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Prevention Of Preterm Labor In Established Cases Of Bacterial Vaginosis With Antibiotics.

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ABSTRACT

Bacteria such as *Lactobacillus lactis* have an intravaginal cleansing effect in normal pregnancies, minimizing the presence of common bacterial species. Recent high-throughput sequencing of 16 S rRNA gene of the vaginal bacterial communities of pregnant women showed that vaginal microbiome becomes more stable and less diverse as pregnancy progresses, which confers a protective role against ascending infection of the genital tract. However, there are intravaginal microorganisms other than *Lactobacillus* species in some pregnancies that cause chorioamnionitis. This is because the normal flora (commensal bacteria) that colonize the vagina during pregnancy do not cause inflammatory conditions or vaginitis, such as occurs with infection by pathogenic bacteria. An imbalance in the normal vaginal bacteria is therefore known as bacterial vaginosis (BV). To find out the prevalence of bacterial vaginosis in spontaneous preterm labor. A complete history was taken with menstrual history and obstetrical history. The gestational age was confirmed from last menstrual period and was correlated with clinical examinations and ultrasonographic gestational age. In the case of previous history of preterm labor, the ultimate fetal and maternal prognosis was carefully analyzed. In the current pregnancy a detailed history of complication associated with pregnancy was taken. Abdominal vaginal and speculum examination were done. Nature of discharge noted and vaginal swabs were taken for bacteriologic study. Without treatment, the preterm delivery rate was higher in the BV subgroup than in the I and normal (N) subgroups ($p = 0.021$) in the EGP, whereas the rates in the BV and I subgroups were higher than in the N subgroup in the MGP ($p = 0.0003$). Although treatment of BV by metronidazole vaginal tablets significantly increased the N subgroup in the MGP ($p = 0.020$), there was no significant improvement in the preterm delivery rate. Decreasing the rate of preterm delivery requires development of treatment methods that will further increase the percentage of patients who test N during the MGP after BV during the EGP.

Keywords: Preterm Labor, Chorioamnionitis Bacterial Vaginosis, Antibiotics.

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INTRODUCTION

Preterm labour with subsequent delivery of the premature baby is the major cause of perinatal morbidity and mortality. Preterm birth is defined as birth before 37 weeks of gestation. Despite major advances in obstetric and neonatal care over the past decade the incidence remained constant at 10-15% [1]. Preterm premature rupture of membranes and spontaneous preterm labour account for approximately 80% of preterm deliveries. The remaining 20% are indicated deliveries for maternal or fetal reasons [2]. Preterm deliveries poses a problem because of the severe neonatal complications that often occur afterwards that includes death, respiratory distress syndrome, sepsis and necrotizing enterocolitis [3]. The etiology of preterm labor (PTL) is multifactorial with increasing evidence that infection is a possible cause in upto 40% of cases. PTL may either be a physiological process occurring too early in pregnancy or a pathological process as a result of an abnormal signal such as infection [4]. Normal genital tract flora are dominated by Lactobacillus which produce lactic acid keeping the vaginal pH below 4.5 so discouraging the growth of other organisms [5]. During pregnancy the concentration of Lactobacillus species increase 10 fold as pregnancy progresses. Increased levels of lactobacilli make the vaginal ecosystem inhibitory to the growth of many pathogens. In Bacterial vaginosis lactobacilli are altered resulting in 1000-fold increase in anaerobes mobiluncus species and the genital mycoplasmas [6]. Bacterial vaginosis has been associated with preterm labour, PROM and with postpartum maternal and neonatal infections. Bacterial vaginosis has been strongly associated with vaginal cuff infections following hysterectomy, PID, post abortal PID and caesarean endometritis [7]. Vaginal infections such as Trichomonas vaginalis and candida generally induce inflammatory response in vaginal wall which is usually accompanied by increase number of leukocytes in vaginal fluid. This is the hallmark of "itis" condition [8]. The term bacterial vaginosis was introduced to describe increased vaginal discharge without signs of clinical inflammation and noticeable absence of leucocyte. The vaginosis was called bacterial because of absence of fungi and parasites as cause of syndrome [9,10].

