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## A case control study evaluating association of preterm Labor with vaginal infection

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### Abstract

**Introduction:** It is estimated that around 60-70% of preterm conveyances are likely because of subclinical infective or provocative causes. The current report was undertaken with an aim to study the role of vaginal infections in preterm labour.

**Methodology:** This prospective observational study was conducted in OB&GY Department of Teerthankar Mahaveer Medical College and Research Center. A total of 137 subjects, 102 in the case group and 35 in the control group were enrolled. Subjects in case group were divided into three groups, group 1 (n=31) had preterm labor without preterm delivery, group 2 (n=37) had preterm labor and spontaneously progressed to labor while group 3 (n=34) had preterm labor and were medically induced into labor for various reasons.

**Result:** In the present study most females were primigravida and were underweight belonged to lower socioeconomic strata. Majority had no history of abortion. Culture of vaginal discharge revealed that organisms were isolated in significantly higher proportion of subjects in PTL, S-PTB & M-PTB group as compared to control group. In the PTL, S-PTB, M-PTB and control group the commonest organisms were mixed microbes (27.27%), candida albicans (23.08%), Escherichia coli (22.22%) / Gardnerella vaginalis (22.22%) and Escherichia coli (25.00%) / Streptococcus agalactiae (25.00%), respectively. Most organisms were sensitive to the commonly used antibiotics. None of the organisms isolated was resistant to colistin.

**Conclusion:** Vaginal infection is commonly associated with preterm labor.

**Keywords:** Vaginal infection, primigravida, multigravida, anemia, UTI, Candida

### 1. Introduction

Preterm delivery as defined by WHO is 'birth of baby prior to 37 completed weeks of gestation'<sup>[1]</sup>. In the developed countries, the incidence of preterm birth is 5-10%, while it is around 25% in developing countries<sup>[2]</sup>. Overall rate of untimely birth goes between 5-18%<sup>[2]</sup>. Preterm birth is the leading cause of neonatal morbidity and mortality (~85%). Preterm birth complications are the leading cause of death among children under 5 years of age, responsible for approximately 1 million deaths in 2015. This is impacted by the maternal morbidity and mortality rates prevalent in the particular country. The maternal mortality rate in India as of 2017 was 145 per 1, 00, 000 live births. The American Association of Paediatrics and ACOG 1997: proposed that Uterine contractions of four in twenty minutes or 8 in 60minutes plus progressive cervical changes; Cervical dilatation of >1cm; Cervical effacement of >80% is preterm labor.

Most of the times, the cause of preterm labour is unknown, but many conditions have been associated with an increased risk of preterm delivery. Common causes of preterm birth embrace manifold pregnancies, infections & chronic ailments such as diabetes and high BP.

To date, causes of prematurity can be found in fewer than half of all cases<sup>[3]</sup>. Some studies have associated preterm delivery with ascending genital microflora<sup>[4]</sup>. It is estimated that around 60-70% of preterm deliveries are due to subclinical infective causes<sup>[5]</sup>. Various tests can be employed for diagnosis of BV, the most commonly used criteria is Amsel criteria which includes: 1) the nearness of slim, homogenous release that clings to the vaginal dividers; 2) a vaginal release pH more prominent than 4.5; 3) an amine, fishy smell with utilization of 10% potassium hydroxide answer for the release (whiff test); and 4) hint cells on saline wet mount. If 3 out of the 4 criteria are present the diagnoses of BV is made regardless of presence of symptoms.

This report aims to study the role of vaginal infections in preterm labour with the objective of evaluating the association between vaginal infections and preterm labour.

## 2. Methodology

This prospective observational case control study was conducted in Department of Obstetrics and Gynecology of Teerthanker Mahaveer Medical College and Research Center from April 2019 to Feb 2020. A total of 137 subjects, 102 in the case group and 35 in the control group were enrolled. The case group consisted of pregnant women, less than 37 weeks of gestation, that had preterm labour associated with uterine contractions of 4 in 20min or 8 in 60 min along with cervical dilatation of  $\geq 1$ cm and effacement of  $>80\%$ . Subjects in case group were divided into three group, group 1 (n=31) consisted of subjects that had preterm labor without preterm delivery, group 2 (n=37) consisted of patients that had preterm labor and spontaneously progressed to labor while group 3 (n=34) consisted of patients that had preterm labor and were medically induced into labor due to reasons for example, rupture of membranes, irregularities of origination, deformities of the embryo, overdistended uterus, hydramnios, various developments, fetal demise, cervical incompetency, uterine oddities, held intrauterine device, genuine maternal ailment, gestational diabetes mellitus, gestational hypertension, and dynamic fundamental disease. Control group consisted of 35 subjects that delivered normally at term. Gestational age was calculated using Naegele's formula and varied using fetal sonography scans.

