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STUDY OF PREVALENCE OF BACTERIAL VAGINOSIS IN PRETERM AND TERM LABOUR- AN OBSERVATIONAL STUDY

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ABSTRACT

Background: Preterm labour is the primary cause of illness and death during pregnancy. Bacterial vaginosis is one of the numerous reasons of preterm labour, occurring in around 30 to 35 percent of cases.

Aims: To investigate the relationship between bacterial vaginosis and preterm labour, as well as the prevalence of bacterial vaginosis in women presenting with both preterm and term labour.

Materials and methods: This observational research investigated the frequency of bacterial vaginosis among women hospitalised for preterm or term labour. Each group had 100 patients evaluated, and the findings were statistically analysed.

Results: Significantly more preterm labour patients than term labour patients had vaginal discharge indicative of bacterial vaginosis (28 percent vs 4 percent respectively) There were more preterm patients who met Amsel's criteria for a BV diagnosis than term individuals (30 percent vs. 4 percent). Neither of the two groups included any indicator cells throughout the current investigation. The most typically generated microorganisms were Enterococcus, Candida, and Group B Streptococcus. Infections of the genital tract were more prevalent in the preterm group than in the late labour group (22 percent vs. 6 percent). In the preterm and term groups, BV-negative moms had more infants with low birth weight than BV-positive mothers. The neonatal and postpartum complications of preterm and term children of BV-positive moms were greater than those of BV-negative mothers. Respiratory distress syndrome was the most prevalent consequence, followed by neonatal sepsis and congenital pneumonia. Puerperal pyrexia was the most prevalent complication, followed by atonic PPH.

Conclusion: It has been shown that bacterial vaginosis plays a crucial role in the development of premature labour. Therefore, early identification and treatment of bacterial

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vaginosis may lower the risk of preterm labour and its associated problems for both mother and child.

Keywords: Amsel's criteria, Bacterial vaginosis, Maternal complications**,** Neonatal complications

INTRODUCTION

One of the most problematic obstetric problems is preterm labour (PTL), along with delivery. PTL is a significant factor in predicting poor baby outcomes in terms of survival and quality of life. About 5-10% of all pregnancies are complicated by it, and 30% of those complications are brought on by intentional medical intervention and the other 40% by spontaneous PTL. Seventy five percent of all perinatal fatalities are linked to PTL. Most of the time, the aetiology of PTL is unclear and possibly multifactorial. Although several approaches have been attempted to predict PTL, their overall predictive value is modest. These include risk scores, bio-physical indicators, and molecular markers. It is challenging to identify nulliparous patients who are at risk for PTL since the most important predictor of PTL is a history of PTL. If this large population of patients goes unidentified, the effectiveness of preventative interventions won't be nearly as good.[1,2]

The incidence of PTL has continuously grown over the previous century, showing modern obstetrics' failure to fathom the complexities of events and develop effective PTL prophylactic interventions. Risk variables are unable to predict up to 70% of PTL. While several strategies for preventing PTL have been studied, transvaginal scan (TVS) and vaginal smear examination for PTL screenings have received the most attention. [2] Six to thirty-two percent of pregnant women are affected with bacterial vaginosis (BV). It is characterised by a vaginal microbiota imbalance, with fewer lactobacilli morphotypes and more anaerobic bacterial morphotypes. Symptoms of BV range from the absence of any symptoms to the development of unpleasant-smelling, excessive vaginal discharge. It's linked to perinatal complications including preeclampsia, prolapsed uterine membranes, and chorioamnionitis, and it raises the odds of a premature birth. A recent meta-analysis of 18 research indicated a strong association between BV and preterm birth, miscarriage, and maternal infection. The investigations included cohort studies, clinical trial control groups, and case-control analyses.[3]

One of the most common vaginal illnesses during pregnancy is bacterial vaginosis. A 2- to 3-fold increase in amniotic fluid infection, chorion and amnion infection, and histology chorioamnionitis are all linked to BV. Because there haven't been many studies in India to assess the link between BV and peripartum and perinatal issues, this study was attempted to establish the prevalence of BV in term and preterm patients.

