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The Prevalence of Symptomatic & Asymptomatic Bacterial Vaginosis and Its Treatment in Managing Preterm and Threatened Preterm Deliveries

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Abstract

Background: 8-10% pregnancies end in preterm labour or threatened preterm labour which has maternal and foetal complications just due to infections such as bacterial vaginosis, which can be identified by simple tests like Amsel Criteria and treated at the earliest with appropriate antibiotics. *Aim:* The prevalence of bacterial vaginosis in preterm & threatened preterm labor based on amsel's criteria and treatment of bacterial vaginosis in managing preterm & threatened preterm deliveries. *Materials and Methods:* The study was carried out in department of obstetrics & gynaecology, Government Rajaji hospital, Madurai medical college, Madurai. 200 women with symptoms of preterm & threatened preterm labour. Examination of vaginal discharge,vaginal pH, microscopy for clue cells and Whiff test, which are Amsel's criteria, were done. Chi-square test was used to find outthe association of variables and p value less than 0.05 was taken as statistically significant. *Results:* There was significant association between bacterial vaginosis and preterm labour.There was significant association between bacterial vaginosis and delivery of low birth weight babies.There was strong evidence that treatment of bacterial vaginosis in preterm & threatened preterm reduces the neonatal complications. *Conclusion:* The prevalence of bacterial vaginosis was 30% in preterm & threatened preterm deliveries. There was a significant association between bacterial vaginosis and preterm labour. There was also significant association of various factors like low socio economic status, low BMI and history of previous preterm deliveries to the study group. There was storng evidence that treatment of bacterial vaginosis in preterm & threatened preterm deliveries reduce the neonatal complications.

Keywords: Bacterial Vaginosis; Gardnerella Vaginalis; Amsel's Criteria.

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Introduction

Preterm labour is defined as the onset of labour prior to the completion of 37 weeks of gestation. It is considered to be established if regular uterine contractions can be documented atleast 4 in 20 minutes or 8 in 60 minutes with progressive change in the cervical score in the form of effacement of 80% or more and cervical dilatation greater than 1 cm. If uterine contraction are perceived in the absence of cervical change, the condition is called threatened preterm labour. The incidence of preterm labour 7 – 10%, nearly 40–50% of preterm births occur following spontaneous labour, 30% due to preterm premature rupture of membranes and the remaining 30% are iatrogenic termination for maternal and fetal benefits. The preterm labour may either be a physiological process that has occurred too soon or a pathological process following an abnormal stimulate like infection. Infection is implicated as the aetiological factor in 40–50% of cases of

preterm labour, among which bacterial vaginosis contributes 30– 40% ,which when treated with appropriate antibiotics can be prevented in upto 70–80% cases.

Bacterial Vaginosis

Bacterial vaginosis is a polymicrobial vaginal infection caused by over growth of anaerobic bacterial like Gardnerella vaginalis, Mycoplasma hominis, Mobiluncus species, ureaplasma urealyticum, Chlamydia trachomatis, Peptostreptococcus, bacteriodes with a corresponding decrease in the number of lactobacillus. Bacterial vaginosis in pregnancy cases preterm labour, preterm premature rupture of membrane, chorioamniontis, amniotic fluid infection, postpartum endometritis, PID, postabortal PID, vaginal cuff infections following hysterectomy.

Aim of the Study

1. The prevalence of bacterial vaginosis in preterm and threatened preterm labour based on Amsel's criteria
2. Treatment of bacterial vaginosis in managing preterm and threatened preterm deliveries.

Review of Litreature

Nearly a century ago, Doderlein described a nonmotile bacillus, which he considered to be the normal flora of vagina of the pregnant women. The doderlein bacillus later became known as lactobacillus. In 1899, menge and kronig reported isolation of both facultative and strictly anaerobic microorganisms, as well as the Dorderlein bacillus from the vagina of most women.

