



Manuscript ID ZUMJ-2110-2367 (R2)
DOI 10.21608/zumj.2021.99190.2367

ORIGINAL ARTICLE

Evaluation of the risk of spontaneous miscarriage in bacterial vaginosis

Ahmed Elsayed Mansor¹, Mohamed Ali Alabiad², Basem Hamed¹

Obstetrics and Gynaecology Department, Faculty of Medicine, Zagazig University, Egypt.

1- Pathology Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding Author:

Dr. Mohamed Ali Alabiad
(corresponding author)

Pathology Department, Faculty
of Medicine, Zagazig
University, Egypt.

Email:

Maabyad@medicine.zu.edu.eg,

Address: Faculty of Medicine,
Zagazig University, Zagazig,
Egypt.

Submit Date 2021-10-02

Revise Date 2021-10-23

Accept Date 2021-11-04

ABSTRACT

Background: Miscarriage is spontaneous expulsion of product of conception from the uterus before viability (20 weeks) or if fetus less than 500 gm, or its length less than 25 cm. Bacterial vaginosis is extremely prevalent condition, although it is not a reportable disease. Up to 50% of pregnant women have been found to have BV.

Methods; In this study, we assessed 219 pregnant women for the association between bacterial vaginosis and first trimester miscarriage by screening for bacterial vaginosis using Nugent gram stain scoring system among the pregnant women at 7 weeks of gestation and follow them up to the end of first trimester. Using Nugent gram stain scoring system and the result of the culture, we divided pregnant women into to 2 groups: **Group I:** Women who are negative for BV (167 women, 76.3%). **Group II:** Positive for bacterial vaginosis (52 women, 23.7%). Then, we followed them up to the end of first trimester. We choose 13 weeks as an end point, as our study was designed to investigate first trimester miscarriage. we compared the two groups regarding the rate of first trimester miscarriage.

Results: In the current study, the prevalence of bacterial vaginosis among the pregnant women included was 23.7 %. Among the 219 women included in the study, 38 women (17.4%) miscarried during the first trimester and 181 women (82%) continued their pregnancies after 13 weeks.

Conclusion there is no between bacterial vaginosis and first trimester miscarriage when comparing pregnant women with bacterial vaginosis to women who are negative for bacterial vaginosis

Keyword: spontaneous miscarriage; bacterial vaginosis; Nugent gram stain

INTRODUCTION

Abortion is the expulsion or extraction from its mother of a fetus or an embryo weighing 500 grams or less. (Approximately equals to 20-22 completed weeks of gestation) (140-154 completed days) or an otherwise product of gestation of any weight and specifically designated (e.g. hydatidiform mole) irrespective of gestational age and whether or not there is evidence of life and whether or not the abortion was spontaneous or induced. The rate of pregnancy loss among clinically diagnosed pregnancies is 8 to 15%. As many as 80% of miscarriages occur before 12 weeks of gestation with miscarriage rate decrease sharply after first trimester (1). In the

United States, abortion refers to pregnancies terminating up to 20 weeks gestational age or delivery of a fetus that weighs less than 500 grams (2). Factors associated with early pregnancy loss include advanced maternal age, alcohol use, cigarette smoking, cocaine use, maternal chronic disease, antiphospholipid syndrome, polycystic ovarian syndrome, maternal infection, vaginal mycoplasma or ureaplasma, listeria, syphilis, toxoplasmosis, Chlamydia, reproductive tract adhesion, previous pregnancy loss and thyroid disease (2). Bacterial vaginosis (BV), also known as vaginal bacteriosis or Gardnerella vaginitis, is a disease of the vagina caused by excessive bacteria. Common symptoms include

increased vaginal discharge that often smells fishy smelling. The discharge is usually white or gray in color. Burning with urination occurs. Itching is uncommon. Occasionally there may be no symptoms. Having BV increases the risk of infection by a number of other sexually transmitted infections including HIV/AIDS. It also increases the risk of early delivery among pregnant women (3). **Donders et al.**, assessed the vaginal flora of women during early pregnancy and determined its relationship to subsequent spontaneous early pregnancy loss. They concluded that bacterial vaginosis, especially when *G. vaginalis* or Mycoplasmas are bred, associated with 5 times the chance of spontaneous abortion. The most likely cause is the increasing spread of the infection accompanied by an inflammatory reaction. They suggested diagnosis and treatment of bacterial vaginosis during pregnancy as soon as possible (4). The aim of the work was to assess the relationship between bacterial vaginosis and the risk of spontaneous miscarriage and to compare mean pregnancy duration in first trimester between women with and without bacterial vaginosis