MATERIALS AND METHOD

Women who were pregnant and were admitted to Warangal's C K M Hospital between December 2019 and October 2021.

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The sample size was decided to be 200 people with a 95% confidence interval in order to give statistically meaningful results with a 5% alpha error and 80% research power.
The Kakatiya Medical College, Warangal, Ethics Committee gave the research the thumbs up. The individuals who were recruited in the research gave informed consent. Maternal age, obstetric history, previous medical and surgical history, sexual history, socioeconomic status, substance abuse history, physical examination results, gestational age at delivery, delivery method, newborn birth weight and conditions, and other relevant information were recorded on a case record form. Gestational age was calculated using the first day of the last menstrual cycle and the earliest available ultrasonography. If there was a discrepancy of greater than seven days between the menstrual and ultrasound estimates of gestational age, the ultrasound estimate was utilised.

The pelvis was checked out, too. The lower vaginal wall was swabbed with a sterile vaginal speculum. This vaginal swab was stained using the Gram method. The wet mount and KOH tests were performed on collected vaginal discharge to look for cellular markers (Whiff test). Litmus paper was used to determine the pH of the vaginal fluid. A vaginal scraping was taken for the aforementioned test if there was no obvious discharge. In order to make a diagnosis of bacterial vaginosis, three or more of the following criteria must be met. (Amsel's criteria)

Gram staining results and the percentages of clearly identifiable bacterial morphologic categories were used to provide a score between 0 and 10. (i.e., large gram-positive rods, small gram-negative or variable rods, and curved rods). There was no point awarded for the presence of lactobacilli in the vaginal flora, however 10 points were given for the presence of Gardnerella, Bacteroides, and Mobiluncus. (Nugent’s scoring)[6].

If a woman satisfied Amsel's criteria and/or had a Nugent's score of 7 or above on Gram's staining of a vaginal smear, she was diagnosed with bacterial vaginosis. All basic queries have been made.

Inclusion Criteria:
Preterm Labor (Group 1): Preterm labour is defined as contractions lasting more than 40 seconds that occur at regular intervals (four or more every 20 minutes or eight or more every 60 minutes), cervical dilatation of at least 1 cm but no more than 4 cm, effacement of at least 80%, and intact foetal membranes, and a gestational age of less than 37 weeks.
Term labor (Group 2): There must be more than 37 weeks of gestation, a spontaneous beginning, regular uterine contractions lasting more than 40 seconds each, cervical dilatation of 1 cm or more but less than 4 cm, and intact foetal membranes.
Exclusion Criteria: Multiple pregnancies, cervical cerclage, structural uterine abnormalities, confirmed foetal anomalies, prior use of tocolytic medications during the current pregnancy, pregnancies complicated by medical conditions like hypertension, diabetes, chronic renal disorders, thyroid disorders, gastrointestinal disorders, severe cardiac disorders, etc., current use of corticosteroids, and patients who initiate labour before 37 weeks are all risk factors for preterm birth.

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Bacterial vaginosis was diagnosed if three or more of the following criteria (Amsel's criteria) were met:

- increased vaginal pH greater than 4.5
- thin, uniform grey-white discharge
- The presence of 'clue cells' (vaginal epithelial cells with fuzzy boundaries owing to associated bacteria) on microscopic inspection of vaginal fluid after the addition of 10% potassium hydroxide (KOH) to vaginal fluid on a glass slide (Whiff test).

Results from Gram staining and the percentages of clearly identifiable bacterial morphologic categories were used to provide a score between 0 and 10. (i.e. large gram-positive rods, small gram-negative or variable rods, and curved rods). According to Nugent's grading scale, a vaginal flora that is dominated by lactobacilli receives a score of 0 and one that is dominated by Gardnerella, Bacteroides, and Mobiluncus receives a score of 10.[3]

In all groups, secondary outcome variables include organisms that have grown on cultures made from high-quality vaginal swabs, CRP, birth weight, the number of NICU hospitalizations, neonatal problems, and post-partum issues.

