Genitourinary infection and preterm labour: a retrospective study

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Abstract

Objectives: The relationship between genito-urinary infections and preterm labour (PTL) is known for ages but still the scenario in developing countries is projecting the same picture as prevalent 2-3 decades earlier. We undertook a study to find out the prevalence of genitourinary infections and PTL with the help of simple laboratory tests so as to enable the various health workers to diagnose and treat them early with the assistance of simple and cost-effective diagnostic methods.

Patients and methods: A retrospective study was undertaken in the department of Obstetrics and Gynaecology/ Microbiology, Government Medical College and hospital, Patiala which comprised of 500 cases in PTL between 28-37 weeks of gestation and 500 normal term cases for comparison. All the cases were subjected to microbiological analysis for bacterial (aerobic), fungal and protozoal examination by two high vaginal swabs and urine samples for routine examination, bacteriological examination, culture and antibiotic sensitivity. Statistical analysis was carried out using chi square and student ''t'' test.

Results: In the intervention group (Group A) of 500 cases of PTL the frequency of genital tract infection, urinary tract infection (UTI) and combined genitourinary infection (GUI) was 44%, 30% and 16% respectively as compared to 10%, 6% and 0% in the Group B, suggesting a statistically significant relationship of prevalence of genital as well as urinary tract infection in patients with preterm labour. The most common causative organisms of UTI were, *Escherichia coli* (14%) and *Klebsiella pneumoniae* (12%), while *Gardnella vaginalis* (16%) and *Candida albicans* (14%) were found to be commonly associated with genital tract infection. The number of low birth weight babies was significantly higher in intervention group than in the normal group.

Conclusions: Integration of a simple infection screening programme into routine antenatal care may reduce the incidence of preterm labour and improve perinatal outcome especially among the rural population of developing countries.

Key words: Preterm labour, genitourinary infections, intrauterine infections, bacterial vaginosis.

Introduction

Preterm labour (PTL) is defined as ''onset of labour with intact membranes after 28 weeks and before 37 weeks of gestation''. About 6-8% of all deliveries are preterm and of these about two-thirds occur between 34 and 37 weeks of gestation[1]. PTL is a heterogeneous condition with numerous associated social and medical risk factors. PTL and delivery is a major cause of perinatal morbidity and mortality in developing countries. The birth of preterm infants is a social, emotional, physical and financial burden not only on the parents but the society as well. Maternal infections of urogenital tract are a relatively frequent cause of preterm labour. The microorganisms may produce large amount of phospholipase A_2, an enzyme capable of liberating arachidonic acid from the phospholipids leading to synthesis of prostaglandins by placental membranes thus initiating the process of labour. The association between asymptomatic bacteruria and preterm delivery is controversial. But the overall high rate of incidence of preterm delivery does seem to favour the existence of a strong association between urinary tract infection (UTI) and

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preterm labour. Assessment of the magnitude is very essential to tackle the problem. There is overwhelming evidence that infection is a major cause of spontaneous preterm labour. Numerous studies have shown the relationship between the genitourinary infections and preterm labour but no study has ever documented how to go about its prevention in a large scale at peripheral level[2,3]. The simplicity and effectiveness of the model is very essential to ideally decrease the prevalence and to initiate the early intervention so as to prevent preterm labour especially in the rural areas which accounts for 65-70% of the total population of India.

Subjects and methods

The present study included 1000 cases which were divided into two clusters: Group A comprised of 500 cases of preterm labour, selected randomly, between 28 weeks to less than 37 weeks of gestation attending the O.P.D./labour ward of Obstetrics and Gynaecology department at Govt. Medical College/ Rajindra Hospital, Patiala. These patients had 2 or more painful uterine contractions in 10 minutes each lasting for 45 seconds with cervical dilatation ≥ 3 cm and 80% or greater effacement but with intact membranes. Group B comprised of 500 normal cases selected randomly for comparison, which carried the pregnancy to full term without any complication. The vaginal swabs and urine samples for culture and antibiotic sensitivity were taken at 28 weeks and at the time of antenatal visit at 37 weeks or more. These patients did not have any history of discharge, bleeding or leaking per vaginum. Patients with antepartum haemorrhage, anaemia, multiple gestation, polyhydramnios, uterine anomaly, fibromyoma uterus, rupture of membranes, pregnancy induced hypertension, eclampsia and those who received antibiotic therapy within 30 days of onset of labour were excluded from the study.