PATIENTS AND METHODS

This study was conducted at Antenatal Care Clinic, to the Obstetrics and Gynecology Department of Zagazig University Hospitals, during the period from' novmber 2017 till novmber 2019. It was designed to investigate the association between bacterial vaginosis and first trimester miscarriage by screening for bacterial vaginosis using Nugent gram stain scoring system among pregnant women at 7 weeks of according to the result of the culture, we divided pregnant women into 2 groups: **Group I:** Women who are negative for BV (167 women, 76.3%). **Group II:** Positive for bacterial vaginosis (52 women, 23.7%). Then, we followed them up to the end of first trimester. We choose 13 weeks as an end point, as our study was designed to investigate first trimester miscarriage. we compared the two groups regarding the rate of first trimester miscarriage

Written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

. Patients:

We recruited 219 pregnant women from attendants of antenatal care clinic during first trimester who were confirmed to have viable embryos by ultrasound examination.

Inclusion criteria:

- Pregnant women of age group 18-38 years, <14week with and without vaginal discharge, confirmed fetal cardiac pulsation by U/S and no threatened abortion and BMI up to 25.

Exclusion criteria:

Multiple gestations, Blighted ovum, and Medical condition predisposing to abortion as: Diabetes mellitus, Chronic hypertension, Endocrinal diseases, Autoimmune diseases, Renal diseases, Blood diseases, and Patients who received antimicrobial therapy within 4 weeks before sampling.

Methods:

For all cases, the following were performed:

1- Careful history taking:

.2-examination;

Full general and abdominal examination and local examination; local steril speculum examination to asses for the presence of abnormal vaginal discharge and signs of vaginitis.

3- Investigations:

Ultrasound examination for confirmation of pregnancy, fetal well- being (+ve cardiac pulsation), dating in early pregnancy and cervical dimension for exclusion of cervical incompetence

4- Collection of samples:

After putting patients in dorsal lithotomy position, sterile vaginal speculum was applied. Samples are collected from posterior vaginal fornix and vault of vagina by sterile cotton swab. The swabs were smeared on clean glass slide and

sent to the lab in the same day. The slides were air dried and labelled with patient study number. The slides were stained by grame stain. Bacterial vaginosis was diagnosed according to the Nugent grame stain scoring system which is gram stain scoring system. The Nugent scor is calculated by scoring the numbers of lactobacilli, Gram-negative, and gram variable rods (i.e,prevotella and gardinerella vaginalis), and curved gram —variable rods (i.e mobilincus). A score of 7-10 is consistant with bacterial vaginosis (5). The slides were read by observer blinded to outcome of pregnancy at the end of the first trimester.

Then, women with positive diagnosis of bacterial vaginosis by Nugent Gram stain scoring were assigned to the first group. and women with negative diagnosis are assigned to the second group. Both groups were followed up by serial ultrasound examinations every two weeks to evaluate fetal viability, till the end of 13th week of pregnancy.

Statistical analysis

Using Epi-Info version 6 and SPP for Windows version 8, data were reviewed and analysed. Level significance: For all above mentioned statistical tests done, the threshold of significance is fixed at 5% level (p-value). The results was considered: Significant when the probability of error is less than 5% ($p < 0.05$). Non-significant when the probability of error is more than 5% ($p > 0.05$), Highly significant when the probability of error is less than 0.1% ($p < 0.001$). The smaller the p-value obtained, the more significant are the results.