R programme will be used to do statistical analysis. Statistics were deemed significant for P values under 0.05. To show all results, descriptive statistics such as the median and interquartile range for skewed distributions and the mean and standard deviation (SD) for normally distributed data will be employed (IQR).

Counts and percentages will be used to display binary and categorical information. The t test, chi square test, and Fisher exact test are employed as statistical tests.

RESULTS

From December 2019 to October 2021, the present research was carried out at the CKM Hospital in Warangal's department of obstetrics and gynaecology. With a p value of 0.47, the mean mother age was similar between the two groups. Both groups had an equal number of primigravida and multigravida.

Preterm labour group admissions' mean gestational age was 33.12 weeks, whereas term labour group admissions' mean gestational age was 38.66 weeks, with a P-Value of highly significant.

Table -1: Previous history of sexually transmitted infections

H/O STIs	Present- N (%)	Absent - N(%)
Preterm Labor	12(12%)	88(88%)
Term Labor	2(2%)	98(98%)
Total	14(14%)	186(186%)

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P value = 0.050 (significant). Preterm patients were significantly more likely to have had an STD in the past than term patients, with a p value of 0.050.

Table-2: Nature of discharge in both the groups.

Type of discharge	Preterm (n = 100)	Term (n = 100)	P-Value
No discharge	28 (28%)	50 (50%)	<0.01
White mucoid	24 (24%)	38(38%)	
White curdy	20(20%)	8(8%)	
Greyish white	16(16%)	4(4%)	
Grey frothy	8(8%)	0	
Greenish frothy	4(4%)	0	
Total (N=200)	100(100%)	100(100%)	

It uses the Fisher exact test. P-Value is highly significant. Compared to the term labour group, the preterm labour group had a higher percentage of patients discharged in various grades. This difference was statistically significant with a p value of less than 0.01.

Table-3: Discharge suggestive of bacterial vaginosis in both the groups

Discharge	Suggestive infection	Not Suggestive of infection	P-Value
Preterm Labor	28(28%)	72(72%)	<0. 01
Term Labor	4(4%)	96(96%)	
Amsel's criteria			
Preterm Labor	30(30%)	70 (70%)	<0. 01
Term labor	4 (4%)	96 (96%)	

Preterm labour patients had substantially more patients with discharges that were indicative of bacterial vaginosis than term labour patients, with a P-Value of < 0.01. (highly significant). Patients in the preterm labour group had a higher prevalence of bacterial vaginosis than those in the term group, as measured by Amsel's Criteria (p <0.01).

Table-4: Vaginal pH in both the groups

Ph	Basic	Acidic	P value
	n (%)	**n (%)**	<0.01
Preterm labor (n=100)	44 (44%)	56 (56%)	
Term labor (n=100)	14 (14%)	86 (86%)	

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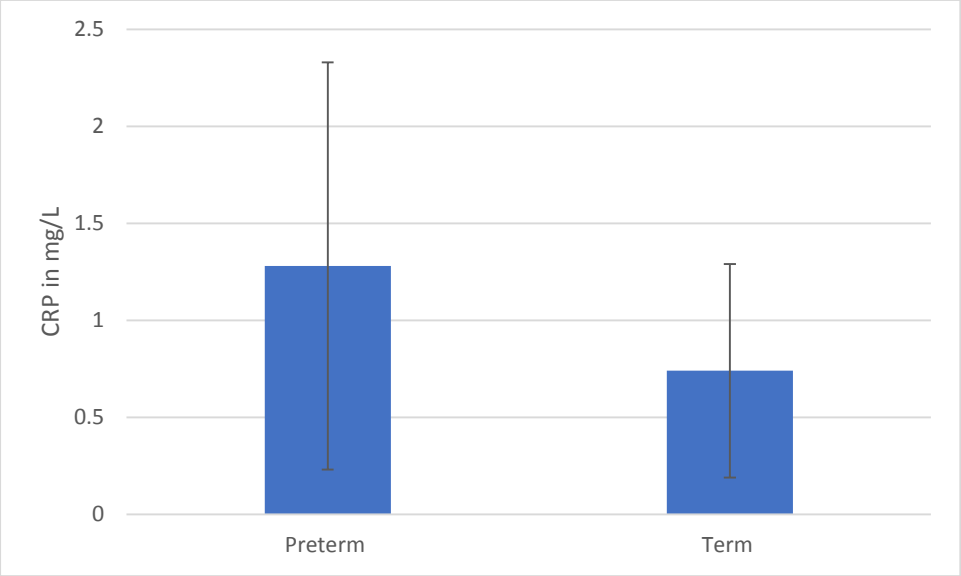
Preterm labour patients were significantly more likely than term labour patients to have basic vaginal pH, with a p value of < 0.01.

