Bacterial Vaginosis in Pregnancy (<28 Weeks) and its effect on pregnancy outcome: A Study from a western up city

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Abstract

Introduction: Bacterial vagiriosis (BV) is an extremely prevalent vaginal condition. BV prevalence in pregnancy is 15-30 percent. BV is a polymicrobial, superficial vaginal infection involving a reduction in the amount of hydrogen-peroxide-producing Lactobacillus and an overgrowth of anaerobic and Gram-negative or Gram-variable bacteria. BV can be symptomatic or asymptomatic. BV in pregnancy has been associated with preterm labour and delivery, premature rupture of membranes amniotic fluid infections and post-partum endometritis.

Materials and Methods: 500 antenatal women of less than 28 are gestation without known risk for PTL admitted or attending antenatal outpatient clinic in Department of Obstetrics and Gynaecology, LLRM and associated SVBP Hospital in last one year were enrolled after a written and informed consent. We studied the presence of bacterial vaginosis in these women uses NUGENTS criteria and correlated it with adverse pregnancy outcome. Prematurity, PROM and post-partum endometritis were considered as adverse pregnancy outcomes.

Result: BV was found in 98 of the 500 women studied. Out of the 98 positive cases, 53 cases were less than 20 weeks gestation and the remaining 45 were between 20-28 weeks gestation. Twenty three of the 98 BV patients had preterm delivery and this association was significant ($p<0.0001$). Out of the 53 patients of BV diagnosed in 11-20 weeks period of gestation, 12 patients had preterm delivery. The remaining 11 preterm deliveries occurred in BV patients diagnosed after 20 weeks gestation. The association of more number of preterm deliveries in patients with BV diagnosed in 11-20 weeks period of gestation was not significant ($p=0.2$). Fourteen patients of BV had PROM and this association was also significant ($p<0.001$). Six patients of BV also had postpartum endometritis.

Conclusion: The above results suggest that screening for BV should start in early pregnancy and a high index of suspicion for preterm delivery should be kept in antenatal patients with BV.

Key Words: Preterm delivery, Bacterial Vaginosis, Bacterial Vaginosis in pregnancy, Prematurity, Premature rupture of membranes

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Introduction

Bacterial vagiriosis (BV) is an extremely prevalent vaginal condition. BV is a polymicrobial, superficial vaginal infection. Bacterial vaginosis is characterized by a change from normal *Lactobacillus* dominated flora to a mixed flora consisting of *Gardnerella vaginalis, Mycoplasma hominis, Mobiluncus* species and other anaerobes.[1,2] The majority of cases of BV are asymptomatic and remain unreported and untreated.[3] BV when symptomatic presents as malodorous[4,3] and increased amount of vaginal discharge which can be greyish to homogenous white[6,7]. Previously considered a benign condition, BV has been linked to many gynaecological conditions like pelvic inflammatory disease (PID)[8,9], post hysterectomy infections[10,11] and post abortal PID[12,13]. Certain obstetrical complications like preterm labour and preterm delivery[3,14,15,16,17], premature rupture of membranes[18], amniotic fluid infections[19] and post-partum endometritis[20] have been linked to occurrence of BV during pregnancy. BV can be diagnosed using Amsel[21], Spiegel[22] or Nugent criteria[23]. These criteria utilize vaginal pH, amine odor test, demonstration of 'clue' cells in vaginal secretion and Gram staining of vaginal discharge. Metronidazole is the drug of choice in the treatment of BV.[24] Metronidazole is inactive against facultative Lactobacilli, therefore, it does not interfere with the recolonization of these organisms after successful therapy. Oral clindamycin has significant effect against anerobic bacteria and G. vaginalis.[25] Intravaginal chlorhexidine, intravaginal metronidazole, clindamycin creams and lactate gels have also been found to be curative.[26] Since BV can be associated with pregnancy complications, we undertook this study to know the prevalence of BV in pregnant women attending antenatal clinic and its correlation with adverse pregnancy outcome.

Materials and Methods

The study was conducted in Department of Obstetrics and Gynaecology and Department of

Microbiology in Lala Lajpat Rai Memorial Medical College (LLRMMC) and associated Sardar Vallabhbhai Patel (SVBP) Hospital over a period of one year extending from September 2009 to October 2010. This study was conducted on 500 pregnant women.

Inclusion Criteria:

1. Single Pregnancy
2. Period of gestation <28 weeks as calculated by last menstrual period or first obstetrical ultrasound if the women was not sure of her last menstrual period.

