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MAJOR ARTICLE

Bacterial Vaginosis and Pregnancy Outcome in Lagos, Nigeria

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Background. Bacterial vaginosis (BV) is a complex clinical syndrome characterized by alterations in the normal vaginal flora and a malodorous discharge when symptomatic. In pregnancy, BV has been associated with adverse outcomes such as miscarriage, premature rupture of membranes, preterm birth, and low birth weight. This study was conducted to determine the prevalence and associations of BV and pregnancy outcomes among pregnant women in Lagos University Teaching Hospital (LUTH).

Methods. We conducted a prospective observational study with high vaginal swabs obtained from consecutive newly registered antenatal women between 14 and 36 weeks gestation. The women were monitored until delivery, and their pregnancy outcome and demographic data were obtained using an interviewer-administered questionnaire.

Results. Bacterial vaginosis was diagnosed by Nugent score in 64 of 246 women, giving a prevalence rate of 26%. Bacterial vaginosis was significantly associated with preterm delivery (risk ratio [RR], 2.68; 95% confidence interval [CI], 1.44–4.98), low birth weight (RR, 3.20; 95% CI, 1.29–7.94), and premature rupture of membranes (RR, 6.75; 95% CI, 3.11–14.67). The association between BV and miscarriage (<28 weeks gestation) and neonatal admission for various morbidities was not statistically significant.

Conclusions. The prevalence rate of BV among pregnant women in LUTH is high and is significantly associated with adverse pregnancy outcome. Routine screening and treatment of women preconceptually may enable interventions to prevent these adverse outcomes.

Keywords. bacterial vaginosis; pregnancy; pregnancy outcome; preterm birth.

Bacterial vaginosis (BV) is a common, complex clinical syndrome characterized by alterations in the normal vaginal flora. When symptomatic, it is associated with a malodorous vaginal discharge and, on occasion, vaginal burning or itching [1]. Under normal conditions, lactobacilli constitute 95% of the bacteria in the vagina and produce several antimicrobial compounds, including lactic acid and hydrogen peroxide (H_2O_2) [2]. Women colonized with H_2O_2-producing lactobacilli are less likely to have BV and remain persistently colonized with lactobacilli [3,4]. Bacterial vaginosis is associated with severe reduction or absence of the normal H_2O_2-producing lactobacilli and overgrowth of anaerobic bacteria, including *Gardnerella vaginalis*, *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Mobiluncus* species, *Prevotella* species, and other anaerobes [1, 5].

The prevalence of BV ranges from 5% to 58.5% depending on the population studied [6]. The risk factors vary, and black race, cigarette smoking, intrauterine device, early age of sexual intercourse, new or multiple sexual partners, vaginal douching, and sexual activities with another woman are the most frequently reported [7, 8]. Bacterial vaginosis was found to be over 2 times more common among black women than white women in the United States [9]. However, a systematic review examining the global epidemiology of BV found that African race per se was not necessarily a risk factor for BV because there is evidence of low prevalence in some African countries. Figures quoted ranged from 6.4% in Burkina Faso and 14.2% in Nigeria to 58.3% in South Africa [6].

Bacterial vaginosis was found to more than double the risk of preterm delivery in both asymptomatic patients and those with preterm labor symptoms in a meta-analysis [10]. The adverse perinatal outcome following preterm delivery is huge, accounting for up to 70% of perinatal mortality worldwide [11]. A perinatal mortality rate of 52% as a result of preterm premature rupture of membranes has been reported in Nigeria [12]. Bacterial vaginosis has also been associated with low birth weight (LBW), premature rupture of membranes (PROM), miscarriage, and chorioamnionitis [13, 14].

However, the results of treatment have been disappointing. There has been no clear evidence that treatment during pregnancy reduces the risk of these associated complications [15]. One study only found a reduction in preterm delivery and miscarriage when women with both BV and intermediate flora were

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treated [16]. It also appears that even when BV resolves during the course of pregnancy, the risks still persist [17].

There are several studies reporting on BV in Nigeria in both pregnant and nonpregnant women, with prevalence rates ranging between 17.3% and 64.3% [18–21]. For pregnant women, the one study noted to report on pregnancy outcome did not find any significant adverse effect of BV on pregnancy despite a relatively high prevalence [22]. Therefore, this study aims to estimate the current prevalence of BV in our pregnant women and to examine for any associated adverse pregnancy outcome.

