P-ISSN : 2527-4627
Warmadewa Medical Journal
Available online http://ejournal.warmadewa.ac.id/index.php/warmadewa_medical_journal

WMJ (Warmadewa Medical Journal), Vol. 11, No.1, May 2026, Page. 17-21

The Association Between Treatment Failure of Bacterial Vaginosis with Metronidazole and the Incidence of the Maternal–Perinatal Composite Index

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Abstract

There is high incidence of Bacterial vaginosis (BV) in pregnancy and increasing rate of treatment failure with metronidazole, the drug of choise in BV in pregnancy. The occurrence of bacterial vaginosis in pregnancy results in morbidity and complications for both the mother and the fetus, especially in untreated cases or cases of treatment failure. This study aims to determine the association between treatment failure and the incidence of the maternal–perinatal composite index (preterm labour, PPROM, low birth weight). This is a cohort study, conducted at Sanjiwani Hospital, Gianyar, from September 2024 to April 2025. involving 52 pregnant less than 20 weeks diagnosed with BV who received metronidazole therapy, divided into two groups, 26 pregnant woman with successful treatment and 26 pregnant woman with treatment failure.The results demonstrated that pregnant women with treatment failure of bacterial vaginosis had a 5.33-fold higher risk of maternal–perinatal complications (OR 5.33; 95% CI = 1.008–28.209; p = 0.049) compared to those with successful treatment.

Keywords: Pregnant women, Bacterial vaginosis, Composite index, Metronidazole

INTRODUCTION

Bacterial vaginosis (BV) is a condition in which the dominant Lactobacillus species in the vagina are replaced by polymicrobial anaerobic microorganisms, and it is classified as a sexually transmitted infection (STI). BV may present in both acute and chronic forms, with either specific clinical symptoms or an asymptomatic presentation. BV is associated with maternal–perinatal morbidity and mortality, particularly chorioamnionitis and preterm birth, especially in infections occurring before 20 weeks of gestation during pregnancy and in cases of treatment failure or recurrence.

The global prevalence of BV is reported to range from 5% to 72% and tends to be higher in developing countries in tropical regions.(1) According to reports from the Ministry of Health of the Republic of Indonesia, the prevalence of BV among pregnant women in several cities in Indonesia ranges from 18.8% to 46.7%.(2) A prevalence study of BV among pregnant women in the Emergency Department of Obstetrics and Gynecology at Sanglah General Hospital, specifically among patients hospitalized with a diagnosis of premature rupture of membranes, reported a prevalence of 68.4%.(3) BV increases the risk of obstetric and gynecologic complications, including cervicitis (13%), chorionitis and chorioamnionitis (8.2%), prematurity (20.5%), premature rupture of membranes (7.3%), neonatal sepsis (2.2%), and contributes to 0.2% of perinatal mortality.(4,5) Approximately 50% of BV cases in pregnant women are asymptomatic, making them frequently undetected and untreated.(6)

Metronidazole has been the treatment of choice for BV since 1985, with a cure rate of 70–80% in acute episodes.(7) However, recurrence rates within the first 1–3 months range from 57–90%, while recurrence within one year ranges from 34–51%. (8) The effectiveness of metronidazole has reportedly declined from 90% at the beginning of its use in the 1960s to 50–80% currently, a reduction associated with bacterial

genotype–phenotype changes and biofilm-forming capability.(9)

Several theories regarding BV treatment failure highlight the role of biofilm formation and polymicrobial composition. (10,11) Treatment resistance in BV is associated with impaired antibiotic penetration into the biofilm, alterations in the microchemical environment, and bacterial morphological changes resembling spores.(12) To date, no studies in Indonesia have examined the relationship between metronidazole treatment failure and the composite index of maternal and neonatal complications. Given the high rates of treatment failure and recurrence in BV, identifying complications associated with treatment failure is essential to improve management through personalized approaches and potentially reduce complication rates.

