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CORRELATION OF MATERNAL BACTERIAL VAGINOSIS WITH NEONATAL SEPSIS

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ABSTRACT

Bacterial vaginosis is a common disease found in pregnant women. Patients presented with white discharge per vaginum are often victims of preterm labor. Babies of mother with excessive white discharge mostly needed ICU admissions. Correlation of maternal infections, with neonatal sepsis was suspected.

INTRODUCTION

The birth of a healthy child is a well orchestrated event that encompasses several facets including prenatal and perinatal factors. However it is not a rare event that the entire gestational period of 280 days is often confronted with innumerable risk factors that affect the birth of a healthy neonate. These factors could be maternal, fetal, placental or of idiopathic origin, of which maternal infection in the form of bacterial vaginosis (BV) is well documented (1).

BV is a polymicrobial syndrome caused due to altered pH conditions of the vaginal niche. As a result the normal vaginal flora is replaced by anaerobic organisms. Commonly, the predominant lactobacillus gets replaced by a mixed population of *Gardnerella vaginalis*, *Peptostreptococci*, anaerobic gram negative bacilli, *Mobiluncus*, *Prevotella* and *Mycoplasma sp.* causing chronic infection and vaginal discharges (2, 3). BV during pregnancy has been associated with increasing risks of spontaneous abortion, preterm labor, premature birth, preterm premature rupture of the membranes, amniotic

fluid infection, postpartum endometritis, and post-cesarean wound infections making the scenario alarming (4, 5). Furthermore increasing association of BV with preterm labor makes antenatal diagnosis of BV mandatory in pregnant women (6). Hence, considering the dreaded sequel of events of BV, its association with the pregnancy/gestation is a matter of deep concern.

Neonatal septicemia is a syndrome diagnosed by systemic signs of infection during the first month of life (7, 8). Sepsis is the leading cause of neonatal morbidity and mortality (30-70%) in India (9). Infection is usually acquired intrapartum or from the maternal birth canal and is transmitted before or during the birth process. Hence imbalance of the normal vaginal flora due to altered biochemical characteristics of the vaginal niche could serve as a potent risk factor causing neonatal infection. So the prospective study was undertaken to determine a probable correlation between BV in pregnancy and the fate of the neonate using sepsis as a monitoring index

MATERIALS AND METHODS

Study population

A total of 100 pregnant women with different gestational stages of pregnancy positive for BV infection were selected as subjects. In parallel, 100 suitable healthy pregnant women without BV served as controls. The study was done in between the period from March 2010 to December 2011. The subjects were selected for the study at carried out in the department of Obstetrics & Gynecology and Department of Microbiology of Jawaharlal Nehru Medical College, AVBRH Sawangi (M), Wardha, as per the following selection criteria mentioned below:

Inclusion criteria

1. Singleton pregnancy
2. Gestational age: two groups, between 28-36i. weeks (preterm) and 36-40 weeks (full term).
3. Painful uterine contractions >2 in 10 minutes each lasting > 45 seconds. ii.
4. Cervical dilatation 1 to 4 cm.
5. Cervical effacement >25% iii.

Exclusion criteria

1. Gestational age <28 weeks
2. History of ante partum hemorrhage, urinary tract infections, respiratory tract infections,iv. diarrhea or any other obvious cause for preterm labor.
3. Medical complications of pregnancy such as moderate to severe anemia, pregnancy induced hypertension and diabetes mellitus.
4. History of leaking per vaginum or absent membranes.
5. Multiple pregnancies
6. Intrauterine growth restriction.
7. Intrauterine fetal death
8. Antibiotic therapy in the last 30 days.

Detailed history of the patient in the respective study population was noted especially to include history of previous abortion, preterm delivery, full term delivery, still birth and neonatal death followed by a thorough general and systemic

examination to exclude exclusion criteria. Additionally the fundal height, abdominal girth, presentation, uterine contractions (intensity, frequency and duration), fetal heart pattern and rate was recorded by detailed obstetrical examination. Speculum examination was done to exclude leaking and the pH and type of vaginal discharge was also noted. The dilatation of cervix and the status of membranes were validated by routine vaginal examination.

