EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 7
Issue: 5
100-106
Year: 2020

STUDY THE ASSOCIATION BETWEEN BACTERIAL VAGINOSIS AND PRETERM AND TERM DELIVERY

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Article Received on 12/03/2020 **Article Revised on 31/03/2020** **Article Accepted on 21/04/2020**

ABSTRACT

Bacterial vaginosis is a clinical condition caused by replacement of the normal hydrogen peroxide producing Lactobacillus spp. in the vagina with high concentrations of characteristic sets of aerobic and anaerobic bacteria. Bacterial vaginosis is believed to be a risk factor for preterm delivery. Bacterial vaginosis is reported in 10-41% of women with an evidence of maternal and fetal morbidity. Studies have shown that spontaneous abortion, preterm delivery (PTD), premature birth, preterm premature rupture of membranes, amniotic fluid infection, postpartum endometritis are increased because of infection with bacterial vaginosis during pregnancy. This observational study aimed to study the prevalence of bacterial vaginosis in women presenting with preterm and term delivery, to analyze the causal relationship between BV and PTD and to analyze the maternal and fetal complications associated with bacterial vaginosis. This current study included 30 patients with preterm and 50 patients with term delivery at Haditha General Hospital/ Iraq. Bacterial vaginosis was determined to be present or absent on the basis of Amsel's criteria. The proportion of patients who fulfilled Amsel's criteria for the diagnosis of bacterial vaginosis was significantly higher in preterm delivery group as compared to term delivery group. In preterm delivery group, a higher number of neonates born to women who had bacterial vaginosis had low birth weight as well as neonatal complications as compared to those born to women without bacterial vaginosis. Maternal postpartum complications were also higher in women with bacterial vaginosis as compared to women without bacterial vaginosis in the preterm delivery group. It can be concluded that bacterial vaginosis is a major risk factor for preterm delivery. Therefore, testing for bacterial vaginosis and its prompt treatment may reduce the risk of preterm delivery. This will also go a long way in the prevention of neonatal complications due to prematurity.

KEYWORDS: Bacterial vaginosis, Preterm delivery, Term delivery.

INTRODUCTION

Preterm delivery (PTD) and delivery are among the most challenging obstetric complications encountered. PTD is the important single determinant of adverse infant outcome in terms of both survival and quality of life. It complicates about 5-10% of all pregnancies and in about 30%, it is due to deliberate medical intervention and in the remainder due to spontaneous PTD. PTD is associated with 75% of all perinatal deaths.[1] In most cases, the exact cause of PTD is not diagnosed and the etiology is likely to be multifactorial. Various measures have been tried to predict PTD, e.g. risk scoring, biophysical, and biochemical markers, but not proved useful and are associated with overall poor predictive value.[2]

Identification of nulliparous patient at risk for PTD remains problematic because the single most important predictor of PTD is a previous PTD. The last century has been marked by a persistent rise in rate of PTD representing the failure of modern obstetrics to understand the complexity of phenomena and to develop effective PTD preventive interventions. Risk factors fail to predict as many as 70% of PTD. Of the many approaches to PTD prevention that have been thoroughly investigated, no single intervention has been thoroughly investigated or thoroughly studied as much as transvaginal scan (TVS) and vaginal smear examination in screening for PTD.[3] Bacterial vaginosis (BV) affects 6-32% of pregnant women. It is characterized by an imbalance in the vaginal microflora which may be symptomless, or it may be accompanied by increased vaginal discharge, which may be foul smelling with a fishy odor. In women with BV, there are usually no clinical signs of infection in the vaginal mucosa. It is a risk factor for preterm delivery and is associated with peripartum complications such as preterm premature rupture of membranes (PPROM), chorioamnionitis, and postpartum endometritis.[4] BV is one of the most common genital infections in pregnancy which is

associated with two to threefold increase in infection of amniotic fluid, infection of the chorion and amnion, and histological chorioamnionitis.[5]

