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Original Research Article

Therapeutic Evaluation of Clindamycin in Bacterial Vaginosis among Pregnant Females

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Abstract

Introduction: Using clindamycin to treat "bacterial vaginosis (BV)" in pregnant women successfully lowers symptoms and improves pregnancy outcomes. Depending on the severity of the infection, it can be given orally or vaginally. It should be used cautiously and under medical supervision despite its relative safety. There are occasions when clindamycin won not work. Therefore, it is important to have backup plans.

Aims and Objectives: This research aims to determine whether clindamycin is effective for treating "bacterial vaginosis" in pregnant women.

Methods: A year-long prospective study was conducted on 100 patients at our hospital's Gynaecology department. The patients were divided into two groups: Clindamycin group (received Clindamycin) and Placebo group (received placebo). The study used a Nugent score of 7 as the threshold for defining bacterial vaginosis. The double-blind, placebo-controlled experiment included women without a history of late miscarriage or premature birth. Participants were randomly assigned to receive placebo.

Results: Table 1 shows the baseline characteristics of Clindamycin and Placebo trial participants. Pregnancies, miscarriages, premature labour, perinatal death, smoking status, maternal age, education, and parity are included. Both groups had 28-year-old mothers and similar gestational weeks. High school or college was the norm. Clindamycin had a greater nulliparous rate (47.3%) than placebo (41.9%). Smoking, miscarriages, inductions, fetal losses, and pregnancy count are also listed. The table compares Clindamycin with Placebo baseline features.

Conclusion: The study has concluded that clindamycin has no fatal maternal and fetal outcomes so it can be used during pregnancy in patients with bacterial vaginosis.

Keywords: Pregnancies, miscarriages, premature labour, "bacterial vaginosis (BV)".

Introduction

Bacterial vaginosis (BV) is a commonly occurring vaginal infection marked by an excess growth of specific bacteria within the vagina [1]. It is especially crucial to address BV in pregnant women due to its association with negative outcomes during pregnancy, such as preterm birth, low birth weight, and an elevated risk of contracting sexually transmitted infections [1-3]. BV is a prevalent condition among women of

reproductive age and is characteristic of imbalances in multiple types of bacteria within the vagina [1]. Its exact causes and mechanisms remain inadequately understood. However, BV has been found to have a notably higher occurrence among black women, particularly in sub-Saharan Africa [1-4]. In specific regions of Nigeria, such as South-East and North-East Nigeria, substantial incidence rates of 17% and 17.3% correspondingly have been reported [5,6].

Bacterial vaginosis (BV) is a condition that affects a significant number of women, with around 50% to 70% of cases being asymptomatic [1]. Symptomatic women may experience a range of presentations, including an increase in grey-white vaginal discharge with an unpleasant odour, which can be more pronounced after intercourse and during menstruation. Other symptoms may include lower abdominal pain and pain during sexual intercourse (dyspareunia) [8]. Identification of bacterial vaginosis typically involves a combination of clinical evaluation and microbiological testing. Various methods, including Gram-stain established norms (Spiegel's and Nugent) and Gas-Liquid chromatography, can provide supporting evidence for the diagnosis [1-7].

Clindamycin, an antibiotic frequently employed for treating bacterial vaginosis (BV) in pregnant women [9], addresses an imbalance in the natural bacteria found in the vagina that leads to this common vaginal infection. It is crucial to address BV during pregnancy due to its association with several negative outcomes, including preterm birth and other complications [10].

Clindamycin is a member of the lincosamides subclass of antibiotics. It functions by inhibiting the growth of bacteria responsible for BV, such as Gardnerella vaginalis and other anaerobic bacteria. Clindamycin can be administered either orally or topically as a cream or gel, depending on the severity of the infection and the healthcare provider's preference [11].

In pregnant females, using clindamycin for treating BV aims to reduce the risk of complications associated with the infection. Left untreated, BV can increase the chances of preterm birth, low birth weight, and post-part most-partum infections. By effectively addressing BV, clindamycin can help minimize these risks and promote a healthier pregnancy outcome [12].