Exclusion Criteria:

1. Women with history of previous preterm labour or threatened preterm labour.
2. Women with known obstetrical complication which can be a confounding factor for preterm labour such as antepartum hemorrhage, severe anemia, pregnancy induced hypertension, essential hypertension, multiple gestation, existing kidney or heart disease, structural and functional abnormalities of the uterus and chronic documented urinary tract infection
3. Cases where preterm labour was induced for any obstetrical and medical condition.

Written consent in patients own language was taken before enrolling patients for the study. Women with period of gestation less than 20 weeks were followed up again at 20 weeks and 28 weeks to assess for presence of bacterial vaginosis if they did not have bacterial vaginosis at the first visit. A detailed history and examination pertinent to an antenatal case was done in all the antenatal women. All women were subjected to routine antenatal investigations. Apart from the routine investigations, vaginal secretion/ discharge were sent to detect bacterial vaginosis by Nugent's criteria.

Nugent's Criteria for diagnosis of Bacterial Vaginosis:

Interpretation from the Gram stained slide was done using Nugent's Criteria. In this criteria, each Gram stained smear was evaluated for the following morphotypes under oil immersion lens:

1. Large Gram positive rods- Lactobacillus morphotype.
2. Small Gram negative rods- Gardnerella morphotype.
3. Small Gram variable rods- Bacteroids morphotype.
4. Curved Gram variable rods- Mobilincus morphology.

Each morphotype was quantified from 0-4+ with regard to the number of morphotypes per oil immersion field.
4+ = > 30 morphotypes / 100Xfield.
3+ = 6 -30 morphotypes/100X field.
2+=1-5 morphotypes/100X field.
1+ = <1 morphotypes /100 field.

A scoring system based on quantification of different morphotypes on the Gram stain slide as given in table (Table 1) below was then applied.

Morphotype	0 point	1 point	2 points	3 points	4 points
Lactobacillus	4+	3+	2+	1+	0
Anerobic rods/ Gardnerella	0	1 +	2+	3+	4+
Mobilincus	0	1+-2+	3+ -4+		

Score:
0-3 = Normal/ Non- Bacterial Vaginosis (NBV)
4-6 = Intermediate
7-10 = Bacterial Vaginosis (BV)

Analysis of Data:
The data was subjected to usual statistical analysis by employing the tests of Chi Square.

Observations and Results

Maximum number of women 216 (43.2%) were in the age group of 21-25 years of age whereas only 34 (6.8%) belonged to age group ≥31 years. Out of the ninety eight women who had BV, 46 (46.9%) women were in the age group of 21-25 years, 33 (33.7%) were in the age group of 26-30 years, 16 (16.3%) belonged to the age group ≤ 20 years and three (3.1%) women were in the age group ≥31 years. The distribution of women with BV according to age was not significant (p= 0.23).

Vaginal microflora was evaluated by Nugent's Criteria in all the women and it was observed that maximum women 350 (70%) had normal vaginal flora. 52 (10.4%) had intermediate flora and 98 (19.6%) had bacterial vaginosis.

Maximum number of women enrolled for study 229 (45.8%) were nullipara, 100 (20%) were primipara, 104 (20.8%) were second para and 67 (13.4%) were third para and above. Sixty six (67.3%) women with BV were nulliparous, twenty (20.4%) were primpara, seven (7.1%) were second para and the remaining five (5.1%) were para

three and above. This distribution shows that BV is significantly seen in nulliparous women (p< .001).

Maximum number of cases 266 (53.2%) belonged to lower class. 167 women (33.4%) belonged to upper lower class and the remaining 67 (13.4%) belonged to lower middle class. None of the women belonged to upper or upper middle class. Seventy five (76.5%) antenatals with BV belonged to the lower class as opposed to twenty (20.4%) who belonged to the upper lower class and three (3.1%) who belonged to the lower middle class. This distribution shows that BV patients are significantly distributed in lower class (p<0.0001).

Maximum number of women 284 (56.8%) were between 21-28 weeks period of gestation. Remaining 216 (43.2%) antenatals were between period of gestation 11-20 weeks. None of the women was under 10 weeks period of gestation. Maximum number of women with BV 53 (54.1%) was in the gestation period between 11-20 weeks. Forty five (45.9%) patients with BV were in the gestation period between 21-28 weeks. The distribution of patients with BV according to period of gestation was not significant distribution.

