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RESEARCH ARTICLE

A study on abnormal vaginal pH in the midtrimester of pregnancy as a screening predictor of preterm labor in asymptomatic patients: a randomized controlled trial

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ABSTRACT

Objectives: The aim of the study is to screen for abnormal vaginal pH in the mid trimester of pregnancy in asymptomatic patients and to assess whether abnormal pH is an indicator of PTB. **Methodology:** Randomised controlled trial conducted in the outpatient department of a tertiary care hospital from March 2019 to August 2020. Total of 170 asymptomatic pregnant women with gestational age between 13 and 22 weeks who had a vaginal pH more than 4.5 were randomised for either treatment with clindamycin vaginal tablet for three days or with no pharmacological intervention. A vaginal smear was also prepared to diagnose bacterial vaginosis. The patients were followed up until delivery and the gestational age at birth, birth weight of the newborn and the perinatal outcome were recorded. **Results:** The preterm delivery was more in the control group (54.8%) than the case group (4%) and was mostly late preterm births. Mean gestational age was 34 weeks and the mean birth weight was 2.2.kg. Gram staining showed bacterial vaginosis in both case and control groups. **Conclusions:** Abnormal vaginal pH is a better predictor of preterm labor even in asymptomatic pregnant women. The study also suggests a method for using intravaginal bacterial findings during pregnancy as a biomarker to evaluate the risk of preterm delivery.

Keywords: Abnormal vaginal pH, bacterial vaginosis, chorioamnionitis, Nugent score, preterm labor.

Preterm birth (PTB), defined as birth before 37 weeks of gestation, is the world's commonest cause of perinatal morbidity and mortality.[1] Approximately 15 million PTBs (~12% of all births) occur annually.[2] Preterm babies that survive commonly have greater risk of developing respiratory, gastrointestinal and neuro developmental complications.[3] Accordingly, the prediction and possible prevention of PTB has become a major health care priority.[4] Approximately two - thirds of PTBs occur without an identifiable cause and follow spontaneous onset of preterm labour (PTL), and preterm premature rupture of membranes (PPROM).[5] About 40-50% of spontaneous PTBs are associated with ascending intrauterine infection, which could be related to changes in the vaginal microflora. The human vaginal microflora is a community of microorganisms (mainly bacteria) that represents a balanced mutualistic relationship which critically influences the reproductive physiology and immunity of the host. Although, opportunistic pathogens are present, this diverse microbial community constitutes a first line of defence against foreign pathogenic organisms.[7] The composition of the vaginal microbial community is dependent on host-environmental interactions varying between and within individuals over time.[8] The vaginal ecosystem can influence conception, the timing of delivery, and risk of acquiring sexually transmitted infections (STIs).[9] An imbalance in the normal vaginal bacteria is therefore is known as bacterial vaginosis. Chorioamnionitis is the main cause of preterm delivery,

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which occurs in the background of bacterial vaginosis. When bacterial vaginosis causes cervicitis or vaginitis it then progresses to inflammation of fetal membranes and causes premature rupture of membranes and labor. Therefore it is important to prevent preterm delivery and associated poor perinatal outcome. Hence the study was conducted to prove the association between abnormal vaginal pH in asymptomatic patients and the risk of preterm birth.

Materials and methods

The present study was conducted in outpatient department of OBG at a tertiary care centre, Thrissur, Kerala. It was a randomised controlled trial with institutional human ethics committee approval conducted during March 2019 to August 2020. The study included asymptomatic, uncomplicated singleton pregnant women in the gestational age group 13 to 22 weeks. Patients with history of preterm birth, complaints of vaginal discharge, suspicion of chorioamnionitis or cervical cerclage during the present pregnancy were excluded from the study. The vaginal pH was tested for every patient using pH paper and a pH more than 4.5 was considered to be significantly associated with bacterial vaginosis. A total of 170 pregnant women satisfying the inclusion criteria were selected and the patient with pH more than 4.5 were divided into two groups by computer generated randomised sampling method. One group was given clindamycin vaginal tablet for 3 days and the other group was not given any pharmacological intervention. A vaginal smear was prepared and gram staining of the smear was done to diagnose bacterial vaginosis according to Nugent score. Both the groups were followed up until delivery and the gestational age at birth, birth weight of newborn and the perinatal outcome were recorded.