As per the study conducted by Saifon et al., the prevalence of bacterial vaginosis in preterm delivery group was higher than in the term delivery group.[4] Intrauterine infection may occur early in pregnancy or even before pregnancy and remains asymptomatic and undetected for months until preterm delivery or premature rupture of membranes (PROM) occurs. Studies conducted by Gregor J et al.[5] showed that combination of vaginal pH with vaginal sialidase and prolinase activities can predict low birth weight and preterm birth.[6,7]

Recent interventional studies by Ugwumadu et al.[8] showed that screening for BV early in pregnancy and subsequent treatment with metronidazole or clindamycin in low-risk women may reduce the risk of spontaneous delivery before 37 weeks and the associated maternal and fetal complications.[8] As per the studies conducted by Eschenbach et al.[9] presence of clue cells is the single most reliable predictor of BV. In women with BV, at least 20 percent of the epithelial cells on wet mount should be clue cells. Using gram stain as the gold standard, the sensitivity of Amsel's criteria for diagnosis of BV is over 90% and specificity over 77%.[9-11]

In Iraq not many studies have been done to estimate the association of BV with peripartum and perinatal complications, hence this study was taken up to know the prevalence of BV in term and preterm patients.

MATERIALS AND METHODS

This observational study was conducted in Haditha General Hospital / Iraq during the period from 2016 to 2018 on (80) patients (30 pre term and 50 term) patients.

A case record form was used to record maternal age, obstetric history, past medical/ surgical history, sexual history, socioeconomic status, history of drug and alcohol abuse, gestational age at admission, physical examination data, gestational age at delivery, the route of delivery and the newborn birth weight and conditions. The gestational age was calculated from the first day of the last menstrual period and earliest available ultrasound scan. If the estimated gestational age by menstrual and ultrasound estimation showed a difference of more than seven days, the ultrasound estimation was used.

Pelvic examination was also performed. Using a sterile vaginal speculum vaginal swab was collected from lower one-third of the vaginal wall. The vaginal swab was subjected to Gram staining. Vaginal discharge was taken for wet mount for detection of clue cells and KOH test (Whiff test). The pH of vaginal discharge was tested using litmus paper. If there was no obvious discharge vaginal scraping was taken for the above test. Bacterial vaginosis was diagnosed based on Amsel's criteria.

Inclusion criteria of preterm group involved gestational age less than 37 weeks, regular uterine contractions (four or more in 20 minutes or eight or more in 60 minutes), each lasting more than 40 seconds, cervical dilatation equal to or greater than 1 cm but less than 4 cm and effacement equal to or greater than 80% and intact fetal membranes.

Inclusion criteria for term delivery group involved gestational age >37 completed weeks, spontaneous in onset, regular uterine contractions (four or more in 20 minutes or eight or more in 60 minutes), each lasting for more than 40 seconds, cervical dilatation equal to or greater than 1 cm but less than 4cm and intact fetal membranes.

Exclusion criteria included Rh isoimmunization, use of antibiotics in the preceding two weeks, multiple gestation, cervical cerclage, structural uterine abnormalities, established fetal anomalies, prior use of tocolytic agents during the current pregnancy, pregnancies complicated with medical disorders like hypertension, diabetes, chronic renal disorders, thyroid disorders, gastrointestinal disorders, severe cardiac disorders etc, current use of corticosteroids, patients who presented with mucous bloody show, patients who were not willing to give consent.

Primary outcome measures

Bacterial vaginosis was diagnosed if 3 or more of the following criteria were present (Amsel's criteria):

a) Elevated vaginal pH>4.5
b) Thin, homogeneous grey-white discharge
c) Amine odor upon the addition of 10% potassium hydroxide (KOH) to vaginal fluid on a glass slide (Whiff test)
d) The presence of 'clue cells' (vaginal epithelial cells with indistinct borders due to attached bacteria) on microscopic examination of vaginal fluid.

A score of 0 to 10 was assigned depending on the Gram staining findings, on the basis of the relative proportions of easily distinguished bacterial morphologic types (i.e. large gram-positive rods, small gram-negative or variable rods, and curved rods). A score of 0 was assigned to the most lactobacillus-predominant vaginal flora, and a score of 10 was assigned to a flora in which lactobacilli were largely replaced by Gardnerella, Bacteroides, and Mobiluncus (Nugent's scoring).[6]

Secondary outcome measures

a) Organisms grown on culture of high vaginal swab in both the groups.
b) CRP in both the groups.
c) Birth weight in both the groups.
d) Number of NICU admissions and neonatal complications in both the groups.
e) Post-partum complications in both the groups.