Table 2: Distribution of preterm labour, prom and post-partum enpqmetritis patients according to vaginal microflora

Category	No. of Women	Preterm Delivery (%)	Prom (%)	Post-partum Endometritis (%)
NBV	350	7(2)	1 (0.3)	0
Intermediate	52	0	1 (1.9)	0
BV	98	23 (23.5)	14 (14.3)	6 (6.1)
Total	500	30	16	6

Twenty three (23.5%) of the 98 patients with BV had a preterm delivery. Out of these twenty three, six delivered at 32 weeks gestation, five delivered at 33 weeks gestation, seven delivered at 34 weeks gestation and the remaining five delivered at 35 weeks gestation. None of the women who had intermediate flora had preterm delivery and only seven (2%) with normal vaginal flora had preterm delivery. Both of them delivered at 36 weeks gestation (Table 2). The occurrence of preterm delivery in patients of BV is quite significant (p<0.0001). As already discussed, BV patients were maximum in the period of gestation between 11-20 weeks. Out of the 53 patients of BV diagnosed in 11-20 weeks period of gestation, 12 patients had preterm delivery, 45 patients of BV were diagnosed in the 21-28 weeks period of gestation. Among these, 11 had preterm delivery. The association of more number of preterm deliveries in patients with BV diagnosed in 11-20 weeks period of gestation was not significant (p= 0.2).

PROM was seen in sixteen patients (Table 2). Fourteen (14.3%) of the 98 patients of BV had PROM. This association is quite significant (p≤ O.OOl). Of the remaining two patients who had PROM, one patient had intermediate vaginal flora and the other one had normal vaginal flora.

Only six patients had postpartum endometritis and all had BV. However, these 6 patients were out of 98 patients of BV. None of the patient with intermediate or normal vaginal flora had postpartum endometritis (Table 2).

Discussion

Infection as a possible cause of preterm labour has caused much interest recently and most of the evidence relating to preterm labour is based on two observations, first, all types of infections relating to ascending bacterial invasions including funisitis, chorioamnionitis, neonatal sepsis and maternal endometritis are more commonly found in preterm births: second, certain organisms in the vaginal flora are more often found in women with preterm labour or premature rupture of membranes.

According to a study by Lavett in 1995, bacterial vaginosis is less common in pregnant than in non-pregnant women (23% Vs 33%).[27] To assess the role of bacterial vaginosis in pregnancy complications in a developing community where mixed cervicovaginal infection are common, Govender et al 1996, found bacterial vaginosis in 52% of the women studied at 30 weeks or more of gestation and was the commonest infection diagnosed.[28] Bacterial vaginosis prevalence in Italian population of asymptomatic pregnant women was found to be 4.9% at 8th or 9th month of pregnancy by Cristiano et al in 1996.[2] The rates of preterm delivery were almost double for women who had bacterial vaginosis in early pregnancy (20.5%) as compared to women who had bacterial vaginosis only in late pregnancy (0.8%) (Riduan et al, 1993). In our study, 350 out of 500 women were diagnosed to be consistent with non-bacterial vaginosis (NBV) (70%) i.e. Nugent's score 0-3, 52 out of 500 were intermediate (10.4%) i.e. Nugent's score 4-6 and 98 out of 500 (19.6%) had Gram stain consistent with bacterial vaginosis (BV) by using Nugent's Criteria

(Nugenf *s* score 7-10).

According to Gravett et al, 1986, patient with and without bacterial vaginosis also did not differ significantly with respect to demographic factors recorded.[18] In our study, age of the women had got no correlation with bacterial vaginosis (p=0.23).

Gravett et al, 1986, prospectively studied the relationship of pregnancy outcome to BV, an anerobic vaginal condition and other selected genital pathogens among 534 gravid women. Patient with BV did not differ significantly with respect to past reproductive performance, prenatal care. However, history of prior first trimester abortions was more common among those with than those without BV ($p<0.05$).[18] In a study by Cristiano et al, 1996, incidence of BV was more common in primipara between gestational ages 11-20 weeks.[29] In our study, woman's obstetric history is significantly correlated with BV ($p<0.001$). It was more commonly found in nullipara women.

In a study by Bhalla et al, 1994, 544 women with vaginitis and 258 asymptomatic women were screened for the presence of bacterial vaginosis. Bacterial vaginosis was present in 50% of the symptomatic cases and 21.8% of asymptomatic cases. Bacterial vaginosis showed a positive correlation with low socioeconomic status.[30] Thakur et al 1986, found that colonization with *Gardnerella vaginalis* was more common among women of low socio economic status, nulliparous.[31] In the article by Jenifer E Allsworth, 2007, the prevalence of bacterial vaginosis in women between ages 14-49 years in USA was lower among those living well above the federal poverty level (24%) compared with those living at or near (34%) or lower (37%) the federal poverty level.[32] In our study, prevalence of BV was most common in lower socioeconomic status ($p< 0.0001$).