However, it is essential to note that any medication during pregnancy should be carefully considered and discussed with a healthcare provider. Based on the patient's situation, they will evaluate clindamycin treatment's potential benefits and risks [13]. In certain instances, healthcare providers may suggest alternative treatment options or adopt a different approach to safeguard the health of both the pregnant woman and the developing fetus. Seeking guidance from a healthcare professional is strongly advised to receive a correct diagnosis and suitable treatment plan for bacterial vaginosis or any other medical condition during pregnancy [14, 15].

Many research investigations have assessed the effectiveness of clindamycin as a treatment for BV among pregnant females. Here are some key findings from the available literature: Clindamycin has shown effectiveness in treating BV in pregnant females. It has been found to reduce the symptoms of BV, restore normal vaginal flora, and improve pregnancy outcomes. Oral vs vaginal administration: Both oral and vaginal formulations of clindamycin have been studied. While oral clindamycin is more commonly used, vaginal administration has also been found to be effective. However, oral administration may be preferred when systemic treatment is required [16].

Clindamycin is generally considered safe for use during pregnancy. However, like any medication, it should be used with caution and under medical supervision. Adverse effects are generally rare, but gastrointestinal disturbances and allergic reactions may occur. Resistance: Clindamycin resistance among BV-causing bacteria has been reported. It is important to consider local antibiotic susceptibility patterns when prescribing clindamycin. In cases of resistance, alternative treatment options may need to be considered [17].

Oral clindamycin has been suggested to offer certain advantages over oral metronidazole in managing bacterial vaginosis, as it has a broader spectrum of action. However, worries were expressed regarding the potential occurrence of post-therapy diarrhoea [7, 8]. In response to these concerns, clindamycin vaginal creams have been utilized as an alternative [10-16]. Notably, Joes et al. highlighted in their research that administering clindamycin vaginal creams may not effectively address pregnancy complications associated with bacterial vaginosis [17]. Based on this premise, an evaluation of the efficacy of clindamycin and its impact on contrary pregnancy consequences resulting from bacterial vaginosis was accepted.

Materials and Methods

Research design

The prospective study was conducted for a year on 100 patients, who visited Gynaecology department of our hospital. The patients were divided into 2 groups, those who received Clindamycin, were assigned to Clindamycin group and those who received placebo, while assigned to Placebo group. Samples were obtained from enrolled Pregnant women for bacterial vaginosis using self-collected vaginal samples. The threshold for defining bacterial vaginosis was a Nugent score of 7. In a double-blind, placebo-controlled experiment conducted at many sites, only women without a history of late miscarriage or premature birth were included. The participants were randomly assigned to receive either a placebo, a four-day course of 300 mg of oral clindamycin twice daily, or three four-day courses of 300 mg twice daily at one-month intervals. The events and outcomes were determined and statistically analyzed.

Inclusion and exclusion

Inclusion

- Gestational age >15 weeks.
- Maternal age of <18 years or older.
- The ability to speak French and provide written informed consent.

Exclusion

- Presence of vaginal bleeding within the week before the proposed screening of bacterial vaginosis.
- Plans to give birth in a different region.
- History of late miscarriage, defined as occurring between 16 to 21 weeks and six days of gestation.

Statistical analysis

The trial results were compared between the placebo group and the combined clindamycin groups, with a secondary analysis evaluating the effects of multiple vs a single clindamycin treatment term. With 900 patients in the placebo group and 1800 in the clindamycin group, the sample size was calculated to detect a drop in late miscarriage or spontaneous preterm delivery rates from 4% in the placebo group to 2% in the clindamycin group. Data on study participants were collected both before and after delivery, then evaluated by blinded researchers and analyzed using intention-to-treat and per-protocol methods. Results were reported using relative risks and 95% confidence intervals, and statistical significance was established at a p-value of 0.05.

Ethical approval

Each patient was explained about the process of the study and the consent was obtained from each of them. The study process has been approved by the Ethical Committee of the concerned hospital.

