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ORIGINAL ARTICLE

Vaginal Bacterial Infection is Associated With the Occurrence of Spontaneous Abortion during the First Trimester

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Abstract

Background: **Recurrent spontaneous abortion (RSA) is a serious disorder that may be detrimental to a woman's health. Bacterial vaginosis is a vaginal microsystem disorder that seems to be connected to a higher risk of abortion, early birth, and puerperal endometritis. Overall, 60% of all vaginitis types are caused by bacterial vaginosis. The purpose of this research was to explore whether vaginal bacterial infection is connected to spontaneous abortion during the first trimester.**

Materials and methods: **This was a cross-sectional study on 120 pregnant women on the first trimester diagnosed with spontaneous abortion during the first trimester.**

Results: **There was no significant difference in clinical data of included participants in both groups. There was significant high prevalence of symptoms in the pregnancy loss group, significant increase in lactobacilli in all grades in the abortion group compared with the evolving pregnancy group, significant increase in pathogenic bacteria in the abortion group, and no significant difference in enteric bacteria. There was a high-significant association between infection and abortion occurrence. All pathogens were significantly associated with pregnancy loss occurrence. Moreover, type *B Streptococci* were significantly associated with abortion occurrence.**

Conclusion: **To exclude out chronic infections, all patients with RSA should be evaluated according on their personal infection risk, which involves a thorough history as well as physical and laboratory examinations. Despite the fact that many patients with RSA are healthy, monogamous, and have a minimal risk of Sexually Transmitted Diseases (STD)s, they should be checked. During the first trimester, vaginal infection may be a risk factor for spontaneous abortion.**

Keywords: Abortion, First trimester, Vaginal bacterial infection

1. Introduction

Recurrent spontaneous abortion (RSA) is a risky condition that may be harmful to a woman's health. According to epidemiological study, the chance of a pregnant abortion is roughly 24% after two clinical abortions; this percentage rises to 30% after three abortions and 40% after four abortions.[1]

RSA depends on many factors including chromosomes,[2] heredity,[3] dissection,[1] the endocrine system,[4] placental abnormality,[5] infection,[6] immunity,[7] thrombosis,[8] and the environment,[9] among others. Among all the cases, 50% still cannot be explained.[10] Researchers discovered that patients with unexplained RSA often experienced recurrent vaginitis or vaginal dysbacteriosis throughout non-pregnancy, pregnancy, and postabortion periods based on study data and results from long-term clinical trials.[1]

A thorough obstetric history, including the gestational age of fetus at the moment of death, cytogenetic data, an ultrasound examination, and pathology, are all necessary for the diagnosis and treatment of RSA. A multidisciplinary approach is required in this complicated reproductive situation

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to study and treat genetic and endocrinologic problems, as well as anatomical, immunologic, infectious, thrombophilic, placental, and iatrogenic causes.[11]

Bacterial vaginosis (BV) is a vaginal microecosystem condition that seems to be linked to an increased risk of abortion, early birth, and puerperal endometritis.[12]

Miranda et al.[13] reported that BV is responsible for 60% of all vaginitis types.

Despite fresh data, infectious illnesses are thought to be the cause of recurrent abortions at a rate as low as 4%.[14] Only a few germs may cause prolonged maternal disease and frequent abortions, despite the fact that many can cause acute infection and subsequent abortion. An estimated 10–15% of pregnancies end in abortion due to embryo-fatal infections; however, this percentage is likely to be underestimated because of early-stage pregnancies ending in abortion owing to untreated subclinical abortions. Only histological study of fetal and placental tissues and isolation of the putative infectious agent by culture or genetic identification may be employed in praxis to detect infection-related abortion.[15]

The present study was aimed to evaluate whether vaginal bacterial infection is associated with the occurrence of spontaneous abortion during the first trimester.

2. Materials and methods

This was a cross-sectional study on 120 pregnant women. In the first trimester diagnosed with spontaneous abortion during the first trimester. The study was conducted in Al-Hussein University Hospital, Al-Azhar University, between May 2021 and February 2022.