MATERIALS AND METHODS

This Prospective study was carried out on pregnant women admitted in the labor ward in the Department of Obstetrics and Gynecology, Sri Venkateshwara Medical College Hospital & Research Institute.Chennai-600 067 between September 2022-september 2023.A total number of 200 women were studied which were divided into 2 groups. The study group included 100 women who came in preterm, With gestational age between 28 and 37 weeks With painful uterine contractions lasting for 45 seconds associated with cervical effacement of 80% and above. Cervical dilatation of less than or equal to 3 cm and with intact membranes. The control group included 100 women who came in term gestation in labor. With painful uterine contractions for 45 seconds associated with cervical effacement of 80% and above .Cervical dilatation of less than or equal to 3 cm and with intact membranes.

Inclusion Criteria

- Booked, unbooked and referral cases were included in thestudy
- Both prime and multi irrespective of socio economic statuswere included.

Exclusion criteria :

Women are excluded from analysis if they had

- GA < 28 weeks
- Multiple pregnancy
- Pregnancy induced hypertension
- Fever, UTI, Diarrhea, Respiratory tract infection
- Anaemia, Heart disease, GDM, DM
- PROM / absent membranes
- Antibiotic therapy within last 30 days

A complete history was taken with menstrual history and obstetrical history. The gestational age was confirmed from last menstrual period and was correlated with clinical examinations and ultrasonographic gestational age. In the case of previous history of preterm labour the ultimate fetal and maternal prognosis was carefully analysed. In the current pregnancy a detailed history of complication

associated with pregnancy was taken. Abdominal vaginal and speculum examination were done. Nature of discharge noted and vaginal swabs were taken for bacteriologic study.

Statistical Analysis

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2018). Using this software range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskul Wallis chi- square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship. Sensitivity, specificity, accuracy, positive predictive value and negative predictive values were calculated using the following formulae and taking 48 hours positivity results with 10 mm induration as cut off value as the Golden standard.

RESULTS

Having excluded patients with known risk factors for preterm labour, the subset of women in idiopathic preterm labour (100) and women in term labours (100) were studied. Nugent's score (Gram staining) taken as gold standard test to diagnose bacterial vaginosis.

Table 1: Age Distribution of Cases

Age groups (in years)	Pre term	Term
< 20	9	9
21 – 24	56	50
25 – 28	22	33
29 – 32	9	6
33 Yrs & above	4	2
Total	100	100

Mean Age in preterm group is 23.6 years $\pm$ 3.8 years and in term group is 23.8 years $\pm$ 3.5 years.X^2-0.5843. P-0.4445 (not significant)On analyzing the table, maternal age did not seem to influence the study group of idiopathic preterm labour as the percentage ofcase in the study group and the control group did not vary much.

Table 2: Distribution of subjects according to obstetric history

Obstetric Code	Study (Pre term)	Control (Term)
Primi	57	45
G2	24	39
G3	14	13
G4	5	2
G5 & above	0	1

57 of women in preterm group and 45 in term group were primigravidas. 5 cases in preterm group and 2 cases in term group belonged to G4. 1 case in term group belonged to G6 and none in the preterm group belonged to G5 & above.X^2-2.42, P-0.1197. The comparison was not significant

Table 3: Distribution of Bacterial vaginosis among the subjects

Bacterialvaginosis	Study (Pre term)	Control (Term)
Positive	27	12
Negative	73	88

According to Nugent's score Bacterial vaginosis was positive in 27% of preterm and 12% of term cases.X^2-6.24, P-0.0125, which is statistically significant. So, the presence of Bacterial vaginosis was significantly associated with preterm labour.