Results

Table 1 shows the baseline characteristics of the women who participated in the trial, split evenly between the Clindamycin and Placebo groups. Information on multiple pregnancies, miscarriages, induced preterm labour, perinatal death, and smoking status at the start of pregnancy, as well as maternal age, education level, and parity, is included in the table below. On average, both groups had about the same number of weeks of pregnancy when randomly assigned. The average maternal age was around 28 years old across all categories. In terms of the level of education, most people in both groups had completed high school or a related technical program. About 37 per cent of those taking clindamycin had completed some college, while 45.7 per cent had completed only high school. There were 37.2% college graduates and 33.3% post-graduates in the placebo group. Women in the Clindamycin group were more likely to be nulliparous (47.3%) than those in the placebo group (41.9%). The table also includes data on smoking habits, previous miscarriages, inductions of premature labour, fetal losses, and the number of pregnancies experienced by each group.

Table 1: Baseline Characteristics of Women According to Study Group

Characteristic	**Clindamycin n=49**	**Placebo n=51**
Weeks of gestation at randomization	12·3· ± 2·2	12·4 ± 2·1
Maternal age – years	27·9 ± 5·4	27·7 ± 5·5
Educational level		
Primary school	5 (11.2)	5 (9.8)
High school or technical school	18 (37.3)	22 (43.1)
Higher education	22 (45.7)	23 (45.0)
Nulliparous	23 (47.3)	29 (56.8)
Smoking at the beginning of pregnancy	11 (22.4)	16 (31.3)
History of miscarriage < 16 weeks	9 (18.4)	10 (19.6)
History of induced preterm labour (22–36 weeks)	1 (2.0)	1 (1.9)
History of perinatal death	3 (6.1)	1 (1.9)
Multiple pregnancy	6 (12.2)	6 (11.8)
Twins	8	7
Triplets	3	1
Nugent score 9 or 10	3 (6.1)	4 (8.4)

Compared to the Placebo group, those taking clindamycin experienced fewer adverse effects, most notably diarrhoea and abdominal discomfort. The Clindamycin group had a greater percentage of unfinished treatments. In contrast, there were no statistically significant differences between the groups regarding preterm birth, spontaneous abortion, bleeding, threatened preterm delivery, abruptio placentae, chorioamnionitis, premature membrane rupture, or gestational age at delivery. These results imply that clindamycin has more tolerability than the placebo, but it has no meaningful effect on the occurrence of these pregnancy problems.

Table 2: Events during pregnancy in each group

Event	Clindamycin n=49	Placebo n=51	P -value
Diarrhea	3 (6.1)	1 (1.9)	0·007
Abdominal	5 (11.2)	5 (9.8)	0·03
Others	18 (37.3)	22 (43.1)	0·31
Incomplete treatment-stopped the protocol	22 (45.7)	23 (45.0)	0·03
Spontaneous miscarriage < 16 weeks	23 (47.3)	29 (56.8)	0·70
Elective abortion or termination of pregnancy for medical reasons ≤ 21 weeks	11 (22.4)	16 (31.3)	0·53
Termination of pregnancy for medical reasons >= 22 weeks*	9 (18.4)	10 (19.6)	0·32
Bleeding during second or third trimester	1 (2.0)	1 (1.9)	0·76
Threatened preterm delivery (hospitalization)	3 (6.1)	1 (1.9)	0·85
Abruptio placentae	6 (12.2)	6 (11.8)	0·20
Prenatal signs of chorioamnionitis	8	7	0·31
Premature rupture of the membranes ≥ 12 h	3	1	0·82
< 37 weeks	3 (6.1)	4 (8.4)	0·57
≥ 37 weeks	9 (18.4	10 (19.6)	0·63

Table 3 shows the results of the mothers' pregnancies who were randomly assigned to the Clindamycin or Placebo groups. The table includes data on the primary outcome, as well as miscarriage after 15 weeks, termination of pregnancy or legal abortion before 21 weeks, termination of pregnancy or legal abortion at or after 22 weeks, fetal death at or after 22 weeks, delivery of liveborn child at or after 22 weeks, gestational age at delivery, mode of delivery, and mode of termination. Primarily, there were no statistically significant differences between the Clindamycin and Placebo groups in terms of preterm delivery (22-36 weeks), spontaneous and induced preterm delivery, miscarriage before 15 weeks, termination of pregnancy or legal abortion before 21 weeks, termination of pregnancy or legal abortion at or after 22 weeks, fetal death at or after 22 weeks, delivery of liveborn child at or after 22 weeks. These results imply that, compared to the placebo, clindamycin has no appreciable effect on these pregnancy outcomes.