MATERIALS AND METHODS

The study was conducted in the Antenatal Clinic and Labour Ward of the Lagos University Teaching Hospital (LUTH), Idi Araba, Lagos State, Nigeria, between August 2012 and January 2013. It was a prospective observational study carried out among healthy pregnant women registering at the antenatal clinic for the first time, ie, booking, between 14 and 36 weeks gestational age with or without symptoms of vaginal discharge. Women with medical conditions including human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) were excluded from the study. Bacterial vaginosis was diagnosed in these women by Nugent score, and they were monitored during and after delivery for pregnancy outcomes. Informed consent of each participant was obtained. Ethical approval of the Joint Ethical and Research Committee of LUTH was also obtained.

Sample Size

We calculated that 240 women would be suitable to determine pregnancy outcome, based on the incidence of preterm labor detected in a similar study [22] of 17.65% in women with BV, with an 80% power at the 5% significance level [23]. Taking into account an attrition rate of 10%, 270 women were enrolled into the study at gestational ages of 14 to 36 weeks.

Specimen Collection

Specimens were collected using sterile cotton swabs incorporated with a transport medium (Amies medium) within a sterile container. This was done by swabbing the lateral and posterior fornices of the vagina after inserting a sterile bivalve speculum into the vagina. The swabs were transported within 45 minutes of collection to the Medical Microbiology Laboratory, Department of Medical Microbiology and Parasitology, College of Medicine, University of Lagos for processing.

Nugent Score

Smears were made from the swab specimens on clean grease-free slides and Gram stained using crystal violet as the primary stain, lugol's iodine as the mordant, acetone as the decolorizer, and safranin as counterstain. Evaluation of the specimen was done using the method by Nugent et al [24]. This scoring system counts the individual morphotype frequency of lactobacilli, *G vaginalis*/Gram-negative rods, and *Mobiluncus* species. Weights are assigned to the morphotypes and summed to give one final score ranging from 0 to 10. A Gram stain score of 7 to 10 was considered positive for BV, a score of 0 to 3 was considered "normal", and a score of 4 to 6 was considered "intermediate". Patients with an intermediate score were also categorized as normal for the analysis.

Follow up

Women diagnosed with BV, whether symptomatic or not, were treated with oral clindamycin 300 mg twice for 7 days as soon as their results were obtained. All of the women were monitored until delivery. Labor ward nurses and doctors were adequately briefed about the study so that pregnancy outcomes were recorded in a register for each patient specifically for this study. A means of identification was provided on the case notes. Follow up was also enhanced by taking the phone numbers of all the women for ease of communication. All neonates in this study were observed for at least 1 week after delivery, especially those admitted into the neonatal intensive care unit.

Data Collection and Analysis

Data were collected using interviewer-administered questionnaires; 270 questionnaires were distributed. The questionnaires included questions on demographic characteristics and adverse pregnancy outcomes studied. Premature rupture of membranes was diagnosed as rupture of membranes occurring at least 1 hour before the onset of labor pains. Miscarriage was diagnosed as spontaneous pregnancy loss occurring before 28 completed weeks of gestation in the current pregnancy, 28 weeks being the age of viability in Nigeria. Preterm delivery was diagnosed as delivery occurring before 37 completed weeks of gestation. Low birth weight was diagnosed as birth weight <2.5 kg at delivery. Data analysis was done with Epi-info 7, 2012. Fisher's exact and χ^2 tests were used for comparison of proportions. Risk ratios were calculated to determine the causal association of BV with pregnancy outcomes including preterm delivery, spontaneous abortions, PROM, LBW, and neonatal unit admissions. The level of significance was set at 0.05.

RESULTS

Two hundred seventy pregnant women were recruited for the study, but 246 women were eventually studied because 24 were lost to follow up. The age range of the study participants was 20 to 44 years (mean age, 30.9 ± 4.5 years), and they were all Southern Nigerian women. A total of 243 women were married, reflecting a percentage of 98.8%, whereas only 3 were unmarried. The majority of the women were professionals (including medical doctors, nurses, accountants, architects etc) and services and sales workers (including traders, caterers, fashion designers, and hair stylists) constituting 26% were professionals and 26% were services and sales workers. Further details are in Table 1.