Statistical analysis

SPSS version 20.0 was used to perform the statistical operations. The categorical data has been represented as frequency and percentages. Pearson's Chi-square test was used to find out the significance of differences in the various categorical data in both the groups. Independent t-test was performed to compare the mean maternal age and mean gestional age at admission in both the groups.

RESULTS

The proportion of patients who had history of sexually transmitted diseases in the past was not significantly more in preterm delivery group as compared to term delivery group with a p value of 0.275 and the mean CRP value recorded in preterm delivery group was significantly more than in term delivery group with a significant difference (p<0.019) as shown in table (1). The pre-term delivery group had more number of patients with the different grades of discharge (66.7%) as compared to term delivery group (54.0%) with no significant difference p= 0.135 as shown in figure (1).

Table (1): Demographical statistics of patients.

Parameters	Preterm delivery (Group 1, n=30)	Term delivery (Group 2, n=50)	P Value
Maternal age (Mean ±SD) (years)	24.7±3.89	25.1±3.95	0.660
Primigravida (%)	15 (50%)	23 (46%)	0.907
Multigravida (%)	15 (50%)	27 (54%)	0.907
Mean gestational age (Mean ±SD) (weeks)	33.2±3.15	39.1±2.10	<0.0001
Sexually transmitted diseases (%)	4 (13.3%)	2 (4.0%)	0.275
CRP	1.31±1.11	0.85±0.62)	0.019

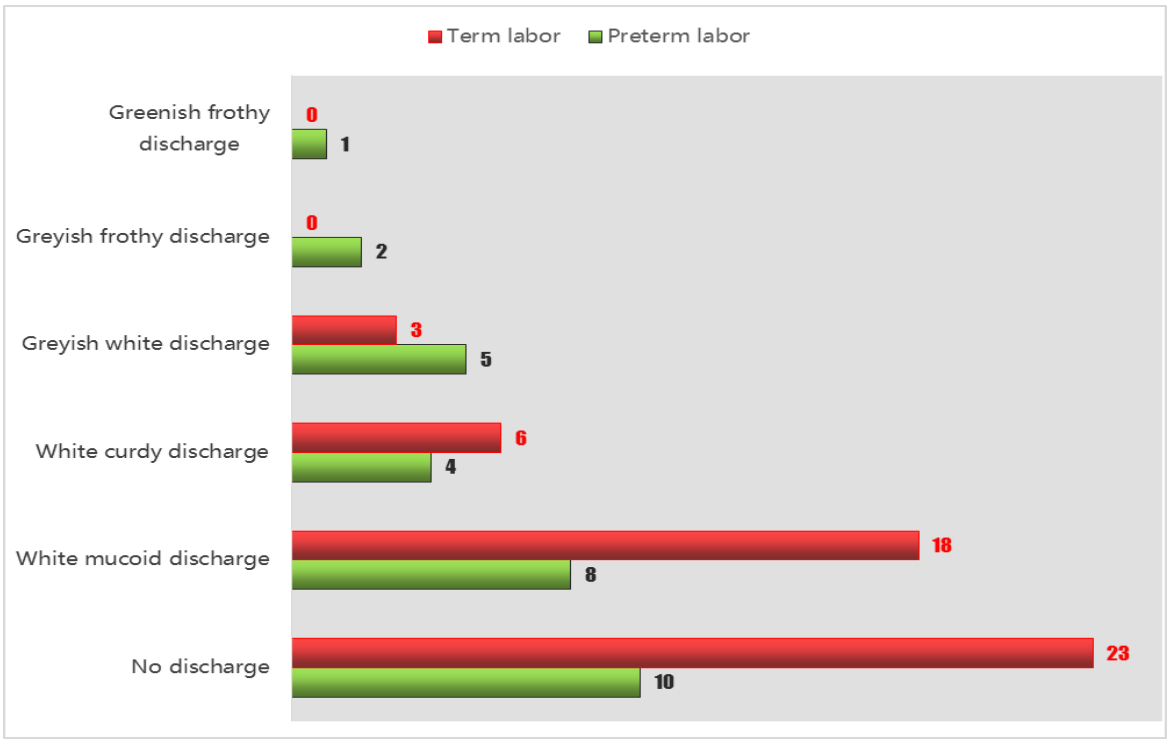

Figure (1): Nature of discharge among both groups.