METHODS

This was an observational study with a cohort design. The case group consisted of pregnant women at <20 weeks of gestation diagnosed with bacterial vaginosis (BV) who experienced treatment failure following metronidazole therapy. The control group consisted of pregnant women at <20 weeks of gestation diagnosed with BV who achieved successful treatment with metronidazole. Both groups were followed to observe the occurrence of maternal or neonatal complications at delivery.

The study was conducted at the Obstetrics Outpatient Clinic of Sanjiwani General Hospital, Gianyar, located on Jl. Ciung Wanara No. 2, Gianyar, Bali. Sample collection was carried out from September to November 2025.

TThe sample consisted of pregnant women at <20 weeks of gestation attending the Obstetrics Outpatient Clinic of Sanjiwani General Hospital, Gianyar, who were selected consecutively from the accessible population after meeting the inclusion and exclusion criteria. Based on the Kelsey formula, the required sample size for each group was 21 participants. After adding a 20% allowance for potential drop-outs, the sample size increased to 25.2, which was rounded up to 26 participants per group. Based on Nugent score criteria, 26 cases (treatment failure) and 26 controls (treatment success) were included in the analysis, resulting in a total sample of 52 participants.

Univariate analysis was performed to describe maternal age, parity, and gestational age characteristics in both the case and control groups, as well as to determine the incidence of premature rupture of membranes (PROM), low birth weight (LBW), and prematurity across groups. Chi-square analysis was conducted to evaluate the association between BV treatment failure following metronidazole therapy and the maternal–perinatal composite complication index. The study was conducted with informed consent and received approval from the Sanjiwani Hospital Ethics Committee.

RESULTS AND DISCUSSION

Characteristics of Maternal Age, Parity, and Gestational Age

The results presented in Table 1 show that the age of respondents in this study ranged from 21 to 42 years, with a mean maternal age of 27.15 ± 3.41 years in the control group and 27.77 ± 4.08 years in the case group. The age group of 26–30 years represents the optimal reproductive phase for women, during which reproductive organs have reached full maturity and the risk of obstetric complications is relatively lower than in younger or older age groups.

Table 1. Distribution of Maternal Age, Parity, and Gestational Age Characteristics in the Case and Control Groups

Variable	Case Group (n=26) (Mean±SD)	Control Group (n=26) (mean ± SD)	*p*
Maternal Age (years)	27.15 ± 3.41	27.77 ± 4.08	0.558
Parity	0.46 ± 0.582	0.8 ± 0.801	0.081
Gestational Age (weeks)	13.54 ± 4.42	14.92 ± 3.09	0.197

DOI: https://doi.org/10.22225/wmj.11.1.13975.17-21

The results showed that most respondents were nulliparous women, meaning women who had never given birth. The mean parity in the case group was 0.46 ± 0.582, while in the control group it was 0.80 ± 0.801. Physiologically, nulliparity may influence vaginal microbiota composition and hormonal stability.

The mean gestational age in the case group was 13.54 ± 4.42 weeks, while in the control group it was 14.92 ± 3.09 weeks. The findings indicated that the majority of participants had a gestational age of 12 weeks, accounting for 11 individuals (19.6%). The prevalence of bacterial vaginosis varies not only between pregnant and non-pregnant women, but also across different gestational ages.(13) In general, the prevalence of BV decreases as gestational age increases.(14)

Composite Index of Maternal–Neonatal Complications

Table 2 presents the occurrence of maternal–neonatal complications in the case group, including preterm birth in 3 participants (11.5%), premature rupture of membranes (PROM) in 7 participants (26.9%), and low birth weight (LBW) in 2 participants (7.6%). In the control group, preterm birth occurred in 2 participants (7.6%), while PROM was observed in 2 participants (7.6%).