Table-5: Results of high vaginal swab culture in both groups

HVS C/S	PRETERM LABOUR (N=100) N (%)	TERM LABOUR (N=100) N (%)	P-Value
Normal Flora	78 (78%)	94 (94%)	0.04
Candida	8 (8%)	6 (6%)	
Group B Streptococcus	2 (2%)	0 (0.0)	
Enterococcus	12 (12%)	0 (0.0)	

With a p value of 0.04, the preterm labour group had substantially more positive vaginal swab cultures than the term labour group.

Figure-1: Mean CRP value in preterm and term labor group.



CRP levels in preterm and term levels are significant on comparion.

Table-6 : Birth weight in preterm labor and term group in bacterial vaginosis positive and bacterial vaginosis negative patients.

Bacterial vaginosis	Low birth weight n(%)	Normal birth weight n(%)	P-Value
Preterm			
Positive (n=30)	16 (53.3)	14 (47.6)	0.23
Negative (n=70)	58 (82.8)	12 (17.2)	
Term			
Positive (n=4)	2(50%)	2(50%)	0.18
Negative (n=96)	18(18%)	78(82%)	

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LBW was evident in 53.3 percent of neonates delivered to BV positive mothers and 82.8 percent of those delivered to BV negative mothers in the preterm group. This difference was unimportant. In the term group, neonates born to BV positive women had LBW at a rate of 50%, compared to just 18% in the BV negative group.

Table-7: Neonatal and post partumcomplications in preterm labor and term group in bacterial positive and negative patients.

Bacterial vaginosis	**Neonatal complications present**	**Neonatal complications absent**	**P-Value**
	n (%)	**n (%)**	
Neonatal complications			
Preterm			
Positive (n=30)	6 (20%)	24 (80%)	**0.33**
Negative (n=70)	8 (11.4%)	62 (88.5%)	
Term			
Positive (n=4)	0 (0)	4 (100.0)	**0.27**
Negative (n=96)	4 (4.1)	92 (95.9)	
Post partum complications			
Preterm			
Positive (n=30)	8 (26.6%)	22 (73.3%)	**0.33**
Negative (n=70)	16 (22.8%)	54 (77.1)	
Term			
0 (0)	4 (100.0)	0 (0)	**0.27**
12 (12.5%)	84 (87.5%)	12 (12.5%)	

Neonatal complications impacted 20% of infants born to BV positive women during preterm labour, compared to 11.4 percent of newborns delivered to BV negative mothers. This difference was unimportant. Neonatal difficulties occurred in 4% of BV negative moms at term delivery, but not in any of the BV positive mothers' neonates. The difference was minor.

DISCUSSION

With a P value of 0.47, the mean mother age in the two groups was similar (25.6 years for preterm labour and 25.3 years for term labour, respectively). The mean mother age in a related research by Chawanpaiboon S et al.[1] was 26.7 years and 26.6 years, respectively. The mean mother age in a research by Deepa Masand et al.[4] was 26 years old and 25.7 years old, respectively. According to Vanhaesebrouck et al.[5], deliveries under 32 weeks account for 1–15 percent of births, while those under 28 weeks account for 0.22–1.5 percent.