In 1913, Curtis demonstrated that (1.) The discharge arose from vagina and not from the uterus. (2.) Women having white discharge did not have large numbers of Doderlein bacilli. (3.) The presence of anaerobic bacteria in vagina, especially anaerobic rods, correlated with vaginal discharge. In 1920s, Schroder reported three types of vaginal flora, acid producing lactobacillus, mixed flora with few lactobacilli and mixed flora without lactobacilli.The recognition of the association of G. vaginalis with non specific vaginitis by Gardner and Dukes in 1955 provided the first clear evidence that G. vaginalis caused non specific vaginitis. In 1980, in honor of Dr. Herman Gardner the name of the organism was changed in to Gardnerella vaginalis and the disease become known as Gardnerella vaginalis vaginitis. In early 1980s, the emergence of evidence that anaerobic bacteria were responsible for characteristic fishy odor of this disease and the term anaerobic vaginosis was coined by Blackwelland associates in 1982. In 1984, the term bacterial vaginosis was advocated to reflect the complex alteration of vaginal flora and to constitute the presence of increased discharge without an apparent inflammatory response.

Epidemiology and Risk Factors

The specific causes and risk factors associated with bacterial vaginosis are poorly understood, however age at first sexual intercourse,change in sexual partners, greater number of lifetime sexual partners,concurrent Sexually Transmitted Diseases, genetic predisposition are possible risk factors. Cigetette smoking and the use of IUDs are both linked to an increased risk of acquiring bacterial vaginosis. Vaginal douching has also been implicated as a risk factor for bacterial vaginosis, by aiding the ascent of microorganisms into the upper genital tract. Bacterial vaginosis is seen to occur more frequently in women of Afro-caribbean origin compared to Caucasian women.

Bacteriology

Bacterial vaginosis is a polymicrobial infection in which the normal hydrogen peroxide producing lactobacillus predominant vaginal flora is replaced with anaerobic bacteria like gardnerella vaginalis, anaerobic gram negative rods (Bacterides, prevotella, Prophyromonas) mobiluncus species and mycoplasma hominis.

Pathogenesis

Bacterial vaginosis results from the replacement of normal vaginal flora (lactobacillus) with a mixed flora consisting of G.vaginalis, anaerobes, M.hominis.The introduction of a particular set of organisms via sexual intercourse may initiate the change in vaginal flora characteristic of Bacterial vaginosis. Lactobacillus species may help normal women to resist vaginal infection and cervical infection.Vaginal lactobacillus inhibit G.vaginalis, mobiluncus species and mycoplasma hominis in vitro. H_2O_2 producing lactobacilli inhibits the growth of anaerobic rods, Gardenerella, Mobiluncus and Mycoplasma by direct activity of H_2O_2 toxicity (or by reacting with halide ion in the preence of cervical peroxidase as part of the H_2O_2 halide peraxidase activities system. So, for no host factor has been identified that increases the susceptibility of bacterial

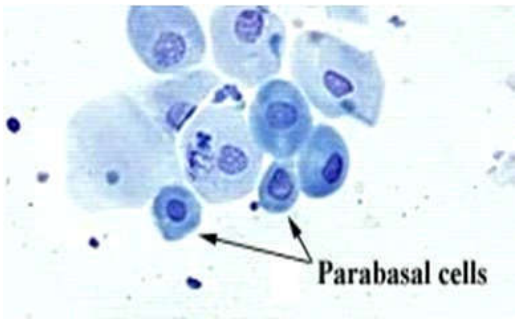
vaginosis. The amines produced by the microbial flora, perhaps via the action of microbial decarboxylases accounts for the characteristic fishy odour, this is produced when vaginal fluid mixed with 10% KOH this is so called whiff test is thought to be due to volatilization of aromatic amines including putrescine, Cedaverine, trimethylmine at alkaline PH The presence of trimethylmine in the vaginal fluidis thought to be largely responsible for symptoms of malodor experienced by women with Bacterial vaginosis. The vaginal fluid of women with Bacterial vaginosis has increased level of endotoxin, sialidease, glycosidases which degrade mucinand decrease its viscosity, in addition secretory leukocyte protease inhibitor is decrease in the vaginal fluid of women with Bacterial vaginosis. In case the vaginal concentration of anaerobic pathogens in Bacterial vaginosis may increase the risk of ascending upper genital tract infection including cervicitis and endometritis.

