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# Bacterial vaginosis as a risk factor of preterm premature rupture of membrane (PPROM)

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## ABSTRACT

**Introduction:** The pathogenesis of PPROM is complex and not fully understood. Recent studies showed that such role of genital tract infection as bacterial vaginosis in the pathogenesis of PPROM turned out to be present. They produce lipase enzymes in which they can form compounds with the fibrous tissue of the amniotic membrane resulting in an increased risk of rupture of the membrane.

**Objective:** This study aims to prove that bacterial vaginosis is a risk factor for preterm premature rupture of membrane.

**Material and methods:** This research used the case-control method. Sampling was using the consecutive sampling method and had fulfilled inclusion and exclusion criteria with age-based matching, then vaginal swab sampling was conducted, painted with gram staining in the Dermatology and Venereology Laboratory of Sanglah Hospital, and Nugent score.

**Result:** Total of 76 pregnant women with 24-36 weeks of gestation were investigated, 38 mothers with PPROM and 38 mothers with normal pregnancy. The average score of Nugent at preterm PROM was 7.18 and in normal pregnancy was 2.37. Bacterial vaginosis risking for PPROM 7 times (OR= 7.0, 95% CI= 1.21-17.68, p= 0.001).

**Conclusion:** Bacterial vaginosis as a risk factor for the occurrence of PPROM.

**Keywords:** Preterm premature rupture of membrane (PPROM), bacterial vaginosis, Nugent, pregnancy

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## INTRODUCTION

Bacterial vaginosis (BV) in pregnancy is a risk factor for various types of complications in pregnancy, including premature rupture of membranes. The etiology and pathogenesis of BV are not entirely clear. This disorder is characterized by reduced Lactobacillus spp., high differences in bacterial species and excessive increases in anaerobic, facultative bacteria such as Gardnerella vaginalis, Atopobium vaginae and other BV-related bacteria including Megasphaera, Sneathia, and Clostridiales spp. compared to healthy individuals.[1,2]

PPROM in premature pregnancies leads to maternal and neonatal complications. Some of the complications caused by PPROM in premature pregnancies include preterm labor, chorioamnionitis, placental abruption, postpartum hemorrhagic, endometritis, premature babies, neonatal sepsis, and even fetal death.[3-5] The prevalence of PPROM in premature pregnancies ranges from 16% and tends to increase. Perinatal morbidity (80.5%) associated with prematurity, early and late neonatal sepsis (25.75%), and moderate-severe asphyxia neonatorum and accompanied by postpartum and febrile puerperal bleeding (34.75%.) Pregnant women with bacterial vaginosis are at risk of developing obstetric complications such as threats to premature labor, premature rupture of membranes, spontaneous abortion, chorioamnionitis, and puerperal infection. Bacterial vaginosis in pregnancy has a 9-fold risk of preterm labor.[6-9] Bacterial Vaginosis in pregnancy has a risk of 9 times the occurrence of premature labor. In another study, PPROM in pregnant women increased 7.3 times if accompanied by BV.[10]

The inflammatory response causes the release of proinflammatory cytokines such as IL-1 beta, IL-6, IL-8, and TNF-α in bacterial vaginosis.[11] This proinflammatory cytokine will stimulate MMP release, especially MMP-8. Neutrophils produce MMP-8 and cause degradation of the membranes. MMP-8 can degrade a large series of proteins from extracellular matrices such as collagen I and III. The infection process shows an increase in MMP-8 levels, and proteoglycan degradation process that composes the membranes. The degradation of the membranes causes premature rupture of the

**Table 1** **Characteristics of the samples**

| Characteristics | BV (+) n =38 (%) | BV (-) n = 38 (%) | Case n = 38 (%) | Control n = 38 (%) |
|---|---|---|---|---|
| **Age** | p = 0.215 | | p = 0.216 | |
| 20-29 years old | 27 (71.05) | 22 (57.89) | 24 (63.16) | 25 (65.79) |
| 30-39 years old | 10 (26.32) | 15 (39.47) | 13 (34.21) | 12 (31.58) |
| 40-45 years old | 1 (2.63) | 1 (2.63) | 1 (2.63) | 1 (2.63) |
| Mean±SD | 26.55±6.04 | 28.29±6.05 | 27.53±6.11 | 27.32±6.12 |
| **Gestational age** | p = 0.001 | | p = 0.001 | |
| 24-27 weeks | 3 (7.89) | 2 (5.26) | 3 (7.89) | 2 (5.26) |
| 28-31 weeks | 9 (23.68) | 14 (36.84) | 10 (26.32) | 13 (34.21) |
| 32-36 weeks | 26 (68.42) | 22 (57.89) | 25 (65.79) | 23 (60.53) |
| Mean±SD | 33.26±1.16 | 34.34±0.91 | 33.32±1.14 | 34.29±0.98 |
| **Parity** | p = 0.633 | | p = 0.632 | |
| ≤ 1 | 30 (78,95) | 23 (60,53) | 30 (78,95) | 23 (60,53) |
| > 1 | 8 (21,05) | 15 (39,47) | 8 (21,05) | 15 (39,47) |
| Mean±SD | 0,79±0,66 | 0,71±0,77 | 0,79±0,74 | 0,71±0,69 |
| **Vaginal pH** | p = 0.001 | | p = 0.001 | |
| ≤ 4.5 | 0 (0) | 33 (86.84) | 0 (0) | 33 (86.84) |
| > 4.5 | 38 (100) | 5 (13.16) | 38 (100) | 5 (13.16) |
| Mean±SD | 6.89±0.45 | 3.92±0.94 | 6.76±0.54 | 4.05±1.25 |
| **Nugent score** | p = 0.001 | | p = 0.001 | |
| ≥ 7 | 38 (100) | 0 (0) | 33 (86.84) | 5 (13.16) |
| 4-6 | 0 (0) | 0 (0) | 0 (0) | 0 (0) |
| 0-3 | 0 (0) | 38 (0) | 5 (13,16) | 33 (86.84) |
| Mean±SD | 8.05±0.87 | 1.5±1.18 | 7.18±2.50 | 2.37±2.45 |