RESULTS

we divided pregnant women included in the study to 2 groups: **Group I:** Women who are negative for BV (167 women, 76.3%). **Group II:** Positive for bacterial vaginosis (52 women, 23.7%). Table1

Then, we followed them up to the end of first trimester. We choose 13 weeks as an end point, as our study was designed to investigate first trimester miscarriage. we compared the two groups regarding the rate of first trimester miscarriage. In the current study, by regular u/s

exam done every 2 weeks we followed the cases and detected the following:

181 cases from 219 women who included in our study complete their pregnancy beyond the first trimester without any negative back draws, 11 cases had come with missed abortion detected on their regular follow up, 6 cases had brought reports which revealed that they had incomplete abortion and come for further management, 6 cases had complete abortion detected by u/s exam done on the regular follow up, and 6 cases had suffered from inevitable abortion 4 cases detected on the regular follow up and the other 2 cases came with reports which revealed that they had inevitable abortion and come for further management. Among the 219 women included in the study, 38 women (17.4%) miscarried during the first trimester and 181 women (82%) continued their pregnancies after 13 weeks. Table 2,3

By comparing the two groups as regard the age, the mean for age was 26.58% with $SD \pm 8.2$ in the women negative for BV, and 27.56 with $SD \pm 9.1$ in the women with bacterial vaginosis. As regard the parity, the mean was 2.82 with $SD \pm 0.9$ among the women negative for BV and 2.61 with $SD \pm 0.8$ among the women with bacterial vaginosis. The results of the contraception history of studied groups are shown in table (2). Bacterial vaginosis was significantly higher in women using IUCD (32/52), and 61.5%, compared to women don't use IUCD (52/167) women, 31.1%. no significance difference was reported in other methods of contraception. Our study showed no statistically significant relation between bacterial vaginosis and first trimester miscarriage when comparing pregnant women with bacterial vaginosis (27%) to women who are negative for bacterial vaginosis (11%) regarding first trimester miscarriage. The rates and types of abortion of the studied groups are illustrated in Table (3). The first trimester miscarriage rate was non significantly higher (21.2%) in women with positive diagnosis of bacterial vaginosis (group b) compared to women with —ve bacterial vaginosis (16.2%).

The types of abortion didnt significantly vary between both groups. Table 4,5

By comparing mean gestational age of abortion in the two groups, we found that it was $7.41 \pm SD 0.84$ in women with normal vaginal flora and $7.22 \pm SD 0.72$ in women with bacterial vaginosis which reveals that miscarriage occurred earlier in women with bacterial vaginosis than women negative for BV Table 4.

no statistically significant relation between bacterial vaginosis and first trimester miscarriage when comparing pregnant women with bacterial vaginosis (27%) to women who are negative for bacterial vaginosis (11%) regarding first trimester miscarriage Table 5. the prevalence of bacterial vaginosis among the pregnant women included was 23.7 %.

Table (1): Shows basic characteristics of studied groups. Both groups are compatible Regarding age, occupation and parity.

Variable	-ve (n=167)		+ve (n=52)		t	P
	No	%	No	%		
Age : (year)						
Mean \pm SD	26.58 \pm 8.2		27.56 \pm 9.1		0.73	0.46
Range	18 - 34		19 - 36			NS
Variable	No	%	No	%	χ^2	P
Age group:						
18 - < 23	22	13.2	8	15.4	0.54	0.76
23 - < 29	112	67.1	32	61.5		
29 - 38	33	19.8	12	23.1		
Occupation:						
Not working(House wife)	98	58.7	38	73.1	3.49	0.06
Working	69	41.3	14	26.9		NS
Parity:					Mean \pm SD	
Mean \pm SD	2.82 \pm 0.9	2.61 \pm 0.8	1.51	0.13	Range	2.82 \pm 0.9
Range	0 - 5	0 - 5		NS		0 - 5
Parity:						
Primgravida	50	29.9	20	38.5	1.32	0.25
Multipara	117	70.1	32	61.5		NS

Table (2): Relation between bacterial vaginosis of the studied group and methods of contraception

Variable	-ve (n=167)		+ve (n=52)		χ^2	P
	No	%	No	%		
Previous Contraception:						
Not use	57	34.1	11	21.2	15.72	0.001**
Hormonal	49	29.3	8	15.4		
IUD	52	31.1	32	61.5		
Barriers	9	5.5	1	1.9		

Table (3): Rates and types of abortion of studied groups:

Variable	-ve (n=167)		+ve (n=52)		χ^2	P
	No	%	No	%		
Abortion:						
Yes	27	16.2	11	21.2		NS

Variable	-ve (n=167)		+ve (n=52)		χ^2	P
	No	%	No	%		
Type:	(n=27)		(n=11)			
Missed abortion	11	40.8	5	45.5	0.38	0.94
Incomplete abortion	6	22.2	3	27.3		
Inevitable abortion	6	22.2	2	18.2		
Complete abortion	4	14.8	1	9		