Sixty-four of the women studied had BV, giving an overall prevalence of 26%. The remaining 182 women were analyzed

Table 1. Sociodemographic Characteristics of Participants

Characteristic	No.	%
Age (in years)		
20–24	19	7.7
25–29	79	32.1
30–34	98	39.9
35–39	46	18.7
40–44	4	1.6
Mean age ± standard deviation	30.9 ± 4.5	
Marital Status	4.4949	
Married	243	98.8
Single	3	1.2
Occupation		
Professionals	64	26.0
Services and Sales Workers	64	26.0
Technicians and Associate Professionals	22	8.9
Managers	21	8.5
Clerical Support Workers	8	3.3
Armed Forces Occupation	4	1.6
Elementary Occupation	3	1.2
Craft and Related Trades Workers	2	0.8
Technician and Associate Professionals	2	0.8
Housewives/Unemployed	56	22.8
Religion		
Christianity	212	86.2
Islam	34	13.8
Parity		
Nulliparous	92	37.4
Parous	154	62.6

as normal. Eighty-two (33.5%) of them had intermediate scores, and 100 (40.5%) had negative scores. Regarding symptoms, only 22 of the BV-positive women admitted to having a vaginal discharge when questioned, 11 had vulval itching, and 9 said the discharge was offensive.

The women were enrolled between 19 and 36 weeks gestation. Ninety-eight (39.5%) of them were recruited before 28 weeks, and the remaining 148 (60.5%) women were recruited between 29 and 36 weeks. The median gestational age at recruitment was 29 weeks, and the median gestational age at delivery was 38 weeks.

Of the 64 women who were positive for BV, 25% had preterm delivery, 14.1% had LBW, and 29.7% had PROM. They had 2.7 times the risk of preterm delivery (95% confidence interval [CI], 1.44–4.98), 3.2 times the risk of LBW (95% CI, 1.29–7.9), and 6.8 times the risk of PROM (95% CI, 3.1–14.7) compared with those who were negative. However, only 4.7% of these positive women had miscarriage, and 18.8% of the newborns were admitted in the neonatal intensive care units: BV was not significantly associated with miscarriage or neonatal unit admission (Table 2).

Table 2. BV Status and Pregnancy Outcome

Pregnancy Outcome	BV Positive (N = 64)	BV Negative (N = 182)	RR (95% CI)	*P* Value
Preterm delivery N (%)	16 (25)	17 (9.3)	2.68 (1.44–4.98)	.002
LBW	9 (14.1)	8 (4.4)	3.2 (1.29–7.94)	.008
PROM	19 (29.7)	8 (4.4)	6.75 (3.11–14.67)	<.001
Miscarriage	3 (4.7)	6 (3.3)	1.42 (0.37–5.52)	.307
Neonatal Unit Admission	12 (18.8)	24 (13.2)	1.42 (0.75–2.67)	.145

Abbreviations: BV, bacterial vaginosis; CI, confidence interval; LBW, low birth weight; PROM, premature rupture of membranes; RR, risk ratio.

DISCUSSION

The prevalence rate of BV of 26% among pregnant women in this study is within the range of other recent local studies, ie, from 17.3% to 64.3% [18–20, 25]. The Nugent criteria used in this study have been shown to have a higher sensitivity and specificity compared with the Amsel criteria [26, 27]. Three of these local studies also used the same Nugent criteria used in our study, and their BV prevalence ranged from 38% to 64.3%. One of them was actually from the same center as this study, and they found a prevalence of 64.3%, which is much higher than ours [19]. These differences could be due to the type of population studied. Ajani et al [19] studied all pregnant women, including those with HIV/AIDS and in the third trimester of pregnancy. In this study, we excluded women with medical conditions including HIV/AIDS and studied women between 14 and 36 weeks.

A higher prevalence rate of 38.9% was also reported from a study done in this center in 1989 using the direct Gram stain method of evaluation of vaginal discharge among 90 consecutive pregnant women attending antenatal clinic [28]. This method only examined *Gardnerella* morphotypes as a diagnostic criterion for BV but did not take into account the polymicrobial nature of the condition.