Table 3: Pregnancy outcomes (mothers) in each group

Outcome	Clindamycin n=49	Placebo n=51	P -value	Relative risk (95% CI)
Primary outcome				
Late miscarriage or spontaneous very preterm delivery 16-32+6	1 (2.0)	1 (1.9)	1 (2.0)	1·10
16-21	9 (18.4)	3 (5.9)		
22-32	3 (6.1)	1 (1.9)		
Preterm delivery 22-36	6 (12.2)	6 (11.8)	0·37	1·15
Spontaneous	3 (6.1)	5 (9.8)	0·40	1·17
Induced	1 (2.0)	1 (1.9)	0·76	1·09
Miscarriage < 15	9 (18.4)	5 (9.8)		
Termination or preg· or legal	11	22		

abortion ≤ 21				
Termination or preg· ≥22	3	8		
Fetal death ≥22 wks of one or both fetuses	3	4		
Delivery of liveborn child ≥ 22 weeks	3	3	0·42	0·82
Gestational age at delivery	3 (6.1)	2(3.9)	0·92	
Cesarean	5 (11.2)	5 (9.8)	0·93	1·05
Cesarean before labor	1 (2.0)	1 (1.9)	0·27	0·86
Fever during labor	9 (18.4)	2(3.9)	0·83	0·95
Post-partumPost-partum fever	3 (6.1)	2(3.9)	0·46	1·20
Post-partumPost-partum wound infection	5 (11.2)	5 (9.8)	> 0·99	1·17

Table 4 shows the fetal and neonatal results for the Clindamycin and Placebo groups, stratified by mother treatment assignment (birth 22 weeks). Births, fetal deaths, gestational ages, birth weights, neonatal sepsis, admission to the neonatal intensive care unit, perinatal deaths, neonatal deaths or severe neonatal morbidity, severe lesions on transfontenellar ultrasound, oxygen therapy at or after 36 weeks, and poor perinatal outcome are all included in the table. Fetal loss, live births, gestational age, birth weight, neonatal sepsis, admission to the neonatal intensive care unit, perinatal death, neonatal death, or severe neonatal morbidity, severe lesions on transfontenellar ultrasound, oxygen therapy at or after 36 weeks, and post-term delivery were all comparable between the Clindamycin and Placebo groups. Based on these results, clindamycin had no more effect on fetal and neonatal outcomes than the placebo.

Table 4: Fetal and Neonatal outcomes according to maternal treatment assignment (birth ≥ 22 weeks)

Outcome	Clindamycin n=49	Placebo n=51	P -value	Relative risk (95% CI)
Termination of pregnancy for medical reasons ≥ 22 weeks	5 (11.2)	1 (1.9)	0·20	0·42
Fetal death ≥ 22 weeks	18 (37.3)	1 (1.9)	0·59	0·75
Live born ≥ 22 weeks	22 (45.7)	7 (13.7)	0·17	1·01
Gestational age	23 (47.3)	5 (9.8)	0·95	
Less than 32+6 weeks	11 (22.4)	1 (1.9)	0·73	1·13
Less than 36+6 weeks	9 (18.4)	1 (1.9)	0·55	1·09
Birth weight	1 (2.0)	7 (13.7)	0·93	
Less than 1500 g	1 (2.0)	4 (7.8)	0·10	2·09
Less than 2500 g	9 (18.4)		0·62	1·07
Neonatal sepsis (suspected or proved) ****	3 (6.1)	7 (13.7)	0·27	0·77
Admission to neonatal intensive care unit	9 (18.4)	5 (9.8)	0·23	1·20
Perinatal death *****	3 (6.1)	1 (1.9)	0·53	0·75
Neonatal death or severe neonatal morbidity c	1 (2.0)	1 (1.9)	0·72	1·20

Neonatal death ≥ 22 weeks	9 (18.4)	4 (7.8)	0.66	
Severe lesions on transfontenellar US	1 (2.0)	7 (13.7)	0.069	
Oxygen therapy ≥ 36 weeks	3 (6.1)	5 (9.8)	0.074	
Poor perinatal outcome	9 (18.4)	6 (11.8)	0.91	0·96