The proportion of patients with discharge, vaginal pH and positive Whiff test suggestive of bacterial vaginosis was significantly higher in preterm delivery group as compared to term delivery group as shown in table (2).

Table (2): Clinical parameters.

Parameters		Preterm Labour (Group 1, n=30)	Term Labour (Group 2, n=50)	P Value
Discharge		11 (33.3%)	3(6%)	0.003
Vaginal pH	Basic	23 (76.7%)	9 (18.0%)	0.001
	Acidic	7 (23.3%)	41 (82.0%)	
Positive Whiff test		14 (46.7%)	8 (16.0%)	0.006

Out of 80 patients in both groups, the proportion of patients who were diagnosed to have bacterial vaginosis according to Amsel's criteria (33.3%) was significantly higher in preterm delivery group than in term delivery group (6.0%), with a P value of 0.004.

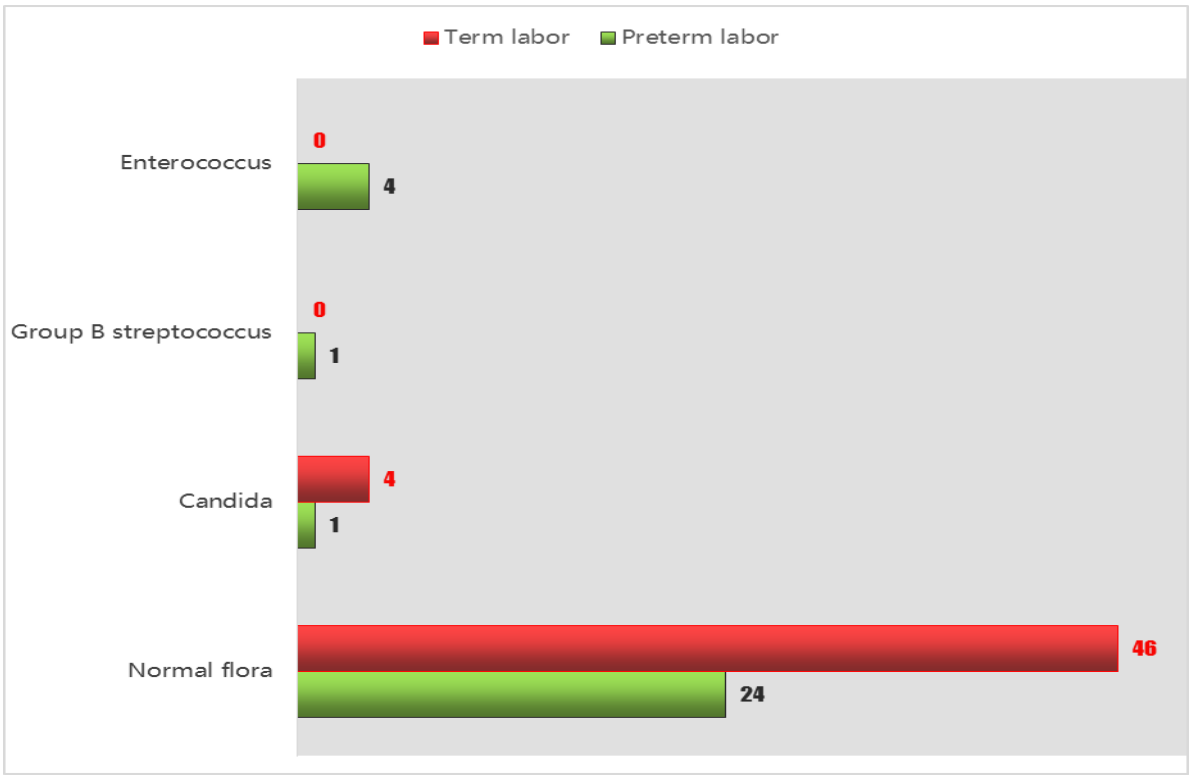

Figure (2): High vaginal swab culture.