Pregnant females that were excluded included those with APH, those with IUD, etc.

For each of the enrolled subject, written informed consent was obtained. After consenting demographic details were collected along with personal, family and obstetrics history. Details on previous pregnancy outcomes including presence of any risk factors, such as genitourinary and respiratory infections, GDM, anaemia, hypertensive disorders, heart disease or any other medical disease, obstetric risks like hydramnios, multifetal gestation, malpresentation and uterine anomalies, in index pregnancy, was collected. A thorough and complete systemic and obstetric examination was conducted for each of the enrolled patient. Patients with GDM and hypertensive disorder of the pregnancy were identified using standard criteria.

In an aseptic environment, cervix and vagina were examined using per speculum. A swab was taken using Q-tip from the posterior fornix of vagina and kept in capped tube. This swab sent to the microbiology department for gram staining and culture sensitivity. Cervical length and dilatation were evaluated using per vaginal examination. *pH* of the vaginal secretions was assessed by placing pH paper on the lateral wall of the vagina. Obstetric ultrasound was performed to determine cervical length, amniotic fluid index, fetal weight, placental localisation and separation. Midstream urine sample was also collected and sent for culture and sensitivity. Patients were monitored for fever, maternal tachycardia, uterine tenderness, foul smelling vaginal discharge or any other features of sepsis.

In microbiology lab the swab was analysed in the following manner:

Microscopic examination of the *wet prep* was done. The slide was warmed briefly (to increase motility of trichomonas) and examined at both medium and high power for trichomonas, clue cells, and yeast. KOH mount preparation was mounted to identify budding yeast or hyphae. *Gram stain* and *Cultures* of the vaginal discharge was done using standard methods.

Data for the study was compiled using MS excel and data was analysed by calculating percentages.

## 3. Results

A total of 137 females subjects were enrolled in the study.

**Table 1:** Distribution of subjects

Group	N	%
PTL	31	22.63%
S-PTB	37	27.01%
M-PTB	34	24.82%
Control group	35	25.55%
Total	137	100.00%

The mean age of the subjects in case was  $26.06 \pm 5.02$  years while that in control group was  $25.64 \pm 4.82$  years. The age distribution of enrolled subjects was as shown in table 2. In the PTL (38.71%) and M-PTB (38.24%) group higher proportion of patients were in the 21-25 years age group while in the S-PTB (35.14%) and control (40.00%) group higher proportion of subjects were in the 18-20 years and 26-30 years age group.

**Table 2:** Age distribution of the subjects

Age Group	PTL		S-PTB		M-PTB		Control group	
	N	%	N	%	N	%	N	%
18-20	7	22.58%	13	35.14%	7	20.59%	9	25.71%
21-25	12	38.71%	11	29.73%	12	35.29%	11	31.43%
26-30	9	29.03%	9	24.32%	13	38.24%	14	40.00%
31-35	3	9.68%	4	10.81%	2	5.88%	1	2.86%
Total	31	100.00%	37	100.00%	34	100.00%	35	100.00%

In the present study most of the females were primigravida as shown in table 2 and most of the subjects were underweight and belonged to lower socioeconomic strata and came from rural parts of society. Majority of the pregnancies were booked and majority had no history of abortion.