There were the same number of primigravida and multigravida in both groups. Preterm women made up 60% of the study's primigravida and 40% of the multigravida, whereas term

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women made up 51.8 % of the primigravida and 48.2 % of the multigravida. The number of primigravida and multigravida was equivalent in a research of a similar kind conducted by Chembeti Kavitha Kiran et al[6].

The term group's mean gestational age at admission was 33.12± 2.5 weeks, whereas the preterm group's was 38.66 ±1.05 weeks, with a P value of 0.01. According to Chawanpaiboon et al.[1], the mean gestational age at admission was 33.6 weeks in the preterm group and 38.6 weeks in the term group. Researchers Deepa Masand et al.[4] observed that the average gestational age at admission was 33.5 weeks for the preterm group and 39.0 weeks for the term group.

A history of STIs was reported by 12% of patients in the preterm labour group and 2% of patients in the term labour group. In the present study, trichomoniasis was the most often reported STD. T. vaginalis was shown to be highly associated to low birth weight and early delivery in the largest prospective study undertaken in the United States.[7] According to Azargoon and Darvishzadeh[8], there was no statistically significant association between T. vaginalis and early labour delivery.

Ureoplasma (47%) and G. vaginalis were the most abundant isolates from the placentas of prematurely delivered women (26 percent). In the preterm group, considerably more patients were released in various grades than in the term group (72 percent vs 50 percent, P 0.01). According to TMMV da Fonseca et al.[9], 43 percent of women in their study had vaginal discharge during pregnancy. In the same research, there was a substantial correlation between pathological vaginal discharge and impending preterm labour; 52 percent of threatened preterms had discharge.

Patients who met Amsel's criteria for the diagnosis of BV were more prevalent in the preterm group (28 percent) than in the term group (4 percent; P = 0.01). Additional investigations supported the conclusion that BV is a significant risk factor for premature labour. According to studies conducted by Hillier and colleagues10, persons with BV had a 40% increased risk of premature birth. Subtil et al.[11] did another research to determine the relationship between BV and an increased risk of premature birth.

Thirty percent of individuals who presented with preterm labour were found to have bacterial vaginosis in the current investigation. Various studies have shown that the incidence of bacterial vaginosis in pregnant women varies.[13] All studies employ a different technique for diagnosing bacterial vaginosis. However, the majority of investigations have noted a strong correlation between clinical diagnostic criteria and laboratory techniques.

Mittal et al. [14] discovered that preterm women had a 30% frequency of bacterial vaginosis. According to Svare et al [15] study's preterm labour patients had a prevalence of 16%.

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In a study by Masand D et al.[4], the frequency of preterm labour was determined to be 38%, whereas that of term labour was found to be 8%. bacterial vaginosis in the first trimester of pregnancy was associated with a 2.6-fold (95 percent CI 1.3-49) increased risk of preterm labour, a 6.9-fold (95 percent CI 2.5-18.8) increased risk of preterm birth, and a 7.3-fold increased risk of preterm, premature membrane rupture, according to Kurki et al.[16] (95 percent CI 1.8 – 29.4).

Individuals with bacterial vaginosis had a 2.6-fold greater risk of preterm labour than healthy controls, according to McGregor et al.[17]. Premature membrane rupture occurs in around one-third of preterm deliveries. These women often had later intrapartum fever and were less responsive to tocolytic therapy. The relative risk of preterm labour for BV participants in this study was 3.8. (RR 3.8).

Patients with vaginal discharge indicative of bacterial vaginosis were considerably higher in the preterm labour group than in the term labour group (28 percent vs. 4 percent, respectively; $P< 0.01$).

According to Chawanpaiboon S et al.[1], patients with preterm labour and term labour had a prevalence of bacterial vaginosis-positive discharge that was 25% and 24%, respectively. With a P value less than 0.01, the preterm group had more patients with a basic vaginal pH than the term group (44 percent vs. 14 percent).

