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ORIGINAL ARTICLE

Urogenital Infections as a Risk Factor for Preterm Labor: A Hospital-Based Case–Control Study

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Abstract

Purpose Preterm labor is a leading cause of neonatal morbidity and mortality. Ascending lower genital tract infection leads to preterm labor and adverse pregnancy outcomes. This prospective case–control study was performed to see the association between preterm labor and urogenital infections.

Methods A total of 104 women were observed for urogenital infections and their association with preterm labor. Case Group I included 52 women with preterm labor after 26 weeks and before 37 completed weeks of gestation with or without rupture of membranes. Control Group II included 52 women at completed or more than 37 weeks of gestation with no history of preterm labor, matched to the case group with respect to age and parity. Midstream urine was sent for cytology and culture sensitivity. Samples from posterior fornix of vagina were taken with two sterilized swabs under direct vision using Cusco/Sims speculum before first vaginal examination and were studied for gram stain characteristics and culture sensitivity by standard methods. Microorganisms isolated on culture were noted, and antibiotics were given according to sensitivity. Data collected were analyzed according to the groups by χ^2 test for categorical variables.

Results In our study, urogenital infection was seen in 19 women in Case Group I (36.54 %) compared with 9 women in Control Group (17.3 %), and the difference was statistically significant (p 0.027).

Conclusion Recognizing and treating the women having urogenital infections at a stage, when it has not become clinically evident, will decrease the percentage of women going into preterm labor and will improve the perinatal outcome.

Keywords Urogenital infection · Preterm labor

Introduction

Preterm labor is defined as the onset of labor before 37 completed weeks of pregnancy and is a leading cause of neonatal morbidity and mortality worldwide. WHO has estimated that 9.6 % of all births (about 13 million) in 2005 were preterm. Africa and Asia accounted for almost 11 million [1]. Evidence suggests that infection plays a role in pathogenesis of preterm labor and delivery [2]. Lockwood [3] reported that an estimated 50 % of spontaneous preterm births were associated with ascending genital tract infections. In 2001, Chhabra and Patil [4] reported that 14 and 28 % of patients in preterm labor had positive urine and cervical cultures, respectively. It has been proven by in vivo and in vitro studies that ascending lower genital

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tract infection leads to preterm labor [5–7]. Decidual invasion by the lower genital tract bacteria is associated with recruitment of leukocytes followed by cytokine production which trigger prostaglandin synthesis in the amnion, chorion, decidua, and myometrium [5]. This leads to contractions of the uterus, dilatation of cervix, membrane exposure, and entry of microorganisms into the uterine cavity. Local action of the lower genital tract bacteria produces enzymes sialidase or mucinase, which weakens the protective cervical mucosa and thus supports bacterial invasion of the upper genital tract.

In pregnancy, asymptomatic urinary tract infection is very common and is linked with preterm delivery. If bacteriuria without symptoms is not treated in pregnant women, then it may lead to acute cystitis and pyelonephritis in 20–40 % of cases. The presence of urinary tract infection may be an indicator for abnormal vaginal flora because of the colonization of the vagina with the same pathogens as found in the urine [8]. In 1989, Romero et al. [9] concluded in their study that nonbacteriuric patients had only about two-third the risk of low birth weight and half the risk of preterm delivery compared to those with untreated symptomatic bacteriuria, and that antibiotic treatment reduced the risk of low birth weight. Recognizing and treating the patients having genitourinary infections at a point, when it has not become clinically noticeable, will reduce the number of patients going into preterm labor resulting in decreased morbidity and mortality in the neonates born to such mothers. Thus, diagnosing and treating infections associated with preterm labor represent a very attractive area for interventions to prevent dire neonatal outcome. This prospective case-control study was designed to see the association between preterm labor and urogenital infections.