**Table 3:** Various demographic and other parameters of subjects

Parameters	PTL		S-PTB		M-PTB		Control group	
	N	%	N	%	N	%	N	%
<b>Gravida status of the females</b>								
Primigravida	16	51.61%	18	48.65%	17	50.00%	18	51.43%
Gravida 2	9	29.03%	8	21.62%	11	32.35%	12	34.29%
Gravida 3	5	16.13%	7	18.92%	4	11.76%	4	11.43%
Gravida 4	1	3.23%	4	10.81%	2	5.88%	1	2.86%
<b>Body Mass Index of Subjects</b>								
Underweight	21	67.74%	20	54.05%	19	55.88%	16	45.71%
Ideal	7	22.58%	8	21.62%	10	29.41%	13	37.14%
Overweight	2	6.45%	5	13.51%	4	11.76%	5	14.29%
Obese	1	3.23%	4	10.81%	1	2.94%	1	2.86%
<b>Rural / urban population</b>								
Rural	17	54.84%	19	51.35%	19	55.88%	20	57.14%
Urban	14	45.16%	18	48.65%	15	44.12%	15	42.86%
<b>Booked / Unbooked pregnancy</b>								
Booked	19	61.29%	24	64.86%	21	61.76%	22	62.86%
Unbooked	12	38.71%	13	35.14%	13	38.24%	13	37.14%
<b>Socioeconomic status of subjects</b>								
Lower	19	61.29%	20	54.05%	21	61.76%	21	60.00%
Lower Middle	8	25.81%	9	24.32%	7	20.59%	7	20.00%
Upper Middle	3	9.68%	7	18.92%	5	14.71%	5	14.29%
Upper	1	3.23%	1	2.70%	1	2.94%	2	5.71%
<b>History of abortion</b>								
0	12	38.71%	13	35.14%	13	38.24%	14	40.00%
1	9	29.03%	11	29.73%	12	35.29%	11	31.43%
2	7	22.58%	9	24.32%	7	20.59%	9	25.71%
3	3	9.68%	4	10.81%	2	5.88%	1	2.86%
<b>History of Pre-term labor</b>								
0	17	54.84%	19	51.35%	21	61.76%	22	62.86%
1	9	29.03%	9	24.32%	8	23.53%	8	22.86%
2	5	16.13%	5	13.51%	5	14.71%	4	11.43%
3	0	0.00%	2	5.41%	0	0.00%	1	2.86%

Culture of vaginal discharge revealed that organisms were isolated in significantly higher proportion of subjects in the PTL, S-PTB and M-PTB group as compared to control group as shown in table 4.

vaginalis (22.22%) and Escherichia coli (25.00%) / Streptococcus agalactiae (25.00%), respectively. Organisms that were isolated from vaginal discharge cultures were as in table 5, figure 1.

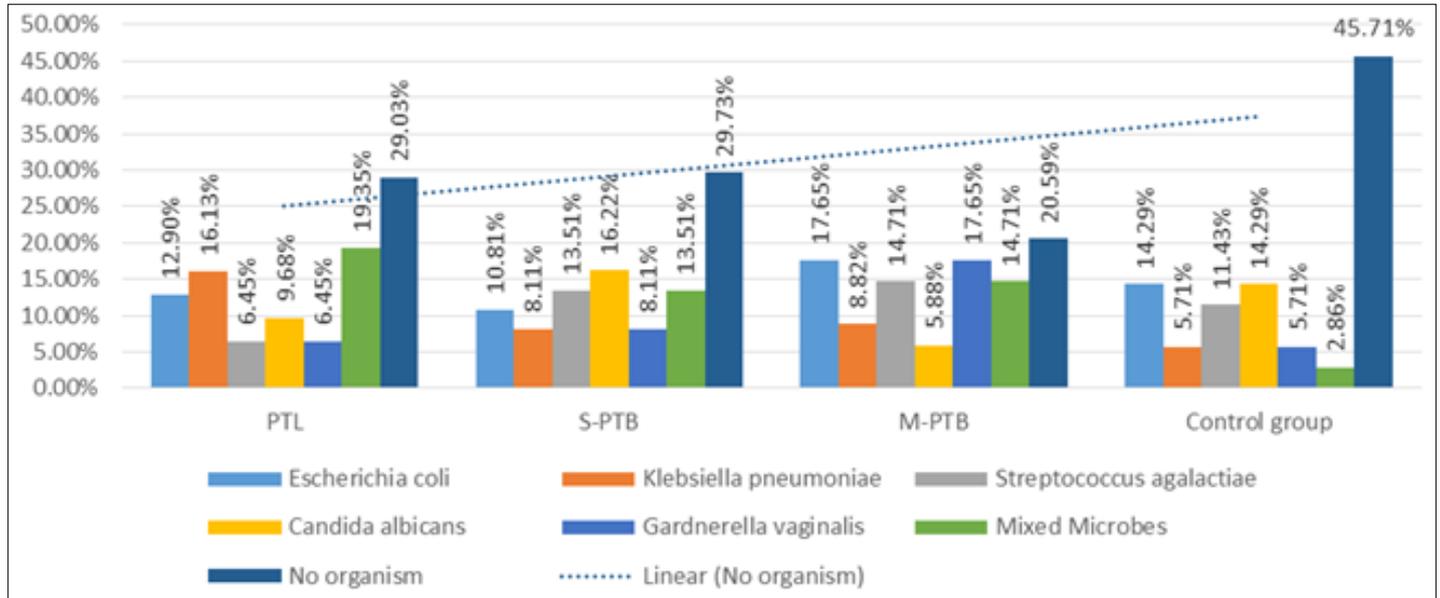
**Table 4:** Presence or absence of organism on vaginal discharge culture