Discussion

In a study conducted by Lamont et al. (2012) [18], the effectiveness of clindamycin vaginal cream (CVC) was examined in 199 pregnant women diagnosed with bacterial vaginosis (BV), comparing them to a placebo group of 205 women. The study monitored the vaginal flora at every call. The results revealed that 71% of women in the CVC cohort showed signs of being cured or experiencing improvement at the subsequent call. In comparison, only 12% in the placebo cohort demonstrated similar outcomes ($P < 0.001$). 90% of individuals who replied effectively after receiving the early CVC intervention were still treated or improving by the third call. By the end of the third appointment, 33% of the women, who did not recover from CVC at first and were given an extra seven-day therapy had cured or improved, as opposed to 15% of the women who did not respond to the placebo at first and were given the identical further therapy ($P = 0.02$).

In contrast, with 26% of the women in the cohort receiving no treatment after the final appointment, 50% of the women in the CVC cohort who obtained extra therapy were still treated or progressed ($P = 0.004$). The CVC cohort gradually transitioned from abnormal towards usual vaginal flora, with percentages rising from 71% at visit 2 to 76% at visit 3 and 79% at visit 4. Even while the cohort receiving a placebo showed an identical pattern, the ratios (12, 24, and 33%) were far smaller. These results highlight the importance of repeat testing and treatment for women who test positively for BV despite early clindamycin management [18].

A study by Ijeoma et al. (2020) in Port Harcourt, Nigeria, compared effectiveness and impact on Metronidazole and Clindamycin pregnancy outcomes in women with bacterial vaginosis (BV). The study found a BV prevalence of 23%, consistent with previous local studies reporting rates ranging from 17.3% to 64.3% among pregnant women [20-22]. Interestingly, the study revealed alike remedy rates for together drugs, with failure rates of 10.4% for clindamycin and 13% for metronidazole ($p = 0.639$). The mean gestational age at delivery was comparable between the metronidazole-treated group (38.67 weeks ± 1.69) and the oral clindamycin group (38.68 weeks ± 1.64) ($p = 0.96$). The rates of pre-labour rupture of membranes and preterm delivery were also similar in both medication groups ($p = 0.73$ for both). Based on these findings, both medications were found to have analogous effectiveness and alike pregnancy consequences in treating bacterial vaginosis in low-risk asymptomatic pregnant Nigerian women, suggesting their interchangeable use [19]. It's important to note that the prevalence of BV can vary significantly amongst nations, races, and different groups within a similar nation [20-22].

The recommended treatments for bacterial vaginosis (BV) by the American College of Obstetricians and Gynecologists (ACOG) and the Centers for Disease Control and Prevention (CDC) involve a seven-day regimen of either oral metronidazole 500mg taken every day twice or oral clindamycin 300mg taken every day twice [23, 24]. Together drugs have shown analogous effectiveness and have not demonstrated significant

differences in pregnancy outcomes. These outcomes include the occurrence of preterm premature rupture of membranes (PPROM), preterm delivery, low birth weight infants, or perinatal death. However, it should be noted that Morency and Bujold [25] recommend oral clindamycin as the first-line treatment for BV in pregnant women and advise against using metronidazole alone in high-risk patients.

Ting et al. conducted a study in 2020 to compare the frequencies, clinical characteristics, and antimicrobial susceptibilities of vaginal microbes before and after treatment with metronidazole and clindamycin. The study involved 140 premenopausal women with bacterial vaginosis (BV) and ten healthy women who underwent routine gynaecological examinations at Beijing Obstetrics and Gynecology Hospital between October 2018 and February 2019. The participants were evaluated using the Vaginal Microecology Evaluation System. Gardnerella vaginalis and Lactobacillus isolates were cultured and assessed. In vitro, the antimicrobial susceptibilities of the clinical isolates to metronidazole and clindamycin were analyzed. Among the 129 samples analyzed, the most isolated species were facultatively anaerobic bacteria, including G. vaginalis (40.31%), Prevotella isolates (14.89%), and Atopobium vaginae (4.65%). In vitro, the clinical isolates showed a significantly higher susceptibility rate to clindamycin than metronidazole (80.00% vs 32.14%; P = 0.002) [26].