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Table 4: Efficacy of various investigations / Homogenous Discharge

Homogenousdischarge	Bacterial Vaginosis	
	Positive(n=39)	Negative(n = 161)
Present (n=36)	31	5
Absent (n=164)	8	156

	Percentage
True positive	86
False positive	14
True negative	95
False negative	5
Sensitivity	79
Specificity	94
Accuracy	94
PPV	86
NPV	95

36 cases (including term and preterm) had homogenous discharge characteristic of bacterial vaginosis. Of these, 31 had bacterial vaginosis according to Nugent's score. The sensitivity was 79% specificity was 94% positive predictive value 86% negative predictive value 95%.

Table 5: pH values of Vaginal Discharge

Ph > 4.5	Bacterial Vaginosis	
	Positive(n=39)	Negative(n = 161)
Present (n=67)	39	28
Absent (n=133)	0	133

	Percentage
True positive	58.2
False positive	41.8
True negative	100
False negative	0
Sensitivity	100
Specificity	83
Accuracy	86
PPV	58
NPV	100

67 cases had pH > 4.5. Of these only 39 cases were positive for bacterial vaginosis. pH value was sensitive to diagnosis all cases of Bacterial Vaginosis. The sensitivity was 100%. Specificity was 83%. positive predictive value was only 58%. Negative predictive value was 100%.44 cases were positive for amine test of these 37 cases were positive for bacterial vaginosis according to Nugent's score. The sensitivity was 95%. specificity 96%. Positive predictivevalue 84%, Negative predictive value 99%.32 cases were positive for clue cells. Of these 30 cases hadBV according to Nugent's score. 9 cases who were negative for clue cells had bacterial vaginosis according to Nugent's score. The sensitivity was only 77%, specificity was 99% positive predictive value was 94% Negative predictive value was 95%.100% cases who were positive for BV by Amsel's criteria had bacterial vaginosis by Nugent's score. Amsel's criteria did not have any false positive cases. But this criterion failed to diagnose bacterial vaginosis in 2 cases who were positive for bacterial vaginosis according to Nugents score. The sensitivity was 95%. specificity 100%. positive predictive value 100%, Negative predictive 99%.

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Table 6: Efficacy of various test results

Tests	Sensitivity	Specificity	Accuracy	PPV	NPV
Nature of discharge	79	94	94	86	95
pH > 4.5	100	83	86	58	100
Amine test	95	96	96	84	99
Clue cells	77	99	95	94	95
Amsel'scriteria	95	100	99	100	99

On analyzing various test results pH value > 4.5 has highestsensitivity (sensitivity 100%)Amine test, Amsel's criteria and clue cells have high specificity Amsel's criteria-100% specific,Clue cells-99%,Amine test-96%,Amine test & Amsel's criteria have good sensitivity and specificityand correlate well with Nugent's score.

Table 7: Impact of bacterial vaginosis on maternal and neonatal outcome

Maternal and neonatal complications	Bacterial vaginosis				X2	P value
	Positive (n=39)		Negative(n=161)			
	No.	%	No.	%		
Neonatal complications Present Absent	 9 30	 23.1 76.9	 22 139	 13.6 86.4	 1.47	0.226 (Not significant)
NICU AdmissionsPresent Absent	 16 23	 41 59	 27 134	 16.8 83.2	 9.55	0.0019, Significant
Maternal Complications Present Absent	 2 37	 66.77 19	 1 160	 33.3 85	 1.8	0.978 (not significant)

From the table, the neonatal complications (including birthasphyxia, RDS, meconium aspiration syndrome, hyperbilirubinemia) were not increased in patients with bacterial vaginosis when compared with patients who did not have bacterial vaginosis.X^2 - 1.47,P- 0.226 (not significant).

NICU admissions in bacterial vaginosis positive group was 41%whereasinbacterial vaginosis negative group the NICU admissions were only 16.8%.X^2-9.55,P-0.0019 which was statistically significant.2 patients in bacterial vaginosis positive group had episiotomy wound infection where as in bacterial vaginosis negative group 1 patient had puerperal fever.X^2 -1.8,P -0.978 which was statistically not significant.

