participate in the study, singleton pregnancy of any gravida/parity were included. Patients with other known risk factors of preterm labour were excluded. A pre-tested semi-structured proforma having sections on socio-demographic profile, anthropometry, obstetric history and clinical findings and laboratory investigations was used for data collection. Universally accepted operational definitions of bacteriuria and preterm labour were used. Patients having bacteriuria were treated with appropriate antimicrobials and followed up until the pregnancy outcome happened. **Result:** A total of 190 urine samples gave positive results for bacteriuria, thus giving a positive proportion of 70.4%. The incidence of preterm labour was found to be 46.7% (n=126) of the participants, and that of preterm birth as outcome of pregnancy was found to be 25.9% (n=70). The most common organism was found to be E. coli, which accounted for nearly half the cases at 49.3% (n=133), followed by Staphylococcus at 10.7% cases (n = 29). Among women with bacteriuria, 51.1% (n=97) were found to be associated with preterm labour which was statistically significant (p=0.026) and 25.3% (n = 48) were associated with preterm birth as pregnancy outcome but statistically insignificant (p=0.702). Combination therapy with Nitrofurantoin, Fosfomycin and Fentoconazole was found to be significantly associated with prevention of preterm labor and preterm birth (p=0.001). **Conclusion:** Bacteriuria was found to be prevalent among the pregnant women in the study area, much higher than reported elsewhere. It was found to be significantly associated with preterm labor. Appropriate treatment significantly could reduce the adverse pregnancy outcomes.

INTRODUCTION

Bacteriuria, also called Urinary tract infection (UTI), is the most common bacterial infection seen during pregnancy. It could be either symptomatic or asymptomatic. Asymptomatic bacteriuria is found in 2-10% of pregnant women.^[1] Since it is asymptomatic, most of the women never seek treatment, while a few go on to develop frank symptoms and signs of urinary tract infection.^[2] Symptomatic bacteriuria which consists of lower tract (acute cystitis) and upper tract (acute pyelonephritis) infections are associated with adverse maternal and fetal outcomes, including preterm birth. Therefore, screening and treatment of bacteriuria during pregnancy have become standard of care recommended by multiple professional organizations.^[3] Preterm labour is a leading cause of neonatal morbidity and mortality worldwide. WHO has estimated that 9.6 % of all births (about 13 million) are preterm.^[4] It is the leading cause of death in the first month of life and preterm neonates are at an increased risk for post-neonatal mortality and a wide range of respiratory, infectious, metabolic, and nervous system morbidities.^[5] Evidence suggests that infection plays a role in pathogenesis of preterm labour and delivery.^[6] Literature regarding the relationship between bacteriuria and preterm labor, although reported from many parts of the world, is hardly available from the north-eastern part of India. This study was conducted with the main objectives of estimating proportion of pregnant women having bacteriuria (symptomatic and asymptomatic) and determining the association between it and preterm labor. Also, the effect of treating such cases with different appropriate antimicrobials to prevent development of preterm delivery was assessed.

MATERIALS AND METHODS

A prospective study was carried out in the Department of Obstetrics and Gynaecology, Jawaharlal Nehru Institute of Medical Sciences, Imphal, Manipur during the period of November 2020 to October 2022. Pregnant women attending the OPD or admitted in the Ward of the Department of Obstetrics & Gynaecology, JNIMS were the study population. Only those women with gestational age up-to 37 weeks of any viable pregnancy, willing to undergo required investigations and participate in the study, singleton pregnancy of any gravida/parity were included. Patients with other known risk factors of preterm labour such multiple gestation, abruptions, smokers, preeclampsia, PPROM, cervical incompetence, domestic violence, retained IUDs, poly/oligohydramnios, maternal age below 16 yrs. or over 40 yrs., congenital abnormalities of uterus or IUGR/IUD were excluded. A sample size of 270 was calculated using probability of event in