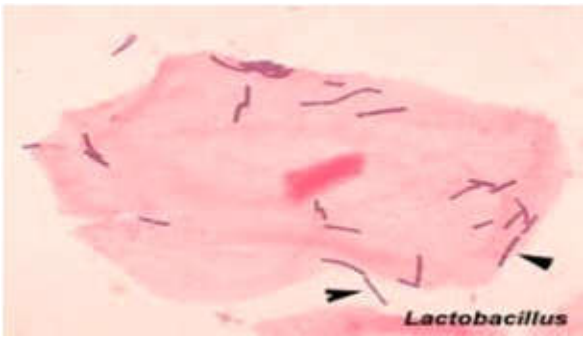
Clinical Manifestations

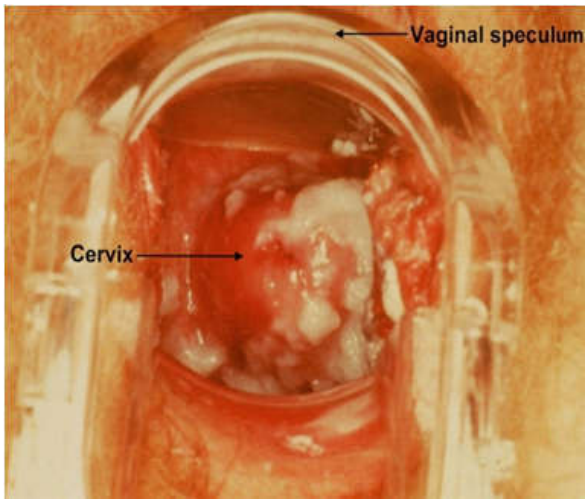
Vaginal malodor (49%) – due to trimethylamine, Vaginal discharge (50%) – Non viscous, homogenous white uniformly adherent, visible in the labia & fourchette,Vaginal PH > 4.5,Fishy odour when mixed with 10% KOH,Presence of clue cells – They are epithelial cells heavily coated with bacteria sufficient

Table 1: Characteristics of Vaginal Discharge

	Normal women	Women with bacterial vaginosis
Discharge	White flocculent	Homogenous grey,white
Odour	Odourless	Malodourous(fishy/musty)
pH	Less than 4.5	More than 4.5
Clue cells	Absent	Present
Lactobacilli	Predominant > 95%	Present in low numbers







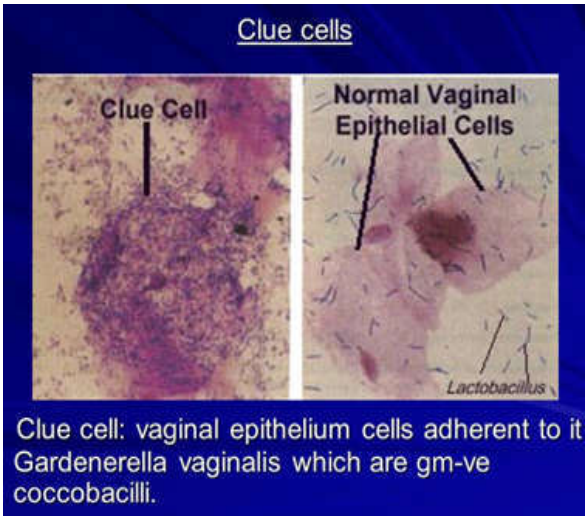


Figure 1-4:

to obscure the cell borders. The bacteria covering the clue cells include G.Vaginalis as well as anaerobes such as mobiluncus.

Complications

Obstetric Complications Associated with Bacterial Vaginosis.

Preterm Labour, Low Birth Weight and PROM

Bacterial vaginosis induces an intramniotic inflammatory response involving the activation of a number of cytokines & chemokines which intern trigger premature contraction, cervical ripening and rupture of membranes. Leucocytes are recruited in response to the infection and undergo activation. IL-6, IL-8, IL-1, TNF alpha – degradation of collagen fibres causing cervical ripening. IL-1 TNF alpha – induces matric metalloproteinases causing membrane rupture. IL-1, IL-2, IL-6 TNF alpha – increase PGE2, PGF2 alpha causing uterine contractions. Approximately 15 – 20% of all pregnant women will have bacterial vaginosis and there women are upto 4 times more likely to have a PTB than women without bacterial vaginosis. In a longitudinal study, Hillier et al, demonstrated that women with bacterial vaginosis are 40% more likely to deliver a preterm, low birth weight infant than women without bacterial vaginosis.