Diagnosis of bacterial vaginosis (BV) in selected subjects

BV was diagnosed in pregnant patients by the tests of Amsel's and Nugent's criteria (10, 11).

The tests of Amsel's criteria were performed using the vaginal discharge and smear of the subjects and controls. They were:

Vaginal pH > 4.5: vaginal pH was determined using pH indicator paper (range 2-10.5) with color scale.

Color and consistency: Thin grayish white homogenous

Whiff test (or Amine test): A few drops of 10 % KOH solution was added to the vaginal discharge, mixed and the emission of a strong fishy odor indicated a positive test.

Detection of clue cells in smear preparation: A wet smear preparation was done, stained with Gram stain and presence of more than 20 % clue cells was considered positive.

Light microscopy of immediate wet mounts was done to identify different microbes. Nugent's score is based on the gram staining of different vaginal morphotypes (11). Their number was enumerated based on the number visualized in oil immersion under 1000X magnification. The Nugent criteria score vaginal flora as normal (0-3), intermediate (4-6) and BV (7-10)

Detection of neonatal septicemia

The study was performed in babies aged 0-28 days delivered from women diagnosed of BV during pregnancy (12, 13). In parallel, babies from healthy women served as control. A

detailed history including the age, sex, birth weight, gestational age and manifestations of clinical septicemia was noted. Subsequently, routine blood culture investigations for diagnosis of infection were performed (14, 15). In brief, blood (4 mL) was drawn in sterile syringe after skin preparation by 2 step process. The organisms were isolated and identified by standard microbiological methods. Culture was monitored for 1-7 days respectively and the observation was correlated with BV, the associated maternal risk factor of the study.

Statistical analysis

Values show the means \pm SD of triplicate results from single representative experiments. Three independent experiments were routinely carried out for each assay. Student's t test was used to determine the level of statistical significance. $P < 0.05$ was considered significant.

RESULTS

We enrolled 100 pregnant women, who were further categorized as preterm and full term pregnancy. The study and the control groups were comparable as per age, weight, gestational age, haemoglobin content, parity and socioeconomic status as shown in Table 1.

The diagnosis of BV was done by performing the tests defining Amsel's criteria. The mean pH of the vaginal discharge of women in the study group was significantly higher (4.72 ± 0.35) as compared to that in the control (BV-) group (3.72 ± 0.55 , $p < 0.01$, Table 2) indicating their positivity for bacterial vaginosis (hence referred as BV +). Interestingly, the mean pH of the vaginal discharge of BV + women in preterm and full term pregnancy was almost similar, the values being (4.72 ± 0.31 and 4.73 ± 0.28).

Additionally, 52 % of pregnant women showed thin white homogenous vaginal discharge that signified presence of BV in them. Similarly, Whiff test or amine test was positive in

increased number (56 ± 2 %) of BV+ pregnant women in the study. In contrast only 15% of BV-ve pregnant women comprising the control group showed positive amine test.

The fourth test of Amsel's criteria to estimate the percent of clue cells was performed with samples taken from the BV+ pregnant women and the results were compared with that of the control group. The study group revealed significantly higher number of pregnant women with clue cells as compared to the control group indicating the occurrence of BV during pregnancy.

Nugent's scoring system based on the identification of the different bacterial morphotypes from individual smear preparation confirmed that 45 % pregnant women were positive for BV. The results corroborating the presence of BV by whiff's test showed a good correlation ($r = 0.98$) with that observed by scoring method.