After eliciting a complete history and physical examination, per speculum and per vaginum examination was done. Maintaining strict asepsis, 2 high vaginal swabs were taken and transported to microbiological unit for culture and sensitivity within 1 hour. One vaginal swab was sent for wet mount and Gram stained smear preparation, while second swab was sent for inoculation of MacConkey's agar, blood agar and Sabouraud's dextrose agar media. A specimen of midstream urine was collected in a sterilized test tube for routine as well as culture and sensitivity examination. Gram staining was carried out for identification of Gram negative intracellular diplococci such as *Neisseria gonorrhoeae* and the presence of clue cells on staining which favours *Gardnerella vaginalis* infection on first high vaginal swab. Trichomonas vaginalis was identified as a flagellated, pear shaped and motile organism on wet mount preparation of normal saline on a clear glass slide. From second vaginal swab, identification of *Escherichia coli* and *Klebsiella pneumoniae* was done with MacConkey's agar medium with appearance of their particular colony characteristics such as 3-4 mm pink, moist and smooth colonies for *E. coli* and 3-4 mm dome shaped mucoid colonies for *K. pneumoniae*. The appearance of 2 mm golden yellow, circular, convex, smooth and opaque beta-haemolytic colonies on blood agar medium suggested the presence of *Staphylococcus aureus* while β-haemolytic streptococci colonies were identified as 0.5-1 mm in size, circular, semitransparent, low convex disc with a clear zone of beta-haemolysis around them. *Streptococcus agalactiae* was suggested by the presence of lysis (Christie, Atkins and Munch Peterson reaction) when staphy-lococcal beta haemolysin was poured on a plate on which group B streptococci were presumed to be present.

Candida albicans growth was seen as cream-coloured, shiny colonies, 2 mm in diameter on Sabouraud's dextrose agar medium and species identification was carried out by Germ tube test.

Gram staining of all the colonies from second vaginal swab was performed by Jensen's modification of Gram's method.

A few patients in preterm labour did present with a varied range of symptoms such as abdominal pain, discharge per vaginum, backache, dragging sensation, dysuria, burning micturition, etc. All these symptoms were attributable to genitourinary infections and were treated symptomatically along with the care of preterm delivery. Blood samples were also sent for toxoplasma IgM antibody titres. Statistical analysis was carried out using appropriate statistical tests like chi-square test, student 't' test, etc.

Results

All the 1000 subjects included in the study satisfied the inclusion and exclusion criteria. The various findings of the study are presented in tabulated manner as follows.

Table 1. Demographic profile of preterm labour and full term women

Demographic characteristics	*Group A*	*Group B*
Number of patients	500	500
Age of the patients in years (Mean ± SD)	23.78 ± 4.56	24.64 ± 3.98
Parity status	Nullipara – 210 Primipara – 140 Multipara – 150	Nullipara – 230 Primipara – 150 Multipara – 120
Educational level	Illiterate-330 Up to 5th class – 110 > 5th class – 60	Illiterate – 280 Up to 5th class – 140 > 5th class – 80
Financial status (family income/month)	<2000 – 350 3000-5000 – 130 >5000 – 20	<2000 – 320 3000-5000 – 140 >5000 – 40
Antenatal booking	Booked – 30 Unbooked – 470	Booked – 170 Unbooked – 330
Location	Rural – 460 Urban – 40	Rural – 420 Urban – 80

The demographic profile was almost comparable in population of both the clusters. Ninety four percent of the cases from Group A were un booked and only 66% patients from Group B were referred from other hospitals and centres. The statistical analysis of educational status revealed that 66% of the patients of group A were completely illiterate as compared to 56% in group B. The 70% of patients in group A and 64% in group B were below poverty line. 92% of patients in group A and 84% of patients in group B hailed from rural background.

Table 2. Microorganisms isolated from the vaginal swabs of preterm labour and normal term women

Groups	*Total no of patients*	*Escherichia coli*	*Klebsiella pneumoniae*	*Streptococcus agalactiae*	*Candida albicans*	*Gardnerella vaginalis*
Group A	500	30 (6%)	-	10 (2%)	70 (14%)	80 (16%)
Group B	500	10 (2%)	10 (2%)	-	20 (4%)	10 (2%)
X^2		1.416	2.010	1.01	3.662	6.815
p		>0.05	>0.05	>0.05	>0.05	<0.001
Statistical significance		NS	NS	NS	NS	HS

S – significant, NS – not significant, HS – highly significant

Table 3. Comparison of wet mount preparation for *Trichomonas vaginalis* from vaginal discharge of preterm and normal term women

Group	*Total no of patients*	*+ve cases*	*-ve cases*
Group A	500	30 (6%)	470 (94%)
Group B	500	-	500 (100%)
X^2	3.092		
p	>0.05		
Statistical significance	NS		

Vaginal swabs of 220 (44%) patients with preterm labour were positive for *E. coli*, *Streptococcus agalactiae, Candida albicans, Gardnerella vaginalis* and *Trichomonas vaginalis* (Table 2 and 3). *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Neisseria gonorrhoea* were not isolated from any patient's vagina. While in women with term pregnancy vaginal swab of only 50 (10%) patients were found positive for *E. coli, Klebsiella pneumoniae, Candida albicans* and *Gardnerella vaginalis*. Statistically *Gardnerella vaginalis* was found to have high significant (p <0.001) relation with preterm labour while the infection with other microorganism was not found to be significant (p>0.05).