Chrioamniotitis & Amniotic Fluid Infection

Clinical signs & symptoms of Chrioamniotitis includesan intrapartum temperature > 100.4^0F, significant maternal tachycardia > 120 bpm, fetal tachycardia > 160 – 180 bpm, purulent or foul smelling amniotic fluid or Vaginal discharge, Uterine tenderness, Maternal Leukocytosis (> 15,000 – 18,000 cells/micro litre). When atleast 2 of the above mentioned criteria are presents the rule of neonatal sepsis is increase, the risk of increases as the duration of ruptured membranes lengthens. Choreoamniotitis initiate uteroplacental bleeding or a placental abruption, labour & delivery may be rapid in the presence of Choreoamniotitis and may cause uterine atony, requiring labour to be augmented with oxytocin, ultimately a poor labour pattern requiring instrumental delivery or a cesarean ection. Recent studies confirm that amniotic fluid sludge which can be identified by ultrasonography at the amniotic fluid interface with the ceramic as hyperechogenic free floating material, and it is a useful market of microbial invasion of the amniotic cavity (MIAC) Neonatal complications of Choreoamiotitis includes respiratory distress pulmonary hemorrhage, pneumonia, apnea, seizures, hypothermia.

Bacterial vaginosis also causes Latemiscarriages and postpartum endometritis.

Gynaeological Complications Associated with Bacterial Vaginosis

Bacterial vaginosis and cervical intra epithelial neoplasia (CIN)

CIN was found in 5% of women with Bacterial vaginosis as compured with 1.4% of women without Bacterial Vaginosis, the possibility is, that Bacterial vaginosis may be a cofactor to the potentially cancer causing HPV. The abnormal vaginal flora in Bacterial vaginosis produces nitrosamines these can be synergistically with HPV to damage epithelial cells aiding in the development of CIN.

PID: PID is a frequent infection in sexually active young women and results in adverse sequelae, like tubal factor infertility and ectopic pregnancy, several investigation have shown an association between Bacterial vaginosis and the development of acute PID.

Infertility: Several studies have examined the possible relationship between Bacterial vaginosis and infertility. One study shows a high prevalence of Bacterial vaginosis was found in women undergoing invitro fertilization than in the general populations.

Post Hysterectomy Vaginal Cuff Infection: Post hysterectomy vaginal cuff infection occurs three to four times more commonly in women with bacterial vaginosis than in those without. The use of prophylactic antibiotic to prevent vaginal cuff infections is now generally practiced.

Post Abortal Sepsis: Pelvic infections following terminaton of pregnancy may be due to vaginal infections particularly with N. gonorrhoeae, C. trachomatis and bacterial vaginosis related organisms. The use of antibiotic prophylaxis before terminations of pregnancy demonstrates a productive effect.

Urethral Syndrome: Uretheral syndrome can be defined as dysuria in women that cannot be explained by the bacteria that normally cause urinary tract infections. C. trachomatis has been implicated in some cases. Bacterial vaginosis is also implicated in the etiology of uretheral syndrome.

Bacterial Vaginosis & HIV: Klebanoff et al., showed that the presence of hydrogen peroxide produicing lactobacilli in the vagina results in the Acidic environment of the vagina that contributes protection against infection. The multimicrobial nature of

Bacterial vaginosis produces a postinflamatory environment consisting of cytokines & toll like receptor (TLR) ligands which increase the susceptibility to HIV infection. M. hominis increase the activity of a soluble HIV inducing factor (HIF) and therefore increase the HIV -1 expression. Genital tract infection with G. Vaginalis stimulate HIV -1 production and hence increase the likelihood of sexual transmission.

Treatment of Bacterial Vaginosis

Metronidazole: Pheifer et al first observed in 1978 that metronidazole used for vaginal trichomoniasis also cleared concurrent nonspecific vaginitis. Studies show that metronidazole therapy treatment for Bacterial vaginosis shows 87% cure rate. Metronidazole 500 mg bid x 7 days.To reduce systemic absorption of metronidazole and decreases side effects, intravaginal metronidazole therapies have developed 0.75% metronidazole gel used once / twice daily for 7 days. The efficacy was similar for both groups with the treatment of Bacterial vaginosis during pregnancy.

Clindamycin: 300 mg bid for 7 days cure rate 94%. Vaginal sustained release clindamycin 2% cream single dose daily for 7 days.