A systematic vaginal speculum examination was performed on women with a live singleton fetus who were evaluated for a routine prenatal consultation at less than 14 complete gestational weeks. They were all new patients who came in on the same weekday and were under 14-week pregnant. Vaginal fluid was collected from the posterior vaginal vault using a wooden Ayre spatula and placed on two separate glass slides. On fresh wet vaginal preparations, phase-contrast microscopy was used to find clue cells.

BV has been shown to exist. Guidelines developed by Amsel et al.[16] were used to diagnose BV, which needed three of the four criteria stated as follows: (1) a vaginal pH of 4.6 or above, (2) uniform vaginal discharge, (3) a fishy odor (amine test), and (4) the presence of vaginal clue cells.

A cotton-tipped swab was introduced into the posterior vault with the help of Amies modified Stuart medium. Following 20 s in an Amies modified Stuart medium, it was introduced into the endocervical canal and spun three times before a second batch of Amies modified Stuart medium was placed after the ectocervical cleaning. An ampicillin-pretreated A3 medium was used to cultivate bacteria associated with BV in vaginal and cervical cultures for 18 h. Based on their ability to hydrolyze urea or L-arginine, *Ureaplasma urealyticum*, and *Mycoplasma hominis* were discovered applying color reactions. The strains of *Escherichia coli*, *Klebsiella*, *Acinetobacter*, *Staphylococcus*, and *Enterococci* were all grown on blood-chocolate agar, as were *Streptococci* and yeasts. As long as their growth was more than the threshold of 1+, patients with normal mixed commensal flora did not have their growth removed (growth covering more than half of the incubation plate).

The results ($n = 10$) were eliminated if cultures were not collected properly, cultures were inadequate, or transfer to the laboratory took more than 6 h.

Lactobacillus morphotypes are recognized. The wet mount was classified using Schröder's original categorization approach. This grading system was developed in response to its clinical use in late pregnancy.

Red blood cells, *Trichomonas vaginalis*, and epitheliolytic squamous epithelial cells have all been discovered.

For leukocytosis in the vaginal fluid, the lowest leukocytosis score was found to be associated with the hpf (400 magnification) with the fewest white blood cells (score of 1). A score of 2 was granted when 5–10 leukocytes/hpf were observed. A sample obtained a score of 3 if there were less than 10 leukocytes per epithelial cell and a score of 4 if there were more than 10 leukocytes per epithelial cell.

We also looked at the importance of finding clue cells on wet mounts or Papanicolaou specimens by various persons or at different dates. After all of this work was done, we looked into the possibility that specific bacteria, such as those connected to BV, may cause miscarriage.

2.1. Statistical analysis

IBM SPSS statistics (Statistical Package for Social Sciences) software was used to analyze computer-generated data. To express quantitative data, percentages, and numbers were employed. Before using the median in nonparametric analysis or the interquartile range in parametric analysis, it was

required to perform Kolmogorov–Smirnov tests to ensure that the data were normal. We used the 0.05 significance threshold to establish the significance of the findings. The chi-square test was used to compare two or more groups. The Monte–Carlo test was used to adjust for any number of cells with a count less than 5. Fisher's χ^2 adjustment was applied to 2 × 2 tables when at least a quarter of cells had a count of less than 5.

2.2. Ethical considerations

The study protocol was submitted for approval by the Institutional Review Board, Al-Azhar University. Each individual who participated in the research provided informed verbal permission. At every stage of the research, confidentiality, and personal privacy were protected.

3. Results

The mean ± SD age was 26.17 ± 3.76 years. The mean ± SD gestational age was 9.54 ± 3.41 weeks. The mean ± SD BMI was 25.1 ± 1.49 kg/m^2 (Table 1). There were 17 cases of pregnancy loss in the first trimester (Tables 2–7).