DISCUSSION

From the study we have confirmed significant association between bacterial vaginosis and preterm labour. Gram staining and analysis by Nugent scoring has been takenas a standard method of diagnosing Bacterial vaginosis in our study because of the reliability and accuracy of Nugent score in the detection of bacterial vaginosis Nugent's score also has the advantage of less inter and intraobserver variation, and the slides can be stored for future references [11]. In our study the prevalence of bacterial vaginosis was 27% in the study group of preterm labour and in 12% in the control group of term labour (p - 0.012) [12]. On analyzing efficacy of various tests homogenous discharge was present in 36 patients of these 31 were positive for bacterialvaginosis. 8 cases of bacterial vaginosis positive cases did not have homogenous discharge the sensitivity was 79% specificity was 94%. PH >4.5 found in 67 patients and diagnosed all of bacterial vaginosis positive cases with the false positivity rate of 41.8% pH>4.5 has the highest sensitivity (100%) and least specificity [13]. However, it is economical, extremely simple and a useful tool to rule out bacterial vaginosis. Amine test was positive in 44 cases of which 37 cases were positive for bacterial vaginosis. Amine test has a good sensitivity (95%) and a specificity (96%). In the absence of microscope, amine test can be used as a specific and relatively sensitive method of detecting BV [14]. Detection of clue cell is the single most specific test but not a sensitive one specificity 99% sensitivity 77%. It has a high PPV (94%) and a NPV (95%). We did not evaluate culture for G.vaginalis since it has repeatedly been shown to be of little diagnostic value.

Eschenbach's group found that more than 55% of normal patients had G. vaginalis positive. Culture play no role in diagnosis because isolation of G.vaginalis and or anaerobic bacteria from vagina does not define the clinical entity and can be observed in women without bacterial vaginosis [15]. In our study, the mean birth weight of babies born to bacterial vaginosis positive mothers was 2.21 Kg.± 0.55kg and in bacterial vaginosis negative group was 2.53± 0.53kg (p – 0.0024). Hence, BVis significantly associated with LBW babies. Whether it is the cause (or) association is not known. In our study, out of 39 patients who had bacterial vaginosis neonatal complications (birth asphyxia, RDS, meconium, aspiration syndrome, hyper bilirubinemia) were present in 9 cases (23.1%). In bacterial vaginosis negative group out of 161 patients in 22 babies (13.6%). So the incidence of neonatal complications in bacterial vaginosis positive and negative group did not vary much (p - 0.226) [16]. In our study, out of 39 patients who had bacterial vaginosis 16 babies (41%) were admitted in neonatal intensive care unit whereasin bacterial vaginosis negative group out of 161 babies, 27 babies (16.8%) were admitted in NICU. So the neonatal admissions in bacterial vaginosis positive group were higher (p – 0.0019) than the bacterial vaginosis negative group [17]. In our study, 4 babies in preterm group and 1 baby in term group died in the early neonatal period. None of these babies were in bacterial vaginosis positive group. So the presence of bacterial vaginosis did not seem to influence the neonatal outcome [18]. Among maternal complications only the infectious morbidity (episiotomy wound infection, fever, foul smelling discharge) was analyzed. 1 patient in study group and 1 patient in control group had atonic PPH and 1 patient in control group developed lumbar plexopathy [19]. All these complications were excluded from analysis.2 Patients in bacterial vaginosis positive group developed episiotomy wound infection and 1 patient in bacterial vaginosis negative group developed fever in the puerperal period. The infectious morbidity in the bacterial vaginosis positive and negative group did not differ much (p – 0.0978) [20].

CONCLUSION

The prevalence of bacterial vaginosis was 27% in preterm group and 12% in term group. There was a significant association between bacterial vaginosis and preterm labour. There was alsosignificant association of various factors like low socio-economic status, low maternal weight and history of previous preterm deliveries to the study group (pre term labour). The neonatal and maternal outcome in the bacterial vaginosis positive and negative group did not differ much.

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