Table 4. Microorganisms isolated from the vaginal swabs of preterm patients and women with term pregnancy

Group	*Total of patients*	*Escherichia coli*	*Klebsiella pneumoniae*	*Streptococcus agalactiae*
Group A	500	70 (14%)	60 (12%)	20 (4%)
Group B	500	10 (2%)	20 (4%)	-
X^2		6.007	2.735	2.540
p		<0.001	>0.05	>0.05
Statistical significance		HS	NS	NS

In patients with preterm labour urine samples of 150 (30%) patients were found positive for *E. coli*, *Klebsiella pneumoniae* and *Streptococcus agalactiae* in comparison to women with term pregnancy, where urine sample of only 30 (6%) patients were found positive for *E. coli* and *Klebsiella pneumoniae* suggesting a highly significant relation of urinary tract infection with preterm labour (p<0.01) (Table 4). Among pathogens, on statistical analysis, *E. coli* was found to have a significant (p<0.001) relationship with preterm labour.

Eight (16%) patients with preterm labour had infection of urinary tract as well as genital tract where as women with term pregnancy did not have it (Tables 1, 2, 3 and 5). In 20 cases (4%), *E. coli* was isolated in both urine and vaginal samples, while in one case urine sample was positive for *E. coli* and vaginal swab for *Trichomonas vaginalis*. There were 30 (6%) patients in whom *Klebsiella pneumoniae* was found in urine and *Gardnerella vaginalis* in vaginal discharge. In one (2%) patient urine was positive for *E. coli* and vaginal sample for *Gardnerella vaginalis*. *Streptococcus agalactiae* was isolated in urine as well as vaginal sample of 10 (2%) patients.

Table 5. Comparison of cases in preterm labour and women with term pregnancy according to the type of infection

Type of infection	*Group A*		*Group B*	
	No. of cases	*% age*	*No. of* cases	*% age*
Genital tract infection	220	44	50	10
Urinary tract infection	150	30	30	6
Asymptomatic	30	6	-	-
Symptomatic	120	24	30	6
Genito urinary infection	80	16	-	-

Statistical analysis	X^2	*DF*	p	*Significance*
Genital infection	14.56	1	<0.001	HS
Urinary tract infection	9.76	1	<0.001	HS

DF – degrees of freedom

Table 6. Incidence of delivery in cases of preterm labour with and without infection

	Infectious		*Non-infectious*		*Total*	
	No. of cases	*% age*	*No. of* cases	*% age*	*No. of* cases	*% age*
Delivered	230	79.31	60	28.57	290	58
Undelivered	60	20.69	150	71.43	210	42
Total	290	100	210	100	500	100

Statistical Analysis	X^2	*DF*	p	*Significance*
Infectious vs. non-infectious	7.024	1	<0.001	HS

In preterm labour patients, 230 (79.31%) out of 290 with positive culture of either urine or vaginal discharge delivered preterm, while 60 patients who delivered preterm had neither infection of urine nor of vagina. On statistical analysis the difference was highly significant (p<0.001).

Table 7. Birth weight of neonates born to preterm and term parturients and their distribution pattern

Birth weight (in kgs)	*Group A*		*Group B*	
	No. of cases	*%*	*No. of cases*	*%*
1-1.5	40	8	-	-
1.6-2	280	56	-	-
2.1-2.5	80	16	40	8
2.6-3	100	20	460	92
Total	**500**	**100**	**500**	**100**

Range	1.5-3.0	2.5-3.0
Mean ± SD	2.0±0.45	2.74±0.13
t value	11.02	
p value	<0.001	
Significance	HS	

Group A comprised of patients with preterm labour while group B comprised of women with term pregnancy.

As is evident from table 7, the majority of the patients (56%) with preterm labour delivered babies with a birth weight of 1.6 - 2 kg as compared to women with term prgnancy where majority (92%) of the delivered babies had a birth weight of 2.6 to 3 kg. On comparison the difference between the two groups was found to be highly significant (p<0.001).

Discussion

The findings of this retrospective study revealed that the majority of the patients with preterm labour were primigravida (42%) from rural areas. They had not received any form of antenatal care previously and reported in obstetric emergency ward of the hospital for the first time which is almost comparable to the earlier study done by Trivedi et al[2]. This reflects on the level of awareness especially among the rural population about the significance of antenatal care which ultimately depends upon the two interrelated conditions, i.e. education and socioeconomic conditions. Infections are responsible for preterm labour in 40% of cases and earlier the abnormal genital tract colonisation, the greater is the risk of adverse outcome[3]. Intrauterine infection is a major cause of preterm labour with or without intact membranes and accounts for 25% of all cases of PTL[4]. In this study, genital tract infection was detected as the causative factor in 44% of cases which is similar with the findings of study done by Lamont[3] but slightly different from the results obtained by Gonclave et al[4]. The reason for this difference is mainly due to the fact that in this study, we examined patients with intact membranes only.