unexposed group as 0.33, probability of event in experimental group as 0.4 with a power of 80% at 95% confidence level. Attrition of 15% was used in the sample size calculation. All eligible cases were enrolled by convenience (consecutive) sampling until the sample size was achieved. A pre-tested semi-structured proforma was used. The operational definition for bacteriuria was urine culture positive cases i.e., colony count of $>1,00,000$ colony forming units (CFU)/mL, with or without symptoms. Preterm labour was defined as onset of labour before 37 completed weeks of pregnancy but after period of viability, with regular uterine contractions occurring once in every 5-8 minutes or less accompanied by \geq one of the following: (a) Progressive changes in cervix (b) Cervical dilatation of more than or equal to 1cm and (c) Cervical effacement of more than or equal to 80%. The study was undertaken after obtaining proper clearance from the ethics committee of JNIMS. Written informed consent was taken from all the study participants. After taking detailed history, general and systemic physical examination including obstetrical examination was done for all participants. Gestational age was estimated by last menstrual period and was confirmed by first trimester scan. Routine investigations were sent either at JNIMS or any accredited laboratories. For screening of bacteriuria, patients were instructed to collect mid-stream urine samples which were then sent for cytology and culture-sensitivity at accredited laboratories at the point of induction into the study and at routine follow ups to detect infection at any point. Those participants who tested positive for Bacteriuria, were treated with appropriate antimicrobial therapy according to culture-sensitivity report – usually Nitrofurantoin or Fosfomycin or both. Such participants were followed up till the termination of their pregnancy and the pregnancy outcomes were noted. Statistical analysis was performed using IBM SPSS version 21. Results were expressed as mean and frequencies and percentages. Differences in categorical variables were tested using a Chi-square test. A p-value < 0.05 was considered statistically significant in all statistical tests.

RESULTS

Completed data sets could be collected from all 270 participants. Their mean age (SD) was found to be 27.30 (\pm 5.58) years, with the minimum age group being 18 years and the maximum being 43 years. The majority of the participants were of the age group of 21-30 years making up 56.7% (n=153). Two-thirds (178; 65.9%) of them belonged to Hindu community. Majority of them (188; 69.6%) were from low-income families. Multipara outnumbered primiparas by 2:1 [Table 1]. A total of 190 urine samples gave positive results for bacteriuria, thus giving a positive proportion of

70.4%. The incidence of preterm labour was found to be 46.7% (n=126) of the participants, and that of

preterm birth as outcome of pregnancy was found to be 25.9% (n=70). [Table 2]

Table 1: Socio- demographic pattern of study participants

Socio-demographic indicator	Frequency (%)
Age in years <ul style="list-style-type: none"> • ≤ 20 • 21-30 • > 30 	33 (12.2) 152 (56.7) 84 (31.1)
Community <ul style="list-style-type: none"> • Hindu • Muslim • Christian 	178 (65.9) 51 (18.9) 41 (15.2)
Socio-economic status <ul style="list-style-type: none"> • Low • Middle 	188 (69.6) 82 (30.4)
Parity <ul style="list-style-type: none"> • Multipara • Primipara 	180 (66.7) 90 (33.3)

Table 2: Distribution of organisms among bacteriuria cases

Outcome indicator	Frequency (%)
Preterm labor <ul style="list-style-type: none"> • Present • Absent 	126 (46.7) 144 (53.3)
Preterm delivery <ul style="list-style-type: none"> • Present • Absent 	70 (25.9) 200 (74.1)

Among the cases of bacteriuria, the most common organism was found to be E. coli, which accounted for 49.3% of cases.