Table (4): Relation between bacterial vaginosis and Gestational age of the studied group:

Variable	-ve (n=167)		+ve (n=52)		t	P
Gestational Age: (Weeks)						
Mean ± SD	7.41 ± 0.84		7.22 ± 0.72		1.6	0.11
Range	5 - 10		5 - 11			NS
Variable	No	%	No	%	χ^2	P
Weeks:						
≤ 7	76	45.5	23	44.2	0.03	0.87
≥ 8	91	54.5	29	55.8		NS

Table (5): Prevalence of bacterial vaginosis among the studied group by vaginal smear using Nugent scoring system;

Variable	(n=219)	
	No	%
Vaginal smear:		
-ve	167	76.3
+ve	52	23.7

DISCUSSION

Miscarriage is a common event that causes considerable morbidity and fetal loss for women in the child bearing period. Early diagnosis and treatment or prevention of the causes of miscarriage is of fundamental importance in avoiding many harmful maternal complication not only fetal loss but also sever hemorrhage, sepsis, bacterial shock, acute renal failure, and also iatrogenic complication as incomplete removal of the fetus and placenta, cervical laceration and uterine perforation during sounding of the uterus, dilatation or curettage (6).

. Classically, women who have a miscarriage are told that natural selection took place and that complex polygenetic or immunological causes may have played a role, the cause of spontaneous miscarriage is misunderstood. There are scant data on the possible role of cervicovaginal infection in causing early pregnancy loss Temmerman et al (7).

Spontaneous abortion was associated with the development of Ureaplasma Urealyticum vaginal and with the presence of streptococci and gonorrhea group B. Chlamydia trachomatis can lead to abortion by excessive maternal immunological reaction to its protein from heat shock (8).

Because most of the previous studies have concentrated on bacterial vaginosis and pregnancy outcomes on the second trimester; however, A strong association of bacterial vaginosis with first-trimester miscarriage remains to be verified as the diagnosis and treatment of bacterial vaginosis is simple and cheap if bacterial vaginosis is associated with first-trimester miscarriage (9).

In this study, we assessed the association between bacterial vaginosis and the first trimester abortion by screening for bacterial vaginosis using Nugent gram stain scoring system among pregnant women at 7 week of gestation and follow them to the end of the first trimester to compare the incidence of

first trimester miscarriage among group of women with normal vaginal flora against group of women with bacterial vaginosis. Using Nugent gram stain scoring system, we divided pregnant women included in the study in 2 groups; **Group I:** women who are negative for BV (167 women, 76.3%). **Group II:** women who are positive for BV (52 women, 23.7%). Then we followed them up to the end of first trimester. We choose 13 weeks as an end point, as our study was designated to investigate first trimester miscarriage.

In the current study the prevalence of bacterial vaginosis among pregnant women included was 23.7%. The average incidence of bacterial vaginosis varies and is reported to be 20-35% in patients visiting gynecological clinics, 15-30% in patients visiting obstetric clinics and 20-45% in patients visiting services of sexually transmitted diseases (10). Among 219 women included in this study, 38 women had 1st trimester abortion giving 1st trimester abortion rate of 17.4% in our study. Similar to our study. Evertte, 1997, reported 1st trimester abortion rate of 15-20%. Also **George et al.**, reported that almost 20% of clinically recognized pregnancies terminate in spontaneous abortion (6). In this study, the rate of first trimester miscarriage was comparable between women with bacterial vaginosis, group 2 (11/52=21.2%), and group of women without it, group 1 (27/167=16.2%), with non significant difference, so bacterial vaginosis isn't associated with increased 1st trimester abortion rate.

Contrary to ours, **Donder et al.**, reported a strong association between bacterial vaginosis and early pregnancy loss. They also reported that bacterial vaginosis before 14 gestational weeks would predict early pregnancy loss in 36% in women with bacterial vaginosis, positive predictive value, whereas absence of bacterial vaginosis would predict normal delivery in 43% of the cases, negative predictive value (4).

The apparent association of bacterial vaginosis and early pregnancy loss in **Donder et al.**, study may be attributed to inclusion of women with past history of pregnancy loss in that study, and so those women may have had an additional cause that made them abort more rather bacterial vaginosis (4).