Based on evidence that metronidazole spares Lactobacillus, it can be inferred that metronidazole promotes improved vaginal acidification compared to clindamycin in vivo. Both metronidazole and clindamycin, recommended by the CDC for managing bacterial vaginosis (BV), have shown comparable clinical efficacy. However, when opting for clindamycin therapy, we suggest administering Lactobacillus probiotics 5 to 7 days subsequently the completion of the antibiotic course [26]. Clindamycin is considered a primary treatment option for bacterial vaginosis (BV), a common vaginal infection. It is typically administered with other antibiotics or probiotics to enhance patient outcomes. Clindamycin is widely recognized as an effective therapeutic choice for addressing BV.

Conclusion

The study has concluded that clindamycin has no fatal maternal and fetal outcomes so that it can be used during pregnancy in patients with bacterial vaginosis. The rate of preterm delivery was not reduced in our experiment, even though clindamycin treatment was initiated early and repeated at suitable dosages. Our results are at odds with a recent meta-analysis by Lamont et al., which found that clindamycin treatment significantly reduced the risk of premature birth and late miscarriage. Our findings are consistent with a recent meta-analysis of the literature published in the Cochrane Database, which concluded that screening for and treating bacterial vaginosis to prevent premature birth was not supported by sufficient evidence. We also found no evidence that the chance of having a miscarriage later in pregnancy was reduced. These results point to the need for additional research and care in assuming the efficacy of clindamycin in avoiding preterm delivery and late miscarriages. Our study is limited by the relatively low rate of preterm birth among its subjects. The individuals' risk of having a premature baby was minimal because they had no history of spontaneous or late miscarriage. This caveat is pertinent to screening for and treating bacterial vaginosis in pregnant women. Most pregnant women do not have a family history of premature birth but are still at risk. Therefore, it is essential to discuss techniques for preventing preterm delivery.

References

1. Hodiwala AB, Koli A. Bacterial vaginosis (Review article). Int J Curr Microbiol App Sci. 2015; 4: 530-538.
2. Anukam K, Osazuwa E, Ahonkhai I, Ngwu M, Osemene G, et al. Augmentation of antimicrobial metronidazole therapy of bacterial vaginosis with oral probiotic Lactobacillus rhamnosus GR-1 and Lactobacillus reuteiri RC-14: randomized, double-blind, placebocon -trolled trial. Microbes and Infection. 2006; 8: 1450-1454.
3. Allsworth J, Peipert J. Prevalence of Bacterial vaginosis: 2001-2004 National Health and Nutrition Examination Survey Data. Obstet Gynecol. 2007; 109: 114-120.
4. Denney JM, Culhane JF. Bacterial vaginosis: A problematic infection from both a perinatal and neonatal perspective. Semin Fetal Neonatal Med. 2009; 14: 200-203.
5. Adinma JI, Okwoli NR, Unaeze A, Unaeze N. Prevalence of Gardnerella vaginalis in pregnant Nigerian women. Afr J Reprod Health. 2001; 5: 50-55.
6. Ibrahim SM, Bukar M, Galadima GB, Audu BM, Ibrahim HA. Prevalence of bacterial vaginosis in pregnant women in Maiduguri, North-Eastern Nigeria. Niger J Clin Pract. 2014; 17: 154-158.
7. Bennett P. Preterm Labour. In: Edmonds DK (ed). Dewhurst's textbook of Obstetrics and Gynaecology 8th Edition. West Sussex: WileyBlackwell publishers. 2012; 338-355.
8. Wristrom J, Noriby SR, Myhrea EB, Ekrisson S, Granstrom G, et al. Frequency of antibiotics associated diarrhoea in 2462 antibiotic treated hospitalized patients, a prospective study. J Antimicrob Chemother. 2000. 47: 43-50.
9. Rao PS, Devi S, Shriyan A, Rajaram M, Jagdishchandra K. Diagnosis of bacterial vaginosis in the rural setup: comparison of clinical algorithm, smear scoring and culture by semiquantitative technique. Indian J Med Microbiol. 2004; 22: 47-50.
10. Leitich H, Brunbauer M, Bodner-Adler B, Kaider A, Egarter C, et al. Antibiotic treatment of bacterial vaginosis in pregnancy: A meta-analysis. Am J Obstet Gynecol. 2003; 188: 752-758.
11. Ferris DG, Litaker MS, Woodward L, Mathis D, Hendrich J. Treatment of bacterial vaginosis: a comparison of oral metronidazole, metronidazole vaginal gel, and clindamycin vaginal cream. J Fam Pract.1995; 41: 443- 449.
12. Andres FJ, Parker R, Hosein I, Benrubi GI. Clindamycin vaginal cream versus oral metronidazole in the treatment of bacterial vaginosis: a prospective double-blind clinical trial. South Med J. 1992; 85: 1077-1080.
13. Chen JY, Tian H, Beigi RH. Treatment considerations for bacterial vaginosis and the risk of recurrence. J Women's Health (Larchmt). 2009;18:1997-2004.
14. Fischbach F, Petersen EE, Weissenbacher ER, Martius J, Hosman J, et al. Effi cacy of Clindamycin vaginal cream versus oral metronidazole in the treatment of bacterial vaginosis. Obstet Gynecol. 1993; 82: 405-410.
15. Schmitt C, Sobel JD, Meriwether C. Bacterial vaginosis: treatment with Clindamycin cream versus oral metronidazole. Obstet Gynecol. 1992; 79: 1020-102.
16. Paavonen J, Mangioni C, Martin MA, Wajszczuk CP. Vaginal Clindamycin and oral Metronidazole for bacterial vaginosis: a randomized trial. Obstet Gynecol. 2000; 96: 256-260.
17. Joesoef MR, Schmid GP, Hillier SL. Bacterial vaginosis: a review of treatment options and potential clinical indication for therapy. Clin Infect Dis. 1999.28: S57-65.
18. Lamont RF, Taylor-Robinson D, Bassett P. Rescreening for abnormal

