Original Article

Pathogen profile and risk factors of aerobic vaginitis in pregnant women: a retrospective cohort study

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Background: Vaginitis is one of the most common gynecological diseases in women and may severely affect the quality of life in patients. However, very few studies have investigated aerobic vaginitis (AV) in pregnant women, and our study was designed to identify the pathogen profile, clinical importance, and risk factors of AV in pregnancy.

Methods: This was a retrospective cohort study enrolling 685 women who attended our hospital between July 2018 and June 2020. Based on the incidence of AV, enrolled women were divided into an AV group and healthy control group, and demographic and clinical characteristics were retrospectively collected by two independent investigators. Some pathogens of AV were tested using quantitative real-time polymerase chain reaction for higher accuracy. Pregnancy outcomes were also retrospectively collected. Univariable and multivariable logistic regression analysis was used to determine the risk factors of AV incidence and adverse pregnant outcomes.

Results: Enrolled women were divided into an AV group of 182 women and healthy control group of 503 women. The proportions of women with a history of cesarean delivery and history of vaginal infection differed between the groups (P=0.002 and <0.001, respectively). The mean gestational week at diagnosis of AV was 22.3±8.6 weeks, and the most common pathogen of AV was *Escherichia coli* (28.6%). After adjustment using multivariable logistic regression, a history of vaginal infection acted as an important risk factor of AV incidence, while a history of cesarean delivery, college education or above, and being employed could protect pregnant women from AV. In addition, the incidences of preterm birth, premature rupture of membranes, neonatal jaundice, and neonatal infection were much higher in the AV group than in the control group, showing significant difference (P<0.001, <0.001, =0.007, and =0.025). After adjustment using multivariable logistic regression, the incidence of AV and older age were important risk factors of premature rupture of membranes and neonatal infection.

Conclusions: Compared with healthy pregnant women, the presence of AV may increase the incidence of adverse outcomes. More attention should be paid to pregnant women with a history of vaginal infection.

Keywords: Pathogen profile; risk factors; aerobic vaginitis (AV); pregnant women; retrospective cohort study

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Introduction

Vaginitis is a common gynecological disease in women of all ages (1), the prevalance of which varies with living habits, living environment, religious beliefs, and economic status. Several pathogens may cause the disease, and may take the form of bacterial vaginitis, mixed vaginitis, Candida vaginitis, Mycoplasma vaginitis, and Trichomonas vaginitis (2), the latter having been the most common type in past decades (3). However, the incidence of Trichomonas vaginitis has been decreasing in recent years, while that of bacterial vaginitis has remained stable (4). Aerobic vaginitis (AV) is more common than anaerobic vaginitis among all bacterial vaginitis (5), and the pathogens of AV include aerobic microorganisms from the gastrointestinal tract such as *Escherichia coli*, *staphylococcus aureus*, coagulase-negative *staphylococci* and group B *streptococcus* (6,7). Patients with AV may suffer from abnormal vaginal discharge and vulvae itching and discomfort, which severely affect their quality of life.

During pregnancy, women will experience various hormonal and physiological changes, which also include changes in the vaginal environment. This may lead to an increased incidence rate of vaginitis and changes to pathogens (8). It has been reported that the pathogen profile of AV in late pregnancy differed from that in non-pregnant women in a Chinese population, with more group B *streptococcus* and less coagulase-negative *staphylococci* and *staphylococcus aureus* (9). The occurrence of AV may worsen the outcomes of pregnant women, resulting in more spontaneous preterm delivery and premature rupture of membranes (9-11). However, previous studies mainly focused on early or late stage pregnancy, and it is hard to understand the incidence of vaginitis across the whole of pregnancy. The study of risk factors of vaginitis in pregnant women also has important clinical significance. Many studies have explored the risk factors of vaginitis in non-pregnant women (12-14), which may differ significantly from those of non-pregnant women, due to hormonal and physiological changes. However, few studies have explored this issue to date, and the risk factors of AV in pregnant women remain unclear.

This study was designed to determine the prevalence and pathogen profile of AV in women at all stages of pregnancy and investigate the effects of AV on pregnancy outcomes. Most importantly, this study aimed to explore the risk factors of AV in pregnant women. The results may assist pregnant women reduce the incidence of AV and improve pregnancy outcomes. We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1710).

Methods

Participant enrollment

We retrospectively enrolled pregnant women who were admitted to the Wuxi Maternity and Child Health Care Hospital of Nanjing Medical University between July 2018 and June 2020, and divided them into a group with AV and a healthy control group. Women older than 18 years old and those who constantly received prenatal examination in our hospital were included, while those who were diagnosed with vaginitis other than AV or mixed vaginitis, did not attend for regular prenatal examinations and were lost to follow up, who received long term antibiotic treatment, who needed to terminate their pregnancy because of severe complications, were excluded. This study was approved by the Ethics Committee of the Affiliated Wuxi Maternity and Child Health Care Hospital of Nanjing Medical University (No. 20200037) and was conducted in compliance with the ethical principles of the Declaration of Helsinki (as revised in 2013). Written informed consent was not required due to the retrospective nature of the study.