	PTL		S-PTB		M-PTB		Control group		P-value
	N	%	N	%	N	%	N	%	
Organism Present	22	70.97%	26	70.27%	27	79.41%	16	45.71%	<0.001
Organism Absent	9	29.03%	11	29.73%	7	20.59%	19	54.29%	

**Table 5:** Organism isolated on vaginal discharge culture

Organism Isolated	PTL		S-PTB		M-PTB		Control group	
	N	%	N	%	N	%	N	%
Escherichia coli	4	18.18%	4	15.38%	6	22.22%	4	25.00%
Klebsiella pneumoniae	5	22.73%	3	11.54%	3	11.11%	2	12.50%
Streptococcus agalactiae	2	9.09%	5	19.23%	5	18.52%	4	25.00%
Candida albicans	3	13.64%	6	23.08%	2	7.41%	3	18.75%
Gardnerella vaginalis	2	9.09%	3	11.54%	6	22.22%	2	12.50%
Mixed Microbes	6	27.27%	5	19.23%	5	18.52%	1	6.25%

In the PTL, S-PTB, M-PTB & control group the commonest isolated organisms were mixed microbes (27.27%), candida albicans (23.08%), Escherichia coli (22.22%) / Gardnerella



**Fig 1:** Organism grown on vaginal discharge culture

The sensitivity pattern of the organisms isolated was as shown in the table 6. Most of the organism isolated were sensitive to the

commonly used antibiotics. None of the organisms isolated was resistant to colistin.

**Table 6:** Sensitivity pattern of organisms

Group	Organism	Sensitivity to Antibiotics										
		Clindamycin	Erythromycin	Chloramphenicol	Levofloxacin	Tetracycline	Ciprofloxacin	Ofloxacin	Clarithromycin	Colistin	Azithromycin	Doxycycline
PTL	EC	75%	75%	25%	75%	25%	75%	75%	100%	100%	75%	75%
	KP	80%	80%	40%	40%	60%	40%	20%	80%	100%	80%	100%
	SA	100%	100%	50%	50%	50%	50%	50%	100%	100%	50%	50%
S-PTB	EC	75%	75%	50%	75%	50%	50%	75%	75%	100%	50%	75%
	KP	100%	67%	33%	67%	33%	33%	67%	100%	100%	100%	100%
	SA	80%	80%	40%	40%	20%	60%	60%	80%	100%	100%	100%
M-PTB	EC	83%	67%	50%	50%	33%	67%	67%	100%	100%	83%	83%
	KP	67%	67%	33%	67%	33%	67%	67%	100%	100%	100%	100%
	SA	80%	60%	40%	80%	40%	80%	80%	80%	100%	80%	80%
Control group	EC	75%	75%	50%	50%	75%	75%	75%	100%	100%	75%	100%
	KP	100%	50%	50%	50%	50%	50%	100%	100%	100%	50%	50%
	SA	50%	50%	50%	75%	25%	75%	75%	100%	100%	100%	75%

S=Sensitive; R=R; EC - Escherichia coli; KP - Klebsiella pneumonia; SP - Streptococcus agalactiae

**4. Discussion**

In the present study, the mean age of the subjects in the case group was 26.06 ± 5.02 years while that in the control group was 25.64 ± 4.82 years and maximum females in the PTL (38.71%) and M-PTB (38.24%) group were in the 21-25 years age group while in the S-PTB (35.14%) and control (40.00%) group they

were in the 18-20 years and 26-30 years age group. Yarlagadda S *et al.*, showed that maximum of subjects were <20 years age (32.75%) and 22.41% of females were between 22-25years. We found that preterm labor occurred in extremes of ages, this was also comparable to reported literature, Yarlagadda S *et al.* in their study found that PTL occurred in 41.37% cases in extremes

of age groups [6]. Samim A *et al.* similarly reported PTL in 36.5% of cases, in extremes of reproductive age group [7]. Contradictory to our findings Shannon FF *et al.* and Renay W *et al.* reported PTL in only 15.8% and 18.8% cases in extremes of age group [8, 9].

In our study majority of cases were primigravida this was contradictory to the study by Yarlagadda S *et al.* wherein 21.55% were primigravida while 78.44% were multigravidas [6]. Shlomo E *et al.* in their study also found that preterm delivery rate was around 93% in multipara. [10] However, Shannon FF *et al.* and Singh U *et al.* found that 45.11% and 47% cases were primigravidas and 54.39% and 53% were multigravidas respectively [5, 8]. Even in the study by Patel U *et al.* and Trivedi DR *et al.*, a higher proportion of subjects with PTL were primigravida [11, 12].