vaginal flora in pregnancy and re-treating with clindamycin vaginal cream significantly increases cure and improvement rates. International journal of STD & AIDS. 2012 Aug;23 (8):565-9.
19. Ijeoma CC, Nyengidiki TK, Bassey G, Ogu RN, Alegbeleye JO, Wariso KT. Oral Clindamycin and Metronidazole in the treatment of bacterial vaginosis in pregnant black women: Comparison of efficacy and pregnancy outcome. Clinical Journal of Obstetrics and Gynecology. 2020 Jan 10;3(1):001-6.
20. Ajani G, Oduyebo O, Haruna M. Nugent scores of pregnant women in a tertiary institution in Nigeria. Adv Microbiol. 2012; 2: 531-536.
21. Awoniyi AO, Komolafe OI, Bifarin O, Olarinde O. Bacterial vaginosis among pregnant women attending a primary health centre in Ile-Ife, Nigeria. Global Adv Res J Medicine Med Sci. 2015; 4: 57-60.
22. Olowe OA, Makanjuola OB, Adekanle DA. Prevalence of vulvovaginal candidiasis, trichomoniasis, and bacterial vaginosis among pregnant women receiving antenatal care in South-Western Nigeria. Eur J Microbiol Immunol. 2014; 4: 193-197.
23. Centers for Disease Control and Prevention, CDC. Division of STD Prevention: 2017.
24. ACOG Committee on Practice Bulletins--Gynecology. Clinical management guidelines for Obstetrician-Gynaecologists, Number 72, May 2006: Vaginitis. Obstet Gynecol. 2006; 107: 1195-1206.
25. Morency AM, Bujold E. The effect of second-trimester antibiotic therapy on the rate of preterm birth. J Obstet Gynaecol Can. 2007; 29: 35-44.
26. Ting Li, Fengjuan Wang, Zhan Zhang et al. Treatment of Bacterial Vaginosis: A Comparison of Metronidazole and Clindamycin on Human Anaerobic Bacteria and Lactobacilli, 23 November 2020, PREPRINT (Version 1) available at Research Square [https ://doi.org/10.21203/rs.3.rs-107727/v1].