The prevalence of vaginal infection was significantly higher in the intervention group than in the normal group. The incidence of detection of infection in the intervention group was highest for *Gardnerella vaginalis* followed by *Candida albicans, T. vaginalis, E. coli* and *Streptococcus aglacticiae* in descending order. *G. vaginalis* was reported to be highly significantly related to PTL, while detection of *C. albicans* and *T. vaginalis* did not have much statistically significant association with PTL. These findings of our study are almost comparable to the earlier studies done by Paul et al[5], Michael et al[6], Yim et al[7] and Sangita et al[8] with some variations especially regarding the prevalence of bacterial vaginosis. This is mainly attributable to a small limitation, as we studied the population only for *G. vaginalis* and not for anaerobic *Bacteroides*, and *Mycoplasma*.

UTI was found to be a significant prevalent factor in most cases of PTL in this study which correlates with the similar findings in some other studies[9]. According to Naheed et al[10] asymptomatic bacteruria was found to be a causative factor for PTL as 21.4% of bacteriuric women went into PTL ($p<0.05\%$) as compared to 4.9% non bactriuric women, the most common offender in such cases being *E. coli.* Meis et al[11] reported bacteruria in 6.2% of cases of PTL. The present study shows a significant relationship between bacteruria and PTL and the prevalence of asymptomatic bacteruria is 6% which is quite comparable with the findings of Meis et al[11] but not with the findings of Naheed et al[10]. The discrepancy is most probably related to our small sample size with gestation between 28 to<37 weeks in contrast to study done by Naheed et al[10] where it was independent of gestation period. Eighty (16%) patients in the present study, had infection of urinary tract as well as genital tract as compared to normal group where it was nil, suggesting the significance of prevalence of combined genitourinary infection in patients of preterm labour.

In recent years, the birth weight of premature babies has been regarded as an important determinant of pregnancy outcome, such that preterm birth is no longer identified solely by gestation age but also in terms of birth weight below 2.5 kg. In our study 56% of the patients delivered preterm babies with birth weight 1.6 to 2 kg which suggests a highly significant association of low birth weight with PTL and the similar results are quoted by Bique Osman et al[12].

Cary et al[13] observed the strong relationship between infection and preterm birth. We also report a statistically significant relationship between rate of delivery of preterm babies and prevalence of genitourinary infection. In this study group, majority of the patients were unbooked and without any antenatal care and most of them were illiterate and hailed from rural background. These patients either ignored the warning symptoms of PTL or they were not aware of them. That is why these patients reported to the emergency obstetric unit in the late stage when they already had 3 cm or >3 cm cervical dilatation.

In 58% of cases infection was detected either of genital tract or urinary tract. More investigations with a larger study population and including isolation of anaerobic organisms are needed for definite answers. The design of our study is quite simple and it is easy to be incorporated into a national programme.

Limitations

1. The study is designed and conducted in an institution and does not include the limitations and shortcomings when conducted in a peripheral health centre. These are the presence of a 24 hour obstetrician, trained paramedical staff, diagnostic facilities and many other such factors. But the study is a pioneer one and it was easier and justifiable to conduct such a study in a controlled atmosphere of an institution.

2. It does not truly represent the entire Indian rural population as some areas are better while some areas are worse, compared to population under study, in providing antenatal health care. It is difficult to conduct such a study in the entire nation at one time but the rural population of one area is almost comparable to that of other areas in demographic profile.

3. The study has not included the anaerobic infections and we have used the routine media only for diagnosis instead of employing special costly media. This was done deliberately as the main aim is to establish such simple and economical diagnostic methods at peripheral health centres later on.

Conclusions

In developing countries, like ours, improvement in socio-economic condition, education, nourishment, life style and personal hygiene, family planning and antenatal care will reduce the risk of preterm labour. Inspite of economic considerations and scarcity of specialized services at rural areas, no antenatal mother should be deprived of these services. The tests and diagnostic interventions followed by us can be easily reproduced at any peripheral health centre as they are highly cost effective. The timely antibiotics, according to sensitivity of infectious organisms, can arrest preterm labour and prevent preterm births and low birth weight babies. The ultimate goal of modern obstetrics is to have a healthy mother and a healthy baby. The crux of our study is aimed at prevention of irreversible damage, that is, rupture of membranes so as to prevent the preterm labour and also to decrease the maternal as well as the infant mortality and morbidity by employing the cost effective methods to cover a larger section of the society.

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