Lactate gel: Lactate gel containing latic acid and growth substate for lactobacilli buffered to PH 3.8, producing a higher curerate. One unit of 5 ml of gel inserted in to the vagina for 7 days, as effective as oral metronidozole 500mg twice daily for 7 days.

Materials and Methods

A. Study Area: The study was carried out in department of obstetrics & gynaecology , Government Rajaji Hospital, Madurai medical college, Madurai.

B. Study Period: 6 months.

C. Study Population: 200 successive cases admitted in labour ward with symptoms of preterm & threatened preterm labour.

Criteria for Established Preterm Labour: With gestational age between 28 and 37 weeks With painful uterine contractions lasting for 45 seconds associated with cervical effacement of 80% and aboveCervical dilatation of less than or eual to 3 cm and with intact menbranes.

Criteria for Threatened Preterm Labour: In case of threatened preterm labour uterine contractions are perceived in the absence of cervical change.

Inclusion Criteria

Booked, unbooked and referral cases were included in the study, Both primi and multi irrespective of socio economic status were included.

Exclusion Criteria

Women are excluded from analysis if they had, GA<28 weeks, Multiple pregnancy, Malpresentation, Placenta previa / APH, Cervical incompetence treated with cervical encerlage, Hydramnios, Pregnancy induced hypertension, Fever, UTI, Diarrhea, Respiratory tract infection,Anaemia, Heart disease, GDM, DM, PROM/absent membranes, Antibiotic therapy within last 30 days, Intra uterine growth retardation, Intra uterine death.

Clinical Study

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.

Bacteriological Study

The specimen was collected by putting the patient in dorsal supine position. Under all aseptic conditions the posterior vaginal wall was retracted with sims speculum and vaginal swabs were taken from posterior fornix by 3 sterile cotton swabs.

pH test: By using a piece of nitrazine paper, pH of the vaginal fluid can be obtained. Care was taken to avoid contact with cervical mucus, as the pH of cervical secretions is approximately-7.

Amine Test: A drop of 10% KOH was added to wet mount specimen and fishy odor was noted.

Clue Cells on wet Mount

Clue cells are found by mixing vaginal fluid with a drop of normal saline on a slide and examining this slide microscopically under high power magnification (x400). Specimens were considered adequate if at least 10 epithelial cells per high power field were seen. The presence of even as few as one clue cell per field in 20 fields (x400) was considered positive. Clue cells were identified as vaginal

epithelial cell with indistinct cell border obscured by the large number of attached organisms.

AMSEL Criteria

Amsel et al claimed that bacterial vaginosis was present if three of these four criteria was present.

1. Homogenous vaginal discharge
2. Vaginal pH > 4.5
3. Fishy odour on alkalinization of vaginal secretion.
4. Presence of clue cells

Gram Staining

With the swab obtained from the posterior fomix a direct smear was made on a clean slide and gram staining was done and smear examined for the presence of clue cells gram negative coccobacilli and other morphological types.

Method of Gram Staining: To a dried smear

Step I: Methyl violet was added, washed with tap water after one minute

Step II: Grams iodine was added, washed with tap water after one minute

Step III: Acetone was added, washed with tap water after 30 seconds

Step IV: Dilute carbol fuschin was added, washed with tap water after one minute

Step V: Smear air dried, study of gram stained smear was done in x 1000 magnification with oil immersion.

Large gram positive bacilli are assumed to be lactobacillus morphotypes and smaller gram variable coccobacilli to be gardnerella morphotypes.

Presence of large number of gram positive lactobacilli morphology alone or greatly exceeding other morphological types is labeled as negative gram stain for bacterial vaginosis.

When lactobacilli morphological types are present at < 2+ levels and if there are 3 + to 4+ levels of mixed flora including Gardnerella cocci, rods, fusiform bacteria or curved rod slides are interpreted as positive for bacterial vaginosis. (Spiegel et al).

Statistical Tools: 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 2008).

Observations, Results and Analysis

Having excluded patients with nown risk factors for preterm labour, the subset of women in idiopathic preterm labour (200) were studied. Amsel's criteria taken as gold standard test to diagnose bacterial vaginosis. The mean age in preterm is 25.0±4.2 years.None of the patients studied were in class I & II socio economic status. 47% of the study group belonged to class IV and 38% belonged to class V group. 39 % of women belongs to G3 and 34% of women belongs to G2. 24% of women belongs to primigravidas. 51.5 % of preterm where in the gestational age of 34 – 37 weeks. 20 % of women where in the gestational age of 28 – 30 weeks.