Table 3: Distribution of organisms among bacteriuria cases

Organism by Urine C/S Reprt	Frequency (%)
E. coli	133 (49.3)
Staphylococcus	29 (10.7)
Klebsiella	18 (6.7)
Enterococcus	4 (1.5)
Streptococcus	1 (0.4)
Proteus	1 (0.4)
E. aerogenes	1 (0.4)

Of the 190 cases of bacteriuria, 51.1% (n=97) were found to be associated with preterm labour which was statistically significant (p=0.026). Among the same cases of bacteriuria, 25.3% (n = 48) were found to be associated with preterm birth as pregnancy outcome, which was statistically insignificant (p=0.702). [Table 4]

Table 4: Association between bacteriuria and preterm labor/delivery

Bacteriuria	Preterm labour (%)		p-value	Preterm delivery(%)		p-value
	Absent	Present		Absent	Present	
Negative	51 (63.8)	29 (36.3)	0.026	22 (27.5)	58 (72.5)	0.702
Positive	93 (48.9)	97 (51.1)		48 (25.3)	142 (74.7)	

Based on culture sensitivity report, 28.5% (n=77) of the 270 participants received combination 1 (Nitrofurantoin + Fosfomycin + Fenticonazole), 41.9% (n=113) cases received combination 2 (Nitrofurantoin + Fosfomycin), while 29.6% (n=80) cases received Fenticonazole alone. Among the participants receiving the combination 1, combination 2 and combination 3, those which progressed to preterm labour were 72.7% (n=56), 36.3% (n=41) and 36.3% (n=29) respectively. The combination containing all the three antimicrobials was found to be significantly associated with lesser proportion of preterm labor (p=0.001).

Table 5: Distribution of preterm labor by different antimicrobial combinations

Antimicrobial combination	Preterm labor (%)		p-value
	No	Yes	
Fentoconazole	51 (63.8)	29 (36.3)	0.001
Nitrofurantoin + Fosfomycin	72 (63.7)	41 (36.3)	
All of the above	21 (27.3)	56 (72.7)	

And, out of the three combinations, Nitrofurantoin + Fosfomycin led the highest proportion of term delivery followed by combination of all the three antimicrobials ($p=0.001$) [Table 6].

Table 6: Distribution of preterm delivery by different antimicrobial combinations

Antimicrobial combination	Preterm delivery (%)		p-value
	No	Yes	
Fenticonazole	58 (72.5)	22 (27.5)	0.001
Nitrofurantoin + Fosfomycin	98 (86.7)	15 (13.3)	

No statistically significant association between preterm delivery and socio-demographic background.

DISCUSSION

Bacteriuria was present in 70.4% of cases. Several previous studies have shown a prevalence of bacteriuria in pregnancy between 20- 35% of cases,^[7] which is lower than what we found. This may be because of the fact that our participants were enrolled from a high-risk hospital-based population group. Of the 190 cases of bacteriuria, 51.1% ($n=97$) were found to be significantly associated with preterm labour. Though the exact mechanism of this association is still not clearly elucidated, it has been shown by several studies that a significant association exists between bacteriuria and preterm labour. Vidhyalakshmi RK et al found that the prevalence of bacteriuria in preterm labour, which was statistically significant. Lai Y J et al,^[8] have found that there was a statistically significant higher rate of preterm delivery before 36 weeks in the bacteriuria group (7.1% vs. 3.3%, $p=0.007$), and also statistically significantly higher rates of preterm premature rupture of membrane (PPROM) in the bacteriuria group before 28 weeks (2.4% vs. 0.1%, $p < 0.001$) or 34 weeks of gestation (3.6% vs. 0.9%, $p=0.001$). Greve VH et al also found that women who gave birth at 28-34 weeks gestation were more likely to have bacteriuria.^[9] Thus, our finding is consistent to the findings of other previous studies where significant association were found between bacteriuria and preterm labour. Of the same cases of bacteriuria, 25.3% ($n=48$) were found to be associated with preterm birth, which is statistically insignificant ($p=0.702$). This may be due to effective treatment of preterm labour associated with bacteriuria at its early stage using appropriate antimicrobial treatments, and also effective management of other factors which could have initiated preterm labour. Of the 78 cases of concomitant infection, 73.1% ($n=57$) cases were associated with preterm labour, which is significant ($p=0.001$), and 43.6% ($n=34$) cases were found to be associated with preterm birth, which is significant ($p=0.001$). In a previous study by Verma Indu et al, urogenital infection was found in 36.54% cases of preterm labour,^[6] which is close to the finding in our study. Hence, the current finding collaborates with those of our earlier studies. Of the total 270 participants, there were 46.7% ($n=126$) cases of preterm labour, 55.6% ($n=70$) progressed to preterm birth, which was statistically significant. This is lower than the global rate of about 75% of