n = number of sample, SD=standard deviation, BV=Bacterial Vaginosis

**Table 2** **Bacterial vaginosis as risk factors for PPROM in premature pregnancy**

| | | BV control | | Total | OR | 95% CI | p value |
|---|---|---|---|---|---|---|---|
| | | Positive | Negative | | | | |
| BV Case | Positve | 3 | 21 | 24 | 7.0 | 1.21-17.68 | 0.001* |
| | Negative | 3 | 11 | 14 | | | |
| | Total | 6 | 32 | 38 | | | |

*Significance if p<0.05, BV=bacterial vaginosis, OR=Odds Ratio, CI=confidence interval

membranes.[10,11] This study aims to prove that BV is a risk factor for PPROM in preterm pregnancy.

## MATERIAL AND METHODS

This case-control research conducted in March 2018 until April 2018. PPROM examination is performed in the Outpatient Clinic and Emergency Department of Obstetrics and Gynecology while Gram examination of the vaginal discharge is carried out at the Laboratory of Dermatology and Venereology. Sample collection by consecutive methods. The inclusion criteria for the case group were all PPROM patients in premature pregnancies who met the diagnostic criteria, Indonesian citizens, women aged 20-45 years, were willing to take part in the study and had signed informed consent. The inclusion criteria for control were non-KPD subjects in premature pregnancy, who visited the Obstetrics and Gynecology polyclinic at Sanglah General Hospital Denpasar, Indonesian citizens (WNI), maternal aged 20-45 years, willing to take part in research and have signed informed consent. Subjects suffering from heart disease, unknown febrile, Gemelli, smokers, obesity, or low BMI were excluded from this study. Premature rupture of membranes is diagnosed based on rupture of the membranes at 24-36 weeks gestation, which is characterized by vaginal discharge, cloudy color, fishy smell, and positive litmus test. Diagnosis of bacterial vaginosis is established based on Nugent scores (if score> 7). A vaginal swab was made into a smear liquid vaginal preparation, fixated, and sent to the laboratory. Statistical tests were carried out with the Statistical Package for Social Sciences (SPSS) program. The research protocol for the Ethical Clearance from the Research Ethics Commission of the Sanglah Hospital in Denpasar was given before the study was conducted.

## RESULTS

A total of 76 people were included in this study (38 match pairs). The characteristics of the research subject can be seen in Table 1.

Based on the normality test between case and control group within the variables, the result was p<0.05. The Mc Nemar test was performed to determine the risk of bacterial vaginosis against the occurrence of PPROM in preterm pregnancies (Table 2).

Based on Table 2, bacterial vaginosis is a significant risk factor for PPROM. Bacterial vaginosis increases the risk of PPROM in premature pregnancies by seven times compared to samples without bacterial vaginosis.

## DISCUSSION

In this study, the most common onset of BV occurred at 32-36 weeks gestation (68.42%). Several previous studies have shown different results, such as research conducted by Redelinghuys et al. resulting BV in the pregnant women found in the second trimester (13-24 weeks gestational age) was 53.85%.[12] Lata et al. also shows different results; BV most commonly occurs at 21-30 weeks gestational age (46.34%).[13] It might because of the patients may not know that they were suffering from BV (asymptomatic). Therefore they come with

complications such as PPROM. In this study, the onset of PPROM in premature pregnancies was also most prevalent at 32-36 weeks' gestation (65.79%). Similar to the study by Rana et al. in India, the highest onset of PPROM in preterm pregnancies was found at 32-36 weeks gestation at 70%.[14]

In this study obtained a statistically different Nugent score between case and control group. The mean score of the case group was 7.18 ± 2.50, and in the control group was 2.37 ± 2.45 (p=0.001). This result similar to previous research by Bharathi et al. to know the relationship between bacterial infections including BV with PPROM using Nugent criteria in establishing a diagnosis of BV.[15] The Nugent score in this study was used to diagnose BV in PPROM. Research by Bharathi et al. also used Nugent criteria and did not use the Amsel criteria in establishing BV diagnosis, because the vaginal discharge could be alkaline due to amniotic fluid that occurs in the PPROM.[19] Nugent criteria are the gold standard in establish diagnosis of BV because it has advantages in terms of objectivity, sensitivity, and specificity.[16]

In the Mc Nemar test, it was found that bacterial vaginosis can increase the risk of developing PPROM in premature pregnancies by seven times compared with no bacterial vaginosis. These results were statistically significant, with an odds ratio of 7 (95% CI 1.21-17.68 and p=0.001). It can be explained that pregnant women with bacterial vaginosis are at risk for obstetric complications such as threats to premature labor, premature rupture of preterm membranes, spontaneous abortion, chorioamnionitis, and puerperal infection, even if cesarean delivery can also result in surgical wound infection.[3] This research is similar to the results of a previous study which stated that bacterial vaginosis in pregnancy carries a 7.3-fold risk for PPROM.[17] In another study by Bharathi et al. also found a significant association between cases of PPROM and BV occurred three times more frequently in PPROM than in pregnancies without PPROM.[18] The weakness in this study did not measure proinflammatory cytokines that might be involved in the pathogenesis of BV. Further research needs to be done to determine the BV as the risk factor of PPROM.

## CONCLUSION

Bacterial vaginosis is a risk factor for PPROM in premature pregnancy.

## CONFLICT OF INTEREST

There is no conflict of interest regarding this article.

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