Data analysis: Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Chi-square test was applied for categorical variables and independent two sample t test was applied for numerical variables. Analyses of neonatal outcome among case and control groups were performed by Fischer's exact test. P value of <0.001 was considered as statistically significant.

Results

In our study the antenatal women with abnormal vaginal pH were divided into two groups of 85 participants. Nearly half of the patients were between the age group 18 to 25 years in both groups while the lowest number of case and control were seen in age groups 31 to 35 year groups (table 1). The mean age of the total population is 26.34 ± 3.8 years. In the control group there was slightly lower mean age of 26.18 ± 3.8 years when compared to 26.51 ± 3.9 years for case group. The gestational age at time of examination were around 13 weeks in both case and control group.

Table 1: Age wise distribution of case and control groups

Age groups (years)	Case n (%)	Control n (%)	Chi-square test
18 to 25 years	36 (42.4)	42 (49.4)	
26 to 30 years	35 (41.2)	30 (35.3)	p value: 0.643
31 to 35 years	14 (16.5)	13 (15.3)	

Table 2: Cervical length in USG

Cervical length in USG (cm)	Case n (%)	Control n (%)	Chi-square test
3 to 3.4 cm	66 (77.6)	65 (76.5)	p value: 0.722
3.5 to 4.1 cm	19 (22.4)	20 (23.5)	
Mean cervical length	3.25 ± 0.30	3.24 ± 0.29	0.876 (T- test)

Table 3: Vaginal pH using pH paper

Vaginal pH	Case n (%)	Control n (%)	Chi-square test
4.5	02 (02.3)	03 (03.5)	p value: 0.569
> 4.5	83 (97.7)	82(96.5)	
Mean vaginal pH	4.913 ± 0.14	4.911 ± 0.14	0.902 (T- test)

The cervical lengths were similar in both the case and control groups. The mean cervical length was almost the same in two groups (table 2). The vaginal pH using pH paper method showed majority of the mothers were more than 4.5 pH levels and they were similar in the both case and control groups (table 3).

Table 4: Gestational age at delivery

Gestational age at delivery	Case n (%)	Control n (%)	Chi-square test
<37 weeks	04 (04.9)	40 (54.8)	
> 37 weeks	77 (95.1)	33 (45.2)	p value: <0.001
Total	81 (100)	73 (100)	

Table 4: Gestational age at delivery

Gestational age at delivery	Case n (%)	Control n (%)	Chi-square test
<37 weeks	04 (04.9)	40 (54.8)	
> 37 weeks	77 (95.1)	33 (45.2)	p value: <0.001
Total	81 (100)	73 (100)	

Table 5: Nugent score for bacterial vaginosis

Gram stain	Case n (%)	Control n (%)	Chi-square test
4 to 6 (Intermediate)	22 (27.2)	19 (26.0)	p value:
7 to 8 (Bacterial vaginosis)	59 (72.8)	54 (74.0)	<0.001
Total	81 (100)	73 (100)	

There were 4 patients excluded from the case group and 12 patients excluded from control group due to lost follow up, asymmetric IUGR, GDM etc. The preterm patients were in total 44, in them only 4 were in case group and 40 in control group. In full term group, 77 patients were in case group and 33 in control group (table 4). This difference was statistically significant.

The gram stain showed bacterial vaginosis were more in both the case (72.8%) and control groups (74.0%) (table 5).

Neonatal outcome showed a greater number of lower birth weight patients in control group. The gestational age at the time of delivery less than 37 weeks was more in the control group (54.8%) than the case group (4%). Late preterm delivery was seen more in control groups when compared to case group; this difference was statistically significant. NICU admission was higher in control group. Respiratory distress syndrome was the highest.