Table 1:

Group	No. (%)
Preterm with Bacterial Vaginosis Positive	60 (30.0)
Preterm without bacterial vaginosis	140 (70.0)
Total	200(100.0)

Table 2:

Birth Weight (in kg)	Group	
	Preterm with Bacterial Vaginosis Positive (n=60) No. (%)	Preterm without bacterial vaginosis (n=140) No. (%)
1.0 – 1.5	1 (1.7)	22 (15.7)
1.6 – 2.0	20 (33.3)	61 (43.6)
2.1 – 2.5	24 (40.0)	39 (27.9)
2.6 – 3.5	15 (25.0)	18 (12.9)
Total	60 (100.0)	140 (100.0)
P value	0.003 (Significant)	

Table 3:

Birth Weight (in kg)	Group	
	Preterm with Bacterial Vaginosis Positive (n=60) No. (%)	Preterm without bacterial vaginosis (n=140) No. (%)
1.0 – 1.5	1 (1.7)	22 (15.7)
1.6 – 2.0	20 (33.3)	61 (43.6)
2.1 – 2.5	24 (40.0)	39 (27.9)
2.6 – 3.5	15 (25.0)	18 (12.9)
Total	60 (100.0)	140 (100.0)
P value	0.003 (Significant)	

Table 4:

Tests	Sensitivity	Specificity	Accuracy	PPV	NPV
Homogenous Discharge	88	94	93	87	95
Amine Test	93	97	96	93	97
Clue Cell	82	97	93	92	93
Amsel's Criteria	95	100	99	100	98
PH>4.5	98	94	96	88	99

Discussion

From the study we have confirmed significant association between bacterial vaginosis and preterm labour. Amsel's criteria has been taken as a standard method of diagnosing bacterial vaginosis in our study and accuracy of amsel's criteria in the detection of bacterial vaginosis. Amsel's criteria also has the advandage of less inter and intraobserver variation. In the study the prevalence of bacterial vaginosis was 30 % . Our study corresponds to Masand D et al (2016), Kiran CK et al. (2017) and Chithrajeyakrishnan et al. (2016).

Study	Prevalence of Bacterial Vaginosis
Masand D et al (2016)	36%
Kiran CK et al(2017)	30%
Chithra jeyakrishnan et al(2016)	48%
Our study	30%

In our study , mean age was 24±4.2 years . the age distribution of cases in the study and control group did not vary much which corresponds to that of Masand D et al. (2016) and to that Kiran CK et al. (2017). In our study, there was a significant association of women in low & very low socio economic status and preterm labour. This corresponds to that study conducted at the department of microbiology, government medical college, Patiala, Punjab (2001).On analyzing efficacy of various tests, homogenous discharge was present in 63 patients of these 53 were positive for bacterial vaginosis. 10 cases of bacterial vaginosis positive cases did not have homogenous discharge the sensitivity was 88% specificity was 94% when compared to sensitivity of 78% and specificity of 90% in Masand D et al. (2016). pH > 4.5 found in 67 patients and diagnosed 59 0f 60 cases of all bacterial vaginosis. It has the highest sensitivity (98%) which was compared to sensitivity of 100% in Chithra jeyakrishnan et al. (2016). It is economical, extremely simple and a useful tool to rule out bacterial vaginosis. Amine test was positive in 60 cases of which 56 cases were positive for bacterial vaginosis. Amine test has a good sensitivity (93%) and a specificity (97%) which was compared to sensitivity of 89% and specificity of 98% in Chithra jeyakrishnan et al. (2016). In the absence of microscope, Amine test can be used as a specific and relatively sensitive method of detecting bacterial vaginosis. Detection of clue cells is the single most specific test but not a sensitive one. It has a specificity of 97% and sensitivity of 82%. It has a high PPV (92%) and a NPV (93%) which was compared to specificity of 94%, sensitivity of 84% , PPV (90%) and NPV (91%) in Masand D et al. (2016). In our study, out of 60 patients who had bacterial vaginosis neonatal complications (birth asphyxia, RDS, meconium aspiration syndrome, hyperbilirubinemia) were present in 5 cases after treatment.when compared with general preterm group it was significant p value is 0.0026 that is preterm with bacterial vaginosis which was treated, neonatal complications were 8.3% but in general preterm group 21.4%neonatal complications occur. So, treatment of bacterial vaginosis in preterm and threatened preterm has great impact on neonatal outcome. In our study, 1 baby in preterm with bacterial vaginosis and 11 babies in general preterm group died in early neonatal period.