A highly significant number of patients in preterm delivery group tested positive on vaginal swab culture sensitivity when compared to term delivery group as shown in figure (2).

In preterm group 60.0% of neonates born to BV positive mothers had low birth weight as compared to 80.0% of neonates born to BV negative mothers with no significant difference (p=0.46). In term group, 33.3% of neonates born to BV positive mothers had low birth weight as compared to 16.0% of neonates born to BV negative mothers with no significant difference (p=0.95) as shown in table (3).

In preterm delivery group, 20.0% of neonates born to BV positive mothers had neonatal complications as compared to 20.0% of neonates born to BV negative mothers with no significant difference. In term delivery group, no neonates of BV positive mothers had neonatal complications, while 4.0% of neonates of BV negative mothers had neonatal complications with no significant difference as shown in table (4).

In preterm delivery group, 30.0% of patients who were BV positive had postpartum complications as compared to 25.0% of patients who were BV negative with no significant difference (p=0.883) (table 5). In term delivery group, none of the patients who were BV positive had post-partum complications, while 10.0% of patients who were BV negative had post-partum complications (p=0.691).

Table (3): Comparison of birth weight in both groups.

Bacterial vaginosis		**Low birth weight, n(%)**	**Normal birth weight, n(%)**	**P Value**
Preterm group	Positive (n=10)	6(60.0%)	4(40.0%)	0.46
	Negative (n=20)	16(80.0%)	4(20.0%)	
Term group	Positive (n=3)	1(33.3%)	2(66.7%)	0.95
	Negative (n=47)	8(16.0%)	39(84.0%)	

Table (4): Comparison of neonatal complications in both groups.

Bacterial vaginosis		Neonatal complications present, n(%)	Neonatal complications absent, n(%)	P Value
Preterm group	Positive (n=10)	2 (20.0%)	8 (80.0%)	0.628
	Negative (n=20)	4 (20.0%)	16 (80.0%)	
Term group	Positive (n=3)	0(0%)	3(100%)	0.248
	Negative (n=47)	2(4.0%)	45(96.0%)	

Table (5): Comparison of postpartum complications in both groups.

Bacterial vaginosis		Postpartum complications present, n (%)	Postpartum complications absent, n (%)	P Value
Preterm group	Positive (n=10)	3(30.0%)	7(70.0%)	0.883
	Negative (n=20)	5 (25.0%)	15(75.0%)	
Term group	Positive (n=3)	0 (0%)	3(100%)	0.691
	Negative (n=47)	5 (10.0%)	42(90.0%)	

DISCUSSION

The mean maternal age in both groups was comparable (24.7 years and 25.1 years in preterm delivery group and term delivery group respectively). A similar study done by Chawanpaiboon et al. found a mean maternal age of 26.7 years and 26.6 years respectively.[4] Both groups had nearly equal number of primigravida's and multigravidas. In the study done by Chawanpaiboon et al., the preterm group had 60% primigravidas and 40% multigravidas, while the term group had 51.8% primigravidas and 48.2% multigravidas. The mean gestational age at admission in preterm group was 33.2 weeks in term group and 39.1 weeks in preterm group. The mean gestational age at admission in the study done by Chawanpaiboon et al. was 33.6 weeks and 38.6 weeks in preterm and term groups respectively.[4]

In the present study the most common sexually transmitted infection reported was Trichomoniasis. According to the results of the largest prospective study in the USA, T. vaginalis was significantly associated with low birth weight and preterm delivery.[12] Azargoon et al.[13] showed that there was no significant correlation between T. vaginalis with preterm labor birth.