Table 6: Neonatal outcome with case and control

Birth weight	Case n (%) (N=81)	Control n (%) (N=73)	Chi-square test
< 1 kg	06 (07.3)	25 (34.6)	
1 to 2.5 kg	66 (81.5)	46 (63.0)	p value: <0.001
2.5 to 3.5 kg	09 (11.2)	02 (2.4)	
Preterm delivery	**Case; n (%) (N=15)**	**Control n (%) (N=29)**	Fischer's Exact test
Late preterm	09 (60.0)	19 (11.1)	
Early preterm	04 (05.5)	04 (04.9)	p value: <0.001
Very preterm	02 (02.7)	04 (04.9)	
Extreme preterm	00 (00.0)	02 (02.5)	
NICU admission	**Case; n (%) (N=81)**	**Control n (%) (N=73)**	Fischer's Exact test
RDS	00 (00.0)	17 (23.3)	
Neonatal jaundice	01 (01.4)	02 (02.7)	
RDS, Hypoglycaemia	00 (00.0)	02 (02.7)	
Hypoglycaemia	00 (00.0)	01 (01.4)	p value: <0.001
Preterm sepsis	00 (00.0)	01 (01.4)	
RDS, Sepsis	00 (00.0)	01 (01.4)	
Sepsis	00 (00.0)	01 (01.4)	

Discussion

Both the groups were comparable with respect to the maternal age, gestational age, cervical length and vaginal pH. The mean age of the total population was 26.34 ± 3.8 years. In the control group there was slightly lower mean age of 26.18 ± 3.8 years when compared to 26.51 ± 3.9 years for case group. There were similar demographic findings in both groups in our study. Which was similar to other studies reviewed by Friese et al, [11] where mean age in study group was 29.74 ± 4.2 years and in control group was 23.8yrs ± 3.5 years. In many of the studies it was found that advanced maternal age (40 years and over) was associated with an increased risk of preterm birth. Lowest risk was in the age group 24-30 years. Preterm birth was mainly spontaneous in younger women (20-24 years) whereas it was more frequently of iatrogenic origin in women over 40 years.

In our study the gram stain showed bacterial vaginosis were more in both the case (72.8%) and control groups (74.0%). We had intermediate group of 22 in case and 19 in the control group and among the bacterial vaginosis group there were 59 in the case group and 54 in the control group. We found the presence of high levels of *Gardnerella vaginalis* and low levels of lactobacillus in the vaginal smear prepared. Todate, *Gardnerella vaginalis* has been consistently linked to bacterial vaginosis and is one of the most common pathogen found among women with preterm prelabor rupture of membranes. In future this study may help to identify women with highest risk of preterm birth based on vaginal flora characteristics during pregnancy. The drawback of the study was that repeat samples were not taken after treatment with clindamycin to ascertain the status after treatment. The neonatal outcome showed a greater number of lower birth weight patients in control group. Which corresponded to the studies by reported by Hauth et al and Goldenberg et al. [12,13] In fact, preterm labour in vaginal pH higher than 5 was seen to be three times more than the vaginal pH below 5. Regarding bacterial vaginosis and alkaline vaginal pH, the findings of the current study is almost consistent with those of Lim KH et al[15] who found that women who were referred for preterm labour had approximately double chance of being diagnosed with bacterial vaginosis. Kumar S et al conducted a prospective trial and concluded that attributive risk of preterm labor in women with bacterial vaginosis was 5.0476 (CI 95% 1.9677 to 12.952). [16] Sendag et al via a prospective study not only found that there is a significant correlation between vaginal pH > 5 and increase risk of preterm delivery (that supports our results), but also found simultaneously, there is a significant correlation between an elevated vaginal pH (> 5.0) and a shortened cervical length ($r = -0.59$, $p < 0.001$).[17] In our study, bacterial vaginosis was related to late preterm births at a mean gestational age of 34 weeks and a mean birth weight of 2.2 kg. The NICU admission showed more significant cases of neonatal complications in control group which corresponds to reviewed study by Fatemeh Foroozanfard et al,[14] who also showed a significant correlation between alkaline vaginal pH.

Conclusion

Bacterial vaginosis and pH of vagina were found to be a good predictor of preterm labour in asymptomatic pregnant women. Patients with abnormal vaginal pH who were not treated for the same were having significantly higher rates of preterm labour and neonatal complications. The results of this study also suggest a method for using intravaginal bacterial findings during pregnancy as a biomarker to evaluate the risk of preterm delivery.

Conflict of interest: None. **Disclaimer:** Nil.

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