Clinical symptoms of neonatal sepsis

The aim of this study was to investigate the probable correlation between the outcomes of neonatal sepsis in the babies delivered from women positive for BV during pregnancy. Primarily to assess the indications of neonatal sepsis, the behavioral attributes of the babies were monitored and as to the babies delivered from the control group. The babies showed refusal of feed, lethargy, hypothermia, irritability, respiratory distress, jaundice, abdominal distension, seizures, and cyanosis. In most of the cases the babies showed an incidence of several features. The blood culture from the babies showed the growth of microorganisms. The microbial flora depicted the profile of neonatal sepsis mostly comprised of Gram negative bacilli. Some of the predominantly occurring culture positive organisms were *Klebsiella sp.*, *Staphylococcus aureus*, *E.coli*, *Pseudomonas aeruginosa*,

Enterobacter sp., *Acinetobacter sp.*, *Candida sp.* Time of culture positivity was significantly observed within 4 days, which saved time for initiation of the required treatment. The incidence of neonate sepsis showed a good correlation (0.99) with the presence of bacterial vaginosis in pregnant subjects.

DISCUSSION

Neonatal sepsis is one of the important factors causing neonatal deaths. It is commonly described as a clinical syndrome of bacteremia manifested with symptoms within the first 4 weeks of life (7, 16). Neonatal sepsis has a wide range of risk factors involving frequent vaginal checkups during pregnancy, premature birth, infected maternal birth canal and infected placenta. However if diagnosed and treated with proper antibiotic therapy sepsis can be cured.

BV is the most common cause of vaginitis. The prospective study demonstrated the presence of BV, as evidenced by Nugent's scoring system and positivity in Amsel's criteria. Amine test which is both highly sensitive and specific was positive in patients with BV. Our study detected 45 % cases by smear examination. The presence of clue cells also predicted BV. Previously, reports have documented the incidence of BV with preterm delivery and the complications associated with it (17-19). In this study we have corroborated the presence of BV in patients all throughout their pregnancy (preterm and full term). Interestingly, since BV culminates in the alteration of the microbial population in the vagina, we observed a good correlation of the incidence of neonatal sepsis in patients positive for BV. The study demonstrated that the neonates from mothers' positive for BV demonstrated signs and symptoms of sepsis which was further confirmed through blood culture studies.

CONCLUSION

Thus we conclude that of the many factors influencing neonatal sepsis, the incidence of bacterial vaginosis poses preponderance for its outcome. Moreover the presence of BV at any phase of pregnancy shows a good correlation with neonatal sepsis. Mothers with bacterial vaginosis invariably had some detrimental effects on their babies.

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Table 1. Demographic profile of study and control group

| Feature | BV + (n = 100) | BV - (n = 100) |
|-------------------------------|----------------|----------------|
| Maternal age (years) | 24.21 ± 4.05 | 23.95 ± 3.56 |
| Gestational age (weeks) | | |
| Preterm | 33.15 ± 1.75 | 33.42 ± 1.95 |
| Full term | 38.05 ± 1.85 | 37.75 ± 2.11 |
| Weight (Kg) | 66.23 ± 5.15 | 65.55 ± 4.44 |
| Haemoglobin (g %) | 10.2 ± 1.05 | 10.5 ± 1.15 |
| Low socio-economic status (%) | 55.45 | 72.84 |
| Uneducated (%) | 52.61 | 48.31 |

Table:2 Vaginal pH in study and control group

| pH | BV + group (n =100) | BV – group (n = 100) |
|-------|------------------------|-------------------------|
| < 3.5 | 8 | 55 |
| 4.0 | 14 | 19 |
| 4.5 | 41 | 15 |
| 5.0 | 26 | 8 |
| 5.5 | 6 | 3 |
| >6.0 | 5 | 0 |

Table: 3 Fetal outcome in BV positive and negative cases.

| Gestational age | Total Number of NICU admissions | BV+ | BV- | NEONATAL SEPTICEMIA |
|-----------------|------------------------------------|-----------|-----|------------------------|
| PRETERM | 76(44.7%) | 35(77.7%) | 21 | 28(36.84%) |
| NEAR TERM | 94(55.29%) | 10(22.2%) | 14 | 17(18.08%) |
| TOTAL | 170 | 45 | 35 | 45 |