Similar to our, Oostrum and et al in their meta-analysis, 2013, reported that BV isn't associated with an increased risk of first trimester abortion (OR 1.20, 95% CI; 0.53-2.75). **Liversedge et al.**, reported that bacterial vaginosis has no significant effect upon fertilization and implantation rates during IVF treatment in spite of high prevalence of bacterial vaginosis in these patients compared to others in antenatal and general gynecological population (11). Similar to **Liversedge et al.**, **Ralph et al.**, reported similar conception rates during IVF treatment in women with bacterial vaginosis and those with normal vaginal flora, but and contrary to our result, they reported a significantly increased risk of miscarriage in first trimester in women with bacterial vaginosis (31.6%) compared to women with normal vaginal flora (18.5%) (11, 12)

In their study to evaluate the association between BV and the history of spontaneous abortion and recurrent pregnancy losses, **another study reported** significant association between BV and 1st and 2nd trimester miscarriage. Their result, were contrary to ours, however, this study was carried out on non pregnant women with a history of miscarriage during preceding 6 months period (13).

Our study, on the other hand was carried out during pregnancy when 1st trimester abortion could be attributed to concurrent BV.

CONCLUSION

The results of our study showed no statistically significant relation between bacterial vaginosis and first trimester miscarriage when comparing pregnant women with bacterial vaginosis to women who are negative for bacterial vaginosis regarding first trimester miscarriage. A large study with large number of cases is required to confirm association between bacterial vaginosis and first trimester abortion.

- **Conflict of Interest:** The authors report no conflicts of interest

REFERENCES

1. DeCherney AH, Nathan L, Laufer N, Roman AS, Education M-H. Current diagnosis & treatment: obstetrics & gynecology: McGraw-Hill Education; 2019.
2. Cunningham F, Norman F, Kenneth J, Larry C, John C. Williams Obstetric Textbook. McGraw-Hill Publishing Company. 2009;23:573-5.
3. Donders GG, Zozzika J, Rezeberga D. Treatment of bacterial vaginosis: what we have and what we miss. *Expert Opin Pharmacother*. 2014;15(5):645-57.
4. Donders GG, Van Bulck B, Caudron J, Londers L, Vereecken A, Spitz B. Relationship of bacterial vaginosis and mycoplasmas to the risk of spontaneous abortion. *Am J Obstet Gynecol*. 2000;183(2):431-7.
5. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. *J Clin Microbiol*. 1991;29(2):297-301.
6. George L, Mills JL, Johansson AL, Nordmark A, Olander B, Granath F, et al. Plasma folate levels and risk of spontaneous abortion. *JAMA*. 2002;288(15):1867-73.
7. Temmerman M, Lopita M, Sanghvi H, Sinei S, Plummer FA, Piot P. The role of maternal syphilis, gonorrhoea and HIV-1 infections in spontaneous abortion. *Int J STD AIDS*. 1992;3(6):418-22.
8. Witkin SS. Immune pathogenesis of asymptomatic Chlamydia trachomatis infections in the female genital tract. *Infect Dis Obstet Gynecol*. 1995;3(4):169-74.
9. 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(4):819-28.
10. Shaffi AF, Balandya B, Majigo M, Aboud S. Predictors of Bacterial Vaginosis among Pregnant Women Attending Antenatal Clinic at Tertiary Care Hospital in Tanzania: A Cross Sectional Study. *EA Health Research Journal*. 2021;5(1):59-68.
11. Liversedge N, Turner A, Horner P, Keay S, Jenkins J, Hull M. The influence of bacterial vaginosis on in-vitro fertilization and embryo implantation during assisted reproduction treatment. *Hum Reprod*. 1999;14(9):2411-5.
12. Ralph S, Rutherford A, Wilson J. Influence of bacterial vaginosis on conception and miscarriage in the first trimester: cohort study. *BMJ*. 1999;319(7204):220-3.
13. Petrova MI, Lievens E, Malik S, Imholz N, Lebeer S. Lactobacillus species as biomarkers and agents that can promote various aspects of vaginal health. *Front Physiol*. 2015;6:81.

Mansour, A., Alabiad, M., Hamed, B. Evaluation of the risk of spontaneous miscarriage in patients with bacterial vaginosis. *Zagazig University Medical Journal*, 2022; (320-326): -. doi: 10.21608/zumj.2021.99190.2367