In the present study around 60% pregnancies were booked; this may be because subjects in the present study belonged to lower socio-economic strata and they have to go out to work apart from doing household chores. These subjects visit the facility infrequently and usually reported late. This results in these patients having co-morbidities such as malnutrition, anemia and increased chances of infections, which remained untreated. Our study found that majority of the subjects belonged to lower and lower middle status and also most of them came from rural set up. Yarlagadda S *et al.* reported 56.89% booked pregnancy cases which had PTL however similar to our study they had 40.51% and 37.06% cases belonging to lower and lower middle socioeconomic class and 70.69% of population coming from rural [6]. It was also observed that majority (46.51%) of the subjects were underweight, belonging to lower socioeconomic status and working had for daily living may be responsible for this.

In the present study it was seen that majority of females had history of atleast one abortion while lesser proportion of females had history of preterm labor in previous pregnancies, similar to this Yarlagadda S *et al.* observed that 38.79% and 32.75% of females had had previous h/o abortion and preterm delivery respectively [6]. Shannon FF *et al.* reported, 35% and 12.11% cases with previous h/o abortions and preterm births, respectively [8]. Samim A *et al.* reported h/o previous preterm births in 15% of the subjects enrolled [7]. History of previous preterm births and abortions was reported in 14.4% cases each in the study by Pandey K *et al.* [13].

Present study revealed that organism growth on vaginal discharge culture were isolated in significantly higher proportion of subjects in the PTL, S-PTB and M-PTB group as compared to control group. In the PTL, S-PTB, M-PTB and control group the commonest isolated organisms were mixed microbes (27.27%), candida albicans (23.08%), Escherichia coli (22.22%) / Gardnerella vaginalis (22.22%) and Escherichia coli (25.00%) / Streptococcus agalactiae (25.00%), respectively. Priestley CJ *et al.* established that the colonization pace of microorganisms in the vagina could be influenced by not just specialized variables, for example, location technique and testing site, yet additionally interior and outer components of every person [14]. In the study by Patel UM *et al.* for the situation gathering (Group An) of 50 instances of PTL the recurrence of genital plot contamination and consolidated genitourinary disease (GUI) was 44%, and 16% separately when contrasted with 10% and 0% in the Group B, which recommended a measurably huge relationship of pervasiveness of genital in patients with preterm work. The most well-known causative living beings of genital diseases were Gardnerella vaginalis (16%) and Candida albicans (14%). G. vaginalis was accounted for to be exceptionally essentially

identified with PTL, while location of C. albicans and T. vaginalis didn't have a lot of factually noteworthy relationship with PTL [11]. The findings of the present study correlate with that of studies by Meis PJ *et al.* and Shilpa M.N *et al.* [15, 16].

The sensitivity pattern of the organisms isolated suggested that most of the organism isolated were sensitive to the commonly used antibiotics. None of the organisms isolated was resistant to colistin. In the study by Choi SN *et al.* it was observed by the authors that the defiance proportions of clindamycin, erythromycin, chloramphenicol, and levofloxacin in 26 GBS isolates were 11.5%, 11.5%, 3.8%, and 7.7%, respectively. All isolates of GBS were susceptible to penicillin, ceftriaxone, and vancomycin. The way of life of M. hominis got from 2 patients were impervious to erythromycin, antibiotic medication, ciprofloxacin, ofloxacin, clarithromycin, and azithromycin and vulnerable to josamycin and pristinamycin. The M. hominis culture from 1 of the 2 patients was helpless to doxycycline. The opposition rates to ciprofloxacin, ofloxacin, tetracycline, azithromycin, erythromycin, clarithromycin, and doxycycline for 56 U. urealyticum detaches were 96.4%, 55.4%, 19.6%, 12.5%, 8.9%, 7.1%, and 7.1%, individually. All the U. urealyticum confines were vulnerable to josamycin and pristinamycin. [17] Thus, it can be seen that vaginal infection is commonly associated with preterm labor.

## 5. Conclusion

Prematurity is associated high rate of neonatal morbidity and mortality. Majority of the causes of preterm labor especially vaginal / urinary infection, anemia, hypertensive disorder of pregnancy are either preventable or easily treatment. It should be made mandatory to screen all the antenatal women for the precipitating causes of PTL especially asymptomatic genitourinary infections and provide necessary measures to manage them as early recognition and prompt treatment will help prevent preterm labor and thereby its associated neonatal morbidity and mortality.

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