Materials and Methods

After clearance from the hospital ethics committee, this case–control study was undertaken in the Department of Obstetrics and Gynecology at Christian Medical College and Hospital Ludhiana, Punjab, India. Written informed consent was obtained from all the women after explaining it to them in the language they best understand. Minimum sample size of women with 7 % prevalence of urogenital infections among antenatal women not having preterm labor and 30 % prevalence of urogenital infections among antenatal women in preterm labor, with a confidence limit of 95 % and a power of 80 was calculated to be 52 in each group using SPS statistical software package (version 17).

Inclusion criteria: Only women with singleton pregnancy were included in this study. Case group I included the antenatal patients admitted in the labor room with threatened preterm labor and in preterm labor with or without rupture of membranes after 26 weeks and before 37 completed weeks of gestation. Control group II consisted of antenatal women visiting antenatal OPD of the hospital for routine antenatal check-up at completed or more than 37 weeks of gestation with no history of preterm labor and matched to the case group with respect to age (teenage pregnancy, pregnancy at 20–30 years, and pregnancy after 30 years) and parity (primigravida or multigravida). Exclusion criteria: Women with twin pregnancy or higher-order pregnancy, and women with antepartum hemorrhage were excluded from the study.

Preterm labor was documented according to ACOG criteria (1997) as four uterine contractions in 20 min or eight in 60 min plus progressive change in the cervix; cervical dilatation greater than 1 cm; and cervical effacement 80 % or greater at gestation <37 completed weeks. Threatened preterm labor was described as four uterine contractions in 20 min or eight in 60 min plus cervical dilatation less than 1 cm; and cervical effacement less than 80 %. Leaking, i.e., rupture of membranes was diagnosed by per speculum examination and confirmed by litmus paper (change of color from red to blue).

All women were evaluated by detailed history compiled with special emphasis to previous history of preterm labor, previous bad obstetric history, and urogenital infections. Gestational age was calculated from date of last menstrual period using Naegeles formula or by first ultrasound in the first trimester of pregnancy. All women underwent general physical, systemic, and obstetrical examinations. Samples from posterior fornix of vagina were taken with two sterilized swabs under direct vision using Cusco/Sims speculum before first vaginal examination and were studied for gram stain characteristics and culture-sensitivity by standard methods. Mid stream urine sample was sent for cytology and culture-sensitivity. Samples for aerobic culture sensitivity were sent immediately to the Microbiology Department of the hospital and taking all aseptic precautions; these samples were inoculated on blood agar and MacConkey's agar using semi-quantitative method of inoculation. The culture plates were incubated at 37 °C for a duration ranging from 24 to 48 h. Isolates were identified by standard methods [10].

Women admitted with preterm labor were put on tocolytics (where required), or steroids therapy (<34 weeks of gestation), and antibiotics (cephalosporins) were started in women with ruptured membranes. Reports of the urine and high vaginal swab cultures were collected and recorded. Antibiotic therapy was started or changed according to the sensitivity reports. Data collected were tabulated and analyzed, according to the groups by means of χ^2 test for categorical variables.

Table 1 Demographic data

		Case Group I	Control Group II	χ^2	*p* value
Antenatal visits	Booked	3	31	17.550	0.000
	Unbooked	49	21		
Modified Kuppuswamy's SE scale status (education, occupation, family income per month in Rs)	Upper	10	12	1.277	0.735
	Upper middle	20	22		
	Lower middle	12	12		
	Upper lower	10	6		
	Lower	0	0		
Past H/O PTL or abortion	Present	11	4	3.817	0.050
	Not present	41	48		
BMI	Normal	41	40	6.661	0.084
	Obese	1	6		
	Overweight	7	6		
	Underweight	3	0		
Work	Working	7	6	0.088	0.767
	Not working	45	46		

Table 2 Overall presence of urogenital infection

		Case GroupI	Control Group II	χ^2	*p* value
Urogenital infections	Positive	19 (36.54 %)	9 (17.30 %)	4.887	0.027
	Negative	33 (63.46 %)	43 (82.70 %)		