According to Chawanpaiboon S et al.[1], patients with preterm labour and term labour had a prevalence of bacterial vaginosis-positive discharge that was 25% and 24%, respectively. With a P value less than 0.01, the preterm group had more patients with a basic vaginal pH than the term group (44 percent vs. 14 percent).

According to Masand et al.[4], the proportion of preterm patients with a positive Whiff test was substantially higher than that of term patients (48 percent vs.20 percent).

In the current investigation, none of the two groups included any indicator cells. It is possible that they experienced a prolonged infection in which IgA antibodies prevented the formation of indicator cells. According to Easmon et al. [18], clue cells are not necessarily required to diagnose BV, and they are not included in Nugent's more systematic scoring technique, which has a 95% specificity.

$P = 0.04$ indicates that the preterm group had more genital tract infections (vaginal swab culture-sensitivity testing) than the term group (22% vs. 6%). In this research, the most prevalent infections were Enterococcus (12 percent), Candida (8 percent), and Group B Streptococcus (2 percent), while the most prevalent infections in the term labour group were Candida (6 percent), Enterococcus (zero percent), and Group B Streptococcus (zero percent).

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According to study by Paulo Cesar Giraldo et al.(2012)[22], UTIs were the most common kind of urogenital infection in pre-term labour patients, with a prevalence rate of 36.7%, followed by bacterial vaginosis at 34.6%. In this research, 34.7 percent of pre-term labour patients and 28.9 percent of term labour patients had bacterial vaginosis.

In the present study, 2% of the individuals in the preterm labour group tested positive for GBS (2 percent in preterm group an 0 percent in term group). Benchetrit et al.[19] discovered that 26% of pregnant women tested positive for GBS.

In the current research, Candida albicans was detected in 8% of preterm labourers and 6% of term labourers. Previous research has shown that vaginal deposition of glycogen and other substrates during pregnancy, as well as elevated levels of circulating strogens, have an influence on this association.[20] Vaginal microbiota are essential for the transmission of illness and the maintenance of a healthy genital tract.

There is a high correlation between upper genital infections (UGIs) during pregnancy and the risk of infection in the infant. Determining the incidence of microbial colonisation in pregnant women is a crucial first step towards understanding neonatal infection. They discovered abnormal bacterial colonisation, the presence of BV-related pathogens such Urea-plasma and Myco-plasma, and chorioamnionitis more often. They believed that infection had a substantial role in a sizable part of idiopathic premature labour. Whether an infection is present or not determines whether tocolytic should be used. The presence of microorganisms from the region between the chorion and the amnion served as a diagnostic marker for histological chorioamnionitis.

Hillier et al[10] In their cohort study the prevalence was found to be 17% in their cohort analysis of 913 pregnant women in the USA using Nugent criteria between 25 and 29 weeks. Asymptomatic bacterial vaginosis affected around 80% of people.

According to the Mathew et al.[21] research, which included 200 pregnant women (150 symptomatic and 50 asymptomatic), the prevalence was 38 percent when utilising the Nugent criteria. In addition, it was shown that individuals with bacterial vaginosis had an increased risk of preterm birth. According to a research by Giraldo PC, et al.[22], lower genital tract infections are fairly common in pregnant women who seem to be in excellent health, with an overall frequency of 40 to 54 percent.

In the preterm labour group, the mean C-Reactive Protein level was 1,287, whereas it was only 748 in the term labour group. In the study undertaken by Halder A et al.[23], 78 (31.2%) of 250 individuals tested positive for CRP, whereas 172 (68.8%) tested negative. Positive CRP levels were connected with preterm labour, with an odds ratio of 2.384%. (95 percent CI: 1.153-4.928 & p value 0.01).