In a study by Hay et al in 1994, 718 pregnant women attending antenatal clinics were studied. At their first attendance and then subsequently, Gram stained vaginal smears were examined and *Mycoplasma hominis* and *Gardnerella vaginalis* were sought by culture. In their conclusion, pregnant women did not commonly develop bacterial vaginosis after 16 weeks of gestation and if present, it remits spontaneously in approximately half of those who reached term. They also noted that bacterial vaginosis was associated with increased rate of 1st trimester miscarriage and preterm delivery. So, they opinioned that any treatment aimed at its eradication in pregnancy should be given no later than the beginning of 2nd trimester of pregnancy.[3] Association of bacterial vaginosis and prematurity in early and late pregnancy in Indonesia was studied by Riduan et al, 1993. 490 pregnant women were evaluated at three-hospitals in Jakarta, Indonesia for bacterial vaginosis at 16-20 weeks and 28-32 weeks and observed till delivery. They found significant differences between preterm delivery and BV diagnosed at 16-29 weeks gestation but not with BV diagnosed at 28-32 weeks gestation. The rates of preterm delivery were almost double for females who had bacterial vaginosis in early pregnancy (20.5%) as compared to women who had bacterial vaginosis only in late pregnancy (10.7%).[14] In our study, none of the woman was under 10 weeks period of gestation. Maximum number of women with BV (53) was in gestation period between 11-20 weeks. This association was however, not significant.

Several recent studies have examined the relationship between BV in pregnancy and preterm delivery. Riduan et al, 1993, found significant associations between preterm delivery (gestational age < 37 weeks) and BV diagnosed at 16-20 weeks gestation, but not with BV diagnosed at 28-32 weeks gestation. The rates of preterm delivery were almost doubled for women who had BV in early pregnancy (20.5%) as compared with women who had BV only in late pregnancy (10.7%).[14] Martius et al, 1988, found significant association between preterm delivery and the recovery of organisms from chorioamnion and histologic chorioamnionitis.[33] BV was associated with 2-6 fold increased risk for preterm labour, a 6.9 fold increased risk for preterm birth and a 7.3 fold increased risk of preterm PROM (Kurki et al, 1992).[34] Hay et al, 1994',' conducted a longitudinal study of BV in pregnancy. They found that BV detected early in second trimester of pregnancy, is strongly associated with late miscarriage and preterm birth. Therefore, women should be screened for BV no later than early in second trimester of pregnancy.[3] Sheehan et al, 1996, concluded in their study on BV that it is the most common cause of vaginal infection. If undiagnosed or untreated, the condition is associated with serious adverse sequelae in both obstetrics and gynecology. If BV is detected early in pregnancy, the women has five fold increased risk of late miscarriage or preterm delivery compared with women without this condition.[35] Govender et al, 1996, showed that 46% of the women studied had poor pregnancy outcome as measured by obstetrical complication, pregnancy loss and/or neonatal morbidity. There was a significant difference in the outcome in women with BV (55 out of 88) compared to those infections other than BV (13 of 31) or no infection (5 of 9). This difference was for obstetrical complications of preterm delivery, PROM and intrauterine infection but not for pregnancy losses and neonatal morbidity.[28] In our study, preterm delivery occurred in 30 out of 500 women studied. The rest of the women delivered at term. The minimum period of gestation at which patient delivered was 32 weeks and the maximum period of gestation.at which labour had to be induced by cerviprime instillation was 42 ± 1 weeks. Out of the 30 antenatal women who delivered preterm, 23 had BV. At the same time, out of the total 98 patients which had BV by Nugent's criteria, 75 delivered after 37 weeks. This association of occurrence of preterm delivery in patients with BV was highly

significant ($p<0.0001$).

Preterm premature rupture of membranes (PPROM) resulting in delivery before 37 Weeks of gestation occurs in about 10% of pregnancies (Gravett et al, 1986). Bacterial vaginosis was significantly associated with PROM (Odds Ratio 2:4) in this study.[18] In our study, a highly significant association was found between PROM occurrence in BV patients ($p<0.001$).

In our study, postpartum endometritis was seen in six women and all of them had BV. Our study further lays credentials to the fact that BV is associated with adverse pregnancy outcome and should be looked for early in pregnancy.

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