Observations and Results

This prospective study was done on 104 married adult pregnant women, divided into Case Group I and Control Group II, matched for age and parity with 52 women in each group. Women in both the groups were in range of 19–38 years of age. Maximum numbers of women (80.77 %, 42/52) were in the age range of 20–30 years, with primigravida comprising 57.69 % (30/52). Table 1 shows that 94.63 % (49/52) of women in the Case Group were unbooked, which was significantly more (P 0.000) than those in the Control Group II, i.e., 40.38 % (21/52). According to modified Kuppuswamy's socioeconomic scale [11], the two groups were comparable (P 0.735) for living standard. Past history of preterm labor or abortion was present in 11 women in Group I compared to 4 in Group II, which was statistically significant (P 0.050). Forty-one women in Group I and 40 women in Group II had normal BMI, while three women were underweight in Group I, and none in Group II. Seven women in Group I and 6 in Control group were going out of house for work which was statistically comparable (P 0.767).

In our study, Table 2 shows that the urogenital infection was seen in 19 women in Case Group I (36.54 %) compared with 9 women in Control Group (17.3 %), and the difference was statistically significant (P 0.027). Table 3 shows the details of only urine, only HVS and both urine and HVS infections in the two groups. Microorganisms cultured in urine were predominantly gram negative bacilli and gram positive bacilli. E coli was the commonest microorganism cultured in the urine in both the groups. Predominant microorganisms isolated in HVS culture were gram positive cocci, gram negative bacilli, gram positive bacilli, and gram negative coccobacilli (Table 4). Gram staining of the vaginal smear was consistent with the culture reports. Commonest microorganisms cultured were Enterococcus fecalis followed by Staphylococcus aureus and E coli in vaginal swab culture. Candida albicans were isolated in one woman each in the two groups. Table 5

Table 3 Details of urogenital infections

	Presence of infection				χ^2	*p* value
	Both+ve	Urine+ve	HVS+ve	None		
Case Group I ($n = 52$)	1 (1.92 %)	7 (13.46 %)	11 (21.15 %)	33 (63.46 %)	7.620	0.050
Control Group II ($n = 52$)	2 (3.84 %)	1 (1.92 %)	6 (11.54 %)	43 (82.69 %)		

depicts the microorganisms cultured and antibiotics used according to sensitivity.

Discussion

In our study, 42 women were in 20–30 years of age group, and 71.42 % (30/42) of these were primigravida. Women in the age group <20 years had 2 primigravida in each group. In the age group more than 30 years (8 in each group), six were primigravida and two were multigravida.

Table 4 Gram staining of high vaginal swab smear (of women with positive cultures)

		HVS	
Case Group I		Gram +ve	Gram −ve
	Cocci	9	0
	Bacilli	0	5
	Yeast like	0	
Control Group II	Cocci	4	0
	Bacilli	2	2
	Coccobacilli	0	1
	Yeast like	1	

Case Group had more of unbooked women compared with Control group which was statistically significant (P 0.000). There was no statistical difference (P 0.735) in the socio-economic status of the two groups. In the Case Group 32 and in Control Group 34 women belonged to upper middle and lower middle class of socioeconomic scale. None of the women in our study were of lower socioeconomic class.

Past history of preterm labor or abortion in previous pregnancy was seen in 61.11 % (11/18) multigravida in Group I compared with 22.22 % (4/18) in Control Group II which was 38.89 % more in the women with preterm labor (Group I) showing a significant association of the past history of abortion or preterm labor and the women going into preterm labor in the present pregnancy. Pandey et al. [12] also reported that past history of preterm births was a significant contributory factor for preterm labor. We also observed that combined urogenital infections were associated in 19 women (36.54 %) with preterm labor compared with 9 women (17.30 %) in Control Group. The prevalence of urogenital infections in women with preterm labor was double compared with women at term gestation.