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In a January 2014 observational study, Najat Nakishbandy BM, et al.[24] found that 93 out of 100 women with premature uterine contractions (PUCs) had elevated CRP levels and 91 percent of them gave birth early, compared to only 9 out of 100 women in the control group who had elevated CRP levels and only 8% of whom gave birth preterm. [8]

Statistics showed the differences were quite substantial. In instances of early uterine contractions, the average CRP level was 9.24 ± 7.91 mg/l, which is greater than the average in the control group (0.92 ± 0.92, $P < 0.001$).

In the current research, however, neonates born to preterm BV-negative mothers were more likely to have a low birth weight (82.8 percent) than those born to preterm BV-positive mothers (53.3 percent). This might be explained by the potential that variables other than BV are responsible for low birth weight, such as anaemia and malnutrition, which were observed in 22 and 16 individuals, respectively, in the present research.

Hillier et al[10] discovered a link between BV and a considerably lower mean birth weight.

According to Svare et al.[15], lower mean birth weight was also seen in bacterial vaginosis. When an ANCOVA was conducted to see whether people with bacterial vaginosis who were positive or negative for the condition had different birth weights, it became obvious that gestational age at delivery had a significant influence ($P< 0.001$).

Bacteriological vaginosis positive individuals had a high rate of preterm delivery, and this preterm birth correlates to a high incidence of newborn jaundice, according to an ANCOVA done for low birth weight, APGAR, neonatal jaundice, and neonatal sepsis. But among those who tested positive for bacterial vaginosis, the APGAR was considerably lower ($p< 0.05$).

Preterm premature rupture of the membranes, preterm labour, and amniotic fluid infection were all substantially correlated with BV. In a research by Hillier et al.[10], the risk of preterm birth was shown to be 1.4 times higher than in controls. Compared to mothers who were not treated, those who received antibiotics saw a lower prevalence of low birth weight infants.

In the group of preterm births, 20% of infants delivered to BV-positive mothers had congenital pneumonia, whereas only 11.4% of children born to BV-negative moms had respiratory distress. In the term labour group, none of the neonates of BV-positive moms encountered neonatal complications, whereas 4.1% of newborns of BV-negative mothers experienced respiratory distress. Our data indicated that BV did not have a role in the aetiology of newborn complications in cases of term labour. In the group of preterm labour patients, 26.6% of BV-positive patients experienced postpartum complications, compared to 22.8% of BV-negative patients; puerperal pyrexia was the most common event. None of the BV-positive patients in the term labour group developed postpartum problems, compared to 12.5% of the BV-negative patients. Five of the six patients with complications had puerperal pyrexia, and one patient had atonic PPH. This research demonstrates that postpartum

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complications in full-term women may be caused by variables other than BV. In the term labour group in the current research, three patients had viral fevers and one had malarial fever.

Eschenbach DA[25] performed one of the first investigations examining the association between bacterial vaginosis and premature delivery. According to their findings, bacterial vaginosis infected 24% of full-term babies and 49% of preterm babies. Later, they discovered a connection between premature labour, chorioaminitis, and bacterial vaginosis. A study involving 3000 women in the United States that examined the prediction of preterm discovered a correlation between bacterial vaginosis and premature labour.

In 2008, Vida Modares Nejad [26] in Iran examined the relationship between bacterial vaginosis and preterm labour using data from 160 participants. They observed that BV was present in 25% of patients with preterm labour and in 11.3% of individuals with term labour. In the current investigation, bacterial vaginosis was detected in 4% of patients with term labour and 30% of patients with preterm labour.

CONCLUSION

The neonatal and postpartum complications of preterm and term children of BV-positive moms were greater than those of BV-negative mothers. Respiratory distress syndrome was the most prevalent consequence, followed by neonatal sepsis and congenital pneumonia. Puerperal pyrexia was the most prevalent complication, followed by atonic PPH.

Current research indicates that bacterial vaginosis is a significant risk factor for premature labour. Therefore, early identification and treatment of bacterial vaginosis may minimise the risk of premature labour. Additionally, this will significantly benefit in reducing premature infant complications.

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