One study showed a prevalence of 11.1% in Iseyin, Oyo state, Nigeria [29]. However, the study was conducted among symptomatic pregnant women with abnormal vaginal discharge. Our own study was conducted among both asymptomatic and symptomatic pregnant women for BV, which may account in part for the higher prevalence rate.

In this study, analysis of the 64 identified patients with BV showed a significantly higher risk of preterm birth with BV infection, which is in agreement with many other studies in the literature [30–33]. Adesiji et al [22] who also worked in South West Nigeria did not find any such association with adverse pregnancy outcome, including preterm birth. The main differences between their study and ours are their use of Amsel criteria for the diagnosis of BV and the fact that they studied women in their first and second trimesters. Our own women were in the second and third trimesters of pregnancy. It has been proposed that there may be differences in the prevalence of BV in the different trimesters. This is because different rates of BV presentation have been found at different phases of the menstrual cycle [34, 35], implying that there might be influence

from endogenous sex hormones. However, most of the trimester-specific studies done have looked at BV in the first and/or early second trimester and have found an increased incidence of preterm labor [13, 32]. Adesiji et al [22] did find a higher incidence of preterm labor of 17.65% in women with BV vs 7.84% in the women with BV, but the difference fell short of statistical significance ($P = .06$). Therefore, it is possible that their finding could have been due to a type II error.

Still, on the trimester of pregnancy, it is interesting that we still found a higher incidence of preterm birth in our study, despite the fact that most of our women were sampled in the third trimester. Other studies have reported that BV discovered in late pregnancy does not have a significant association with preterm birth when compared with BV in early pregnancy [17, 36]. However, because our women only provided one sample, and previous studies have reported that BV does not frequently develop during late pregnancy if absent earlier on [17, 37], it is likely that they had BV from the beginning of pregnancy.

Apart from preterm birth, several reports have linked BV with LBW, PROM, neonatal morbidity, and spontaneous miscarriage [10, 13, 17, 38]. Our study also showed a statistically significant association of BV with LBW and PROM but not with miscarriage or neonatal admissions into the neonatal intensive care unit. For miscarriage, the reason for this could be the fact that the number of women providing samples before 28 weeks gestation, which is still the age of fetal viability in Nigeria, was actually less than half of the total sample size, and there was not enough power for that outcome. Other studies found BV to be associated with spontaneous second trimester miscarriage, but they studied the women in their first trimesters and had larger sample sizes [39, 40]. In order to exclude spontaneous pregnancy loss due to other causes in the first trimester in our own study, the women were recruited after 14 weeks gestation.

We did not find any significant difference in neonatal admissions. We assumed this to be due to the fact that as a tertiary center, many neonates are admitted into the neonatal unit sometimes for observation, and our study was not sufficiently powered for this outcome. Other proxies such as duration of neonatal intensive care unit stay or incidence of respiratory distress (as examined by another study [38]) may have been more useful in detecting neonatal morbidity.

This study also corroborates reports that treatment of BV during pregnancy does not necessarily reduce the incidence of adverse outcome because all of our BV-positive women were treated with oral clindamycin, which has been reported to be as effective as metronidazole in the treatment of BV in pregnancy [1, 15]. It is possible that because they were recruited and therefore treated from the second trimester, the inflammatory processes leading to the adverse outcomes had already been triggered. However, until it can be proven that treatment early in pregnancy can reduce adverse pregnancy outcome, it seems expedient to continue to advocate for appropriate testing and treatment before pregnancy, such as in preconception and infertility clinics.

It is worthy to note that strict exclusion criteria of women with obstetric complications or medical conditions that could influence pregnancy outcome were adhered to in this study. Therefore, we believe our findings to be accurate, because most of the confounding variables have been considered from the outset of the study.

CONCLUSIONS

The prevalence rate of BV among pregnant women in LUTH is high and is significantly associated with preterm delivery, LBW, and PROM. Awareness of the condition and treatment before pregnancy may help reduce the adverse outcome associated with it. Studies assessing treatment of BV with clindamycin in the first trimester of pregnancy may clarify whether adverse outcome may be avoided in our women.

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