4. Discussion

A spontaneous miscarriage has no recognized cause. According to women who miscarry, natural selection has occurred, and intricate polygenetic or immunologic factors may have played a role. There is scant evidence that cervicovaginal infection causes miscarriage. *Chlamydia trachomatis* may induce miscarriage owing to an overly immunogenic maternal response to its heat shock protein 60 antigen,[17] whereas other studies have established a link between vaginal *U. urealyticum*, *group B streptococci*, and gonorrhea.[18]

Several studies have been conducted to investigate the relationship between bacterial vaginosis and early pregnancy outcomes. According to Kurki et al.,[19] premature labor, preterm delivery, and early membrane rupture before the 18th week of pregnancy may be predicted by the presence of bacterial vaginosis at the first prenatal visit. As a result, the question of whether bacterial vaginosis causes miscarriage in the first part of pregnancy remains unsolved. In a trial including 1260 women on their first prenatal visit, McGregor et al.[20] reported that bacterial vaginosis was connected to a threefold increase in the chance of miscarriage for the course of the study's follow-up.

Table 1. Basal characteristics of included participants.

Parameter	Value (N = 120)
Age (years)	26.17 ± 3.76
GA (weeks)	9.54 ± 3.41
BMI (kg/m^2)	25.1 ± 1.49
Co-morbidities	
HTN	34
DM	26
Pregnancy loss in first trimester	17

DM, diabetes mellitus; GA, gestational age; HTN, hypertension.

Table 2. Clinical data of included participants.

	Pregnancy loss (N = 17)	Evolving pregnancy (N = 103)	P value
Age	27 ± 3.92	26.03 ± 3.74	0.33
GA	9.88 ± 3.66	9.49 ± 3.38	0.66
BMI	24.7 ± 1.79	25.13 ± 1.44	0.28
Co-morbidities			
HTN	6	28	0.49
DM	3	23	0.66

There was no significant difference in clinical data of included participants in both groups.
DM, diabetes mellitus; GA, gestational age; HTN, hypertension.

Table 3. Symptoms in participants in both groups

	Pregnancy loss (N = 17)	Evolving pregnancy (N = 103)	P value
Discharge	7	12	0.002
Itching	10	19	0.003
Pain	5	6	0.0018

There was a significant high prevalence of symptoms in the pregnancy loss group.

Table 4. Microscopic findings in both groups.

	Pregnancy loss (N = 17)	Evolving pregnancy (N = 103)	P value
Lactobacilli grade			
I	3	38	0.001
IIa	3	42	
IIb	4	14	
III	7	9	
Clue cells	4	13	0.23
Red blood cells	3	26	0.498
Epithelial cytolysis	2	23	0.32
Vaginal leukocytosis			
<5 leukocytes/hpf	1	6	0.98
<10 leukocytes/hpf	4	20	
≥10 leukocytes/hpf and <1 Leukocytes/epithelial cell	6	40	
≥10 leukocytes/hpf and >10 Leukocytes/epithelial cell	6	37	

There was a significant increase in lactobacilli in all grades in the abortion group compared with the evolving pregnancy group.
hpf, high-power field.

Table 5. Comparison of vaginal cultures in both groups.

	Pregnancy loss ($N = 17$)	Evolving pregnancy ($N = 103$)	P value
Bacterial vaginosis			
Gardnerella vaginalis	4	6	0.14
Ureaplasma urealyticum	5	8	0.008
Mycoplasma hominis	3	4	0.025
Enteric bacteria			
Enterobacteriaceae	1	22	0.1331
Enterococci	2	29	0.15
Group B *streptococci*	2	32	0.102

There was a significant increase in pathogenic bacteria in the abortion group. There was no significant difference in enteric bacteria.

Table 6. Correlation between pregnancy loss and patient characteristics.