spontaneous onset preterm labour which progress to preterm birth as found in a study conducted by Vogel JP et al.^[5] This may be due to small sample size of the study, and the more or less identifiable causes of preterm labour for the participants of our study, i.e. bacteriuria, which are mostly manageable with appropriate treatments and counselling, although other factors which could contribute to preterm labour cannot be definitely ruled out. The most common infective organism found in cases of bacteriuria in the study was *E. coli*, accounting for nearly half of the total 190 cases of bacteriuria at 49.3%, followed by *Staphylococcus* species at 10.7%, both together accounting for 60% of all cases of bacteriuria. Other previous studies with similar findings, such as those done by Abdel-Aziz Elzayat M et al, Nteziyaremye J et al and Baer RJ et al.^[10-12] which have found *E. coli* to be the most common organism in their studies, accounting for upto 60-70% of bacteriuria cases. Regarding antimicrobial therapy, 28.5% ($n=77$) of the 270 participants received combination 1 (Nitrofurantoin + Fosfomycin + Fenticonazole), 41.9% ($n=113$) cases received combination 2 (Nitrofurantoin + Fosfomycin), while 29.6% ($n = 80$) cases received Fenticonazole alone. Among those receiving the combination 1, combination 2 and combination 3, those which progressed to preterm labour were 72.7% ($n = 56$), 36.3% ($n = 41$) and 36.3% ($n = 29$) respectively. This was a statistically significant association between antimicrobial therapy and prevention of preterm labour ($p=0.001$). The pregnancy outcome of the patients in relation to its progression to term pregnancy were found to be 57.1% ($n=44$), 86.7% ($n=98$) and 72.5% ($n=58$) of similar combination respectively. This is also statistically significant ($p=0.001$). Both these findings show that, the treatment regimens were effective in preventing onset of preterm labour and preterm birth. Selection bias and information bias could not be completely excluded. That was one limitation of our study. Some potential confounding factors like mistaken LMP, history of previous preterm birth, personal and perineal hygiene, nature of daily activity or work during pregnancy, maternal gestational weight gain, anaemia, prediabetes or gestational diabetes, pregnancy-induced hypertension, diet structure, sexual activity and sexual partner(s), psychological state such as anxiety and stress, which may have direct or indirect impact on onset of preterm labour and preterm birth,

were missing in our study due to high percentage of missing information. Spontaneous onset preterm labour is also a major contributor in the global incidence of preterm labour and preterm birth in general, whose contribution in the overall prevalence cannot be definitely ruled out. These may affect the development of preterm labour or birth in the patients. Therefore, further studies with larger population base are needed to confirm the findings of the current study.

CONCLUSION

Bacteriuria was found in 70.4% of pregnant women which is higher than reported elsewhere. The incidence of preterm labour was found to be 46.7%, and that of preterm birth as outcome of pregnancy was found to be 25.9%. *E. coli* was most commonly detected in nearly half of the bacteriuria cases, which was followed by *Staphylococcus*. Bacteriuria was found to be significantly associated with preterm labor but not with preterm delivery. Regarding treatment effect, combination of Nitrofurantoin + Fosfomycin + Fenticonazole was found to be significantly associated with lesser proportion of preterm labor and preterm birth.

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