In a study by Chhabra and Patil [4], 14 % urine infection and 28 % cervical colonization in women with preterm labor were reported. Our preterm group showed urinary

Table 5 Microorganisms isolated on culture and their respective sensitive antibiotics

	URINE		HVS	
	Microorganism	Antibiotic	Microorganism	Antibiotic
Case Group I	$n = 8$[a]		$n = 12$[b]	
	E. Coli 4 (50 %)	Cephalexin, Piperacillin + tazobactum	E. Coli 2 (16.67 %)	Cefoperazone + sulbactum
	Enterrococcus fecalis 1 (12.5 %)	Amoxycillin + clauvulinic acid	Enterrococcus fecalis 5 (41.67 %)	Linezolid, Amoxycillin + clauvulinic acid
	Pseudomonas aeruginosa 1 (12.5 %)	Cephalexin	Pseudomonas aeruginosa 1 (8.33 %)	Cefoperazone + sulbactum
	Proteus vulgaris 1 (12.5 %)	Ciprofloxacin	Proteus vulgaris 1 (8.33 %))	Piperacillin + Tazobactum
	Staphylococcus aureus MSSA 1 (12.5 %)	Amoxycillin + clauvulinic acid	Staphylococcus aureus 4 (33.33 %)	Cefoperazone + sulbactum, linezolid
	Candidia albicans 1 (12.5 %)	Fluconazole	Enterobacter aerogenes 1 (8.33 %)	Linezolid
Control Group II	$n = 3$		$n = 8$[c]	
	E. Coli 2 (66.67 %)	Cefexime, ofloxacin	E. Coli 2 (25.00 %)	Cefexime, cefoperazone
	Staphylococcus aureus MSSA 1 (33.33 %)	Amoxycillin + clauvulinic acid	Staphylococcus aureus MSSA 1 (12.5 %), MRSA 1 (12.5 %)	Amoxycillin + clauvulinic acid
			Enterococcus fecalis 4 (50 %)	Ampicillin, linezolid
			Gardinella vaginalis 1 (12.5 %)	Cefixime
			Candida albicans 1 (12.5 %)	Clotrimazole

[a] Two microorganisms isolated in urine of one woman, Group I

[b] Two microorganisms isolated in HVS of two woman, Group I

[c] Two microorganisms isolated in HVS of two woman, Group II

tract infection in 13.46 % and genital tract infection in 21.15 %, while one woman had both cultures positive which is comparable to the observations by Chhabra and Patil [4]. Commonest microorganism isolated in urine culture was E coli and that in high vaginal swab was Enterococcus fecalis. In Control Group II, urinary tract infection was seen in 1(1.92 %), positive high vaginal swab culture in 6 (11.54 %), and both in 2 (3.84 %) women.

In the Case Group, overall urinary tract infection was detected in 15.38 % (8/52) which was 2.67 times more than that in the control group (5.77 %, 3/52). This shows that women in preterm labor had 2.67 times more incidence of urinary tract infection than their counterparts with term pregnancy. Our observations are similar to the results of Pandey et al. [12], who reported urinary tract infection in 20.34 % of women in preterm labor and those of McPheeters et al. [13] who reported 17.1 % of urinary tract infection in women with preterm labor and 10.9 % in women without preterm labor. In our study, positive high vaginal swab cultures were noted in 23.08 % (12/52) in the Case Group and 15.38 % (8/52) in Control Group. Lajos et al [14] reported the prevalence of endocervical colonization to be 14.20 % in preterm labor or premature of membranes.

Conclusion

We conclude that in our study, urogenital infection was 2.1 times (36.54 %) more in women with preterm labor compared to those in control group (17.30 %), which indicates a significant association of urogenital infections in preterm labor. Urogenital infections contribute significantly to the preventable causes of preterm labor. We recommend that women coming for first antenatal checkup should be investigated for the presence of asymptomatic genitourinary infections. Making early diagnosis of urogenital infections and treating them adequately with the antimicrobials will go a long way in decreasing the incidence of preterm labor, preterm births, and the associated neonatal and maternal morbidities.

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