Summary

Two Hundred women in preterm & threatened preterm were studied.Maternal age and parity did not seem to influence the study group. There was significant association of women belonging to low socioeconomic status class IV to study group.There was significant association between bacterial vaginosis and preterm labour. There was significant association between bacterial vaginosis and delivery of low birth weight babies. There was strong evidence that treatment of bacterial vaginosis in preterm & threatened preterm reduces the neonatal complications.

Conclusion

The prevalence of bacterial vaginosis was 30% in preterm & threatened preterm deliveries. There was a significant association between bacterial

vaginosis and preterm labour. There was also significant association of various factors like low socio economic status, low BMI and history of previous preterm deliveries to the study group. There was storng evidence that treatment of bacterial vaginosis in preterm & threatened preterm deliveries reduce the neonatal complications.

References

1. Chawanpaiboon S, Sutantawibul A. Preterm birthrate in Siriraj hospital: a seven-year review (2002-2008BE). Thai J Obstet Gynaecol. In press 2009.
2. Klebanoff MA, Hillier SL, Nugent RP, MacPhersonCA, Hauth JC, Carey JC, et al. Is bacterial vaginosisa stronger risk factor for preterm birth when it isdiagnosed earlier in gestation? Am J ObstetGynecol 2005;192:470-7.
3. McDonald HM, Brocklehurst P, Gordon A.Antibiotics for treating bacterial vaginosis in pregnancy. Cochrane Database Syst Rev 2007;(1):CD000262.
4. Okun N, Gronau KA, Hannah ME. Antibiotics for bacterial vaginosis or Trichomonas vaginalis in pregnancy: a systematic review. Obstet Gynecol 2005; 105:857-68.
5. Screening for bacterial vaginosis in pregnancy to prevent preterm delivery: U.S. Preventive Services Task Force recommendation statement.Ann Intern Med 2008;148:214-9.
6. Hadlock FP, Shah YP, Kanon DJ, Lindsey JV. Fetal crown-rump length: reevaluation of relation to menstrual age (5-18 weeks) with high-resolution real-time US. Radiology 1992;182:501-5.
7. Vatish M, Groom K, Bennett P, Thornton S.Management of threatened preterm labor. In:Norman J, Greer I, editors. Preterm labor: managing risk in clinical practice. Cambridge: Cambridge university press; 2005.pp.92-203.
8. American Academy of Pediatrics and American College of Obstetricians and Gynecologists. Guidelines of perinatal care. 4th ed. Elk Grove Village, IL: American Academy of Pediatrics; 1997.
9. Amsel R, Totten PA, Spiegel CA, Chen KC, Eschenbach D, Holmes KK. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. Am J Med 1983;74:14-22.
10. Hillier SL. Diagnostic microbiology of bacterial vaginosis. Am J Obstet Gynecol 1993;169(2 Pt 2): 455-9.
11. Eschenbach DA, Hillier S, Critchlow C, Stevens C, DeRouen T, Holmes KK. Diagnosis and clinical manifestations of bacterial vaginosis. Am J Obstet Gynecol 1988;158:819-28.
12. Leitich H, Bodner-Adler B, Brunbauer M, Kaider A, Egarter C, Husslein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis.Am J Obstet Gynecol 2003;189:139-47.
13. Klebanoff MA, Hauth JC, MacPherson CA, Carey JC, Heine RP, Wapner RJ, et al. Time course of the regression of asymptomatic bacterial vaginosis in pregnancy with and without treatment. Am J Obstet Gynecol 2004;190:363-70.
14. Brocklehurst P, Hannah M, McDonald H. Interventions for treating bacterial vaginosis in pregnancy. Cochrane Database Syst Rev 2000;(2):CD000262.
16. Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. N Engl J Med 2000;342:1500-7.