Table 2. Distribution of Composite Index Outcomes in the Case and Control Groups

Variable	Case Groups (%)	Control Groups (%)
Preterm Birth	3 (11.5)	2 (7.6)
Premature Rupture of Membranes (PROM)	7 (26.9)	2 (7.6)
Low Birth Weight (LBW)	2 (7.6)	0
Composite Index	8 (30.7)	2 (7.6)
Total	20 (76.7)	6 (22.8)

In this study, preterm birth was observed in 11.5% of cases, whereas it occurred in 7.6% of the control group. These findings are consistent with previous research, which reported that the incidence of preterm birth in BV-positive cases was lower, with 6 cases (25%), compared to 40 cases (18.8%) in BV-negative subjects, with a p-value of 0.742.(15) Bacterial vaginosis (BV) has been shown to be significantly associated with an increased risk of preterm birth, low birth weight (LBW), and premature rupture of membranes (PROM).(16) Women with untreated or recurrent BV have a 2–3-fold higher risk of experiencing preterm birth compared to women without BV.

In this study, premature rupture of membranes (PROM) was identified in 7 participants (26.9%) in the case group, whereas only 2 participants (7.6%) in the control group experienced PROM. The incidence observed in the case group was substantially higher than the prevalence of PROM in the general population, which ranges from 8–10% of all pregnancies.(17) A retrospective study reported a p-value < 0.05, indicating a significant association between BV and PROM, with an odds ratio (OR) of 4.35.(14) Excessive matrix metalloproteinase (MMP-2 and MMP-9) activity leads to collagen degradation, thereby reducing the tensile strength of the amniotic membrane and rendering it fragile and susceptible to rupture.

Low birth weight (LBW) in this study was observed only in the case group (7.6%). The mechanisms underlying LBW are multifactorial and may result from two primary processes: preterm birth and intrauterine growth restriction (IUGR). Both mechanisms are generally associated with placental dysfunction, inflammation, oxidative stress, and maternal factors that impair the transfer of nutrients and oxygen to the fetus.

DOI: https://doi.org/10.22225/wmj.11.1.13975.17-21

Association Between Treatment Failure and the Maternal–Perinatal Composite Complication Index

Table 3 shows that there were 8 cases (15.4%) of maternal–perinatal complications in the treatment failure group, compared to 2 cases (3.8%) among those with successful treatment. Accordingly, pregnant women with BV who experienced treatment failure had a 5.33-fold higher risk of composite adverse outcomes (OR 5.33; 95% CI 1.008–28.209; p = 0.049) compared to those who achieved treatment success.

Table 3. Composite Risk Index (Preterm Birth, Premature Rupture of Membranes, and Low Birth Weight) in the Case and Control Group

	Groups		OR	OR (95%CI) (1,008 – 28,209)	*p*
	Composite Index (+)	Composite Index (-)			
Treatment failure	8 (15.4%)	18 (34.6%)	5,33	1,008 – 28,209	0,049
Treatment success	2 (3.8%)	24 (46.2)			

Chi-square analysis demonstrated a p-value < 0.05 (p = 0.049), indicating a significant association between treatment failure of bacterial vaginosis in pregnant women and the occurrence of maternal–perinatal composite complications, including low birth weight (LBW), premature rupture of membranes (PROM), and preterm birth. Pregnant women with BV who experienced treatment failure had a 5.33-fold higher risk of composite adverse outcomes (OR 5.33; 95% CI 1.008–28.209; p = 0.049) compared to those who achieved successful treatment.

A meta-analysis demonstrated that women with persistent BV after treatment have approximately a threefold higher risk of late miscarriage and preterm birth, whereas women with recurrent BV have nearly a tenfold higher risk compared to those without recurrence.(18)

CONCLUSION

Pregnant women who experience treatment failure of bacterial vaginosis have a higher risk of maternal–perinatal complications compared to those who achieve successful treatment. The high rate of complications affecting both mother and fetus highlights the importance of effective management of bacterial vaginosis during pregnancy, particularly in women who experience treatment failure. This group is at elevated risk for maternal and neonatal complications. Further studies are needed to investigate optimal management strategies for patients with treatment failure in order to prevent adverse maternal and neonatal outcomes.

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