The preterm group had significantly higher number of patients with different grades of discharge as compared to term group (66.7% vs. 54.0% respectively). Various studies have proved that lower genital tract infections are very common among apparently healthy-looking pregnant women with an overall prevalence of 40-54%.[14]

The number of patients who fulfilled Amsel's criteria for diagnosis of BV were more in preterm group (33.3%) as compared to term group (6.0%). This observation was correlated with other studies where it was concluded that BV is one of the important risk factors for preterm delivery. Hillier et al.[15] and Subtil et al.[16] showed that patients with BV were 40% more likely to have preterm delivery. In the present study, bacterial vaginosis was diagnosed in 30% of patients who presented with preterm delivery. Mittal et al.[17] and Svare et al.[18] showed 30% and 16% prevalence of bacterial vaginosis in preterm group. The number of patients having vaginal discharge suggestive of bacterial vaginosis in preterm delivery group were significantly higher than in term delivery group (28% vs. 4% respectively). In the study conducted by Chawanpaiboon et al., discharge suggestive of bacterial vaginosis was present in 24% and 25% of patients with preterm delivery and term delivery respectively.

Preterm group had a greater number of patients with basic vaginal pH as compared to term group (76.7% vs. 18.0%). The number of patients having positive Whiff test in preterm group was significantly higher as compared to term delivery group (46.7% vs. 16.0%). In the present study, clue cells were not detected in either of the two groups. Absence of clue cells can be explained by the possibility of them to have chronic infection in which clue cells were absent due to local immune response to IgA antibodies. According to Easmon et al.[19], it is not always necessary to see clue cells to make a diagnosis of BV and it is not included in the scoring system by Nugent which is more systematic and has a specificity of 95%.

The number of patients who had other genital tract infections (vaginal swab culture sensitivity tested) were higther in preterm group as compared to term group (20.0% vs. 8.0%). The commonest infections found in this study were Enterococcus (13.3%) followed by Candida (3.3%) and Group B Streptococcus (3.3%) in preterm group and Candida (8.0%) in term group. Benchertriit et al.[20] showed the presence of GBS colonization in 26% pregnant women evaluated. Simões et al.[21] studied Candida albicans and found a prevalence of 19.3% for vaginal candidiasis in normal pregnant women in the third trimester.

Microbiota that inhabit the vagina play an important role in the spread of illnesses and the maintenance of a healthy genital tract. The correlation between upper

genital infections (UGIs) during pregnancy and the possibility of infection in the newborn is high. Thus, as a first step towards the understanding of infection in newborns, it is imperative to determine the prevalence of microbial colonization in the pregnant women. The mean C- Reactive Protein value recorded in preterm delivery group was 1.31 and in term delivery group it was 0.85. In the study done by Halder A et al.[22] out of 250 patients, 78 (31.2%) were CRP positive and 172 (68.8%) were CRP negative.

Hillier et al.[15] showed the relation of BV with a significantly reduced mean birth weight. Svare et al.[18] showed lower mean birth weight in bacterial vaginosis. In the present study, however, a greater number of neonates born to preterm BV negative group (80.0%) had low birth weight as compared to neonates born to preterm BV positive mothers (60%). This can be explained by the probability of factors other than BV responsible for low birth weight like anemia and malnutrition which was present in 13 and 10 patients respectively in the present study.

In preterm delivery group, 30.0% of patients who were BV positive had postpartum complications as compared to 25.0% of patients who were BV negative; the most commonly seen complication was puerperal pyrexia. In term delivery group, none of the patients who were BV positive had post-partum complications, while 10.0% of patients who were BV negative had post-partum complications. Out of the patients who had complications, 4 patients had puerperal pyrexia and 1 patient had atonic PPH. This finding probably suggests the possibility of factors other than BV giving rise to post-partum complications in term women.

Eschenbach et al were among the first researchers who studied the relationship between bacterial vaginosis and preterm delivery. In their study, 49% in preterm group and 24% in full term group had bacterial vaginosis. Later they showed the correlation between bacterial vaginosis and chorioaminiotis and preterm delivery.[23] A prematurity prediction study carried out on 3000 women in the United States has shown the relationship between bacterial vaginosis and preterm delivery.[24] Nejad et al. carried out a study to establish the association of bacterial vaginosis and preterm delivery on 160 patients in Iran in 2008, reporting 25% prevalence of BV in patients with preterm delivery and 11.3% prevalence in term patients.[25] In the present study, bacterial vaginosis was diagnosed in 33.3% of patients with preterm delivery and 6.0% of patients in term delivery.

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