Age	
Pearson correlation	0.090
P value	0.327
Infection	
Pearson correlation	0.540**
P value	0.000
BMI	
Pearson correlation	−0.099
P value	0.284
GA	
Pearson correlation	0.041
P value	0.658
HTN	
Pearson's correlation	0.063
P value	0.496
DM	
Pearson's correlation	−0.040
P value	0.667

There was highly significant association between infection and abortion occurrence ($P < 0.0001$).
DM, diabetes mellitus; GA, gestational age; HTN, hypertension.

Table 7. Correlation between abortion and other infectious events.

	Age	Loss
Gardnerella vaginalis		
Pearson's correlation	0.139	0.223*
P value	0.129	0.014
Ureaplasma urealyticum		
Pearson's correlation	0.163	0.243
P value	0.075	0.008
Mycoplasma hominis		
Pearson's correlation	−0.030	0.307
P value	0.745	0.001
Enterobacteriaceae		
Pearson's correlation	0.057	−0.137
P value	0.533	0.135
Enterococci		
Pearson's correlation	−0.223*	−0.110
P value	0.014	0.234
B. streptococci		
Pearson's correlation	0.007	−0.255
P value	0.943	0.005

All pathogens were significantly associated with pregnancy loss occurrence. Moreover, *B. Streptococci* were significantly associated with abortion occurrence.

We focused particularly on the first trimester of pregnancy and found a highly significant association between infection and abortion occurrence ($P < 0.001$). All pathogens were significantly associated with pregnancy loss occurrence. Moreover, *B. Streptococci* were significantly associated with abortion occurrence.

Other studies reported about other infectious species. *Brucella* spp. were originally identified as an infectious agent causing recurrent abortion in humans after being discovered in fetal or placental tissues, after similar results in animals.[21] Seoud et al.[22] found spontaneous abortion and intrauterine mortality rates of 40 and 46%, respectively, among women with acute brucellosis caused mostly by *Brucella melitensis*. Acute human brucellosis, on the contrary, seldom causes abortion, most likely owing to a lack of erythritol in the human placenta, which is a critical substrate for brucella attachment and subsequent transmission to the fetus.[23]

We can consider infection as a dependent factor associated with occurrence of spontaneous abortion during the first trimester. A total of 39 (25.2%) women in the prior conception only and birth groups had a history of spontaneous abortion, according to the study by Nasioudis et al.[24] One abortion was performed by 26 (16.8%) women, 11 (7.1%) women had two abortions, and two (1.3%) women had performed three abortions.

Despite the increased frequency of bacterial vaginosis in these patients compared with those in the prenatal and general gynecological population, Liversedge et al.[25] showed no significant influence of bacterial vaginosis on fertilization and implantation rates during in-vitro fertilization therapy. When it came to the risk of miscarriage during in-vitro fertilization therapy, women with bacterial vaginosis had the same risk as those without it, according to Ralph et al.,[26] but no difference in the rate of conception during the first trimester between the two groups (18.5%).

In concordance with our results, Donders et al.[27] discovered a clear association between the first prenatal visit's diagnosis of bacterial vaginosis and a future early pregnancy loss (relative risk: 5.4; 95% confidence interval: 2.5–11). (relative risk: 5.4; 95% confidence interval: 2.5–11). The 95% confidence interval for the relative risk is 2.5–11. However, multivariate analysis indicated that bacterial vaginosis, *M. hominis*, and *U. urealyticum* were still connected with a greater risk of miscarriage, but not other germs.

A recent Egyptian study by Mansour et al.[28] went against our results and reported that there is no between bacterial vaginosis and first trimester

miscarriage when comparing pregnant women with bacterial vaginosis with women who are negative for bacterial vaginosis.

4.1. Conclusion

To exclude out chronic infections, all patients with RSA should be evaluated according on their personal infection risk, which involves a thorough history as well as physical and laboratory examinations. Despite the fact that many patients with RSA are healthy, monogamous, and have a minimal risk of STDs, they should be checked. During the first trimester, vaginal infection may be a risk factor for spontaneous abortion.

Authors contribution

All authors have made a substantial contribution to the article.

Conflict of interest

There are no conflicts of interest.

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