Data collection

Following enrolment, the baseline characteristics of patients was collected including age, body mass index, multifetal pregnancy, parity, history of cesarean delivery, history of vaginal infection, history of hypertension and diabetes mellitus, level of education, history of smoking, and occupational status. The data were collected by two independent investigators to minimize errors.

All enrolled participants underwent a gynecological examination, and a sterile cotton swab was used to obtain samples of vaginal discharge. The diagnosis of AV was determined by *lactobacillary* grade, leukocyte number, proportion of toxic leukocytes, background flora, and proportion of parabasal epitheliocytes according to microscopic examination. Pathogens of AV were tested by conventional bacterial culture and biochemical analysis. Part pathogens were tested using quantitative real-time polymerase chain reaction for amplification of specific targets, followed by specific probe test for bacterial vaginosis markers, including Enterococcus group, bacterial vaginosis-associated bacterium 2, and Megasphaera 1. The

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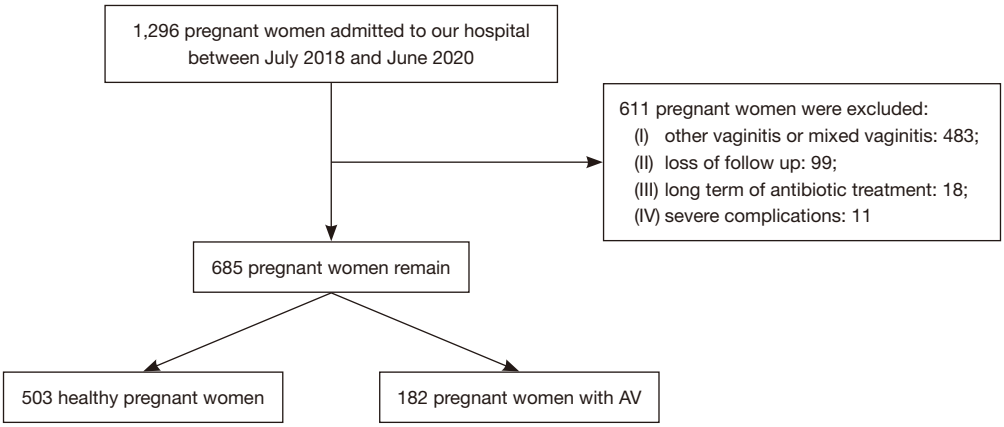

Figure 1 Flow chart of this study. AV, aerobic vaginitis.

gestational week of participants when diagnosed with AV was also recorded.

Pregnancy outcomes

All participants were followed up until 1 month after delivery. Some pregnant outcomes were recorded in this study for further analysis, including delivery mode, preterm birth, premature rupture of membranes, birth weight, Apgar score, neonatal jaundice, neonatal infection, and stillbirth.

Statistical analyses

Continuous variables were shown as mean with standard deviation and categorical variables were shown as number with percentage. Comparisons between continuous variables were analyzed using student *t*-test and those between categorical variables using Chi-square test. Univariable logistic regression analysis was performed to preliminarily determine the risk factors of adverse pregnant outcomes and AV. Multivariable logistic regression analysis was then used to verify the real risk factors after adjusting confounding variables according to univariable logistic regression analysis. Statistical analysis was performed using SPSS 20.0 (IBM Corporation, NY, USA) and P value less than 0.05 was considered statistically significant.

Results

We enrolled pregnant women who had attended our hospital over a 2-year period and the flow chart is shown in *Figure 1*. In total, 1,296 women were admitted and 685 were enrolled in the study after 611 women failed to meet the exclusion criteria. Those included in the study were then divided into an AV group of 182 women and a healthy control group of 503.

Demographic and clinical characteristics of both groups are shown in *Table 1*. In the control group, the mean age was 27.7±6.0 years and mean body mass index was 24.0±4.9. Four women had multifetal pregnancies, and more than half of the control group were primiparas. A history of cesarean delivery was seen in 101 women, 48 women had a history of vaginal infection, 40 had a history of smoking, 15 had hypertension, and eight women had diabetes. High school education or below was recorded in 322 women in the control group, and 419 were currently employed.

In the AV group, the mean age was 26.8±5.4 years and mean body mass index was 23.9±11.0. Three women had multifetal pregnancies and 117 women were primiparas. A history of cesarean delivery was seen in 18 women, 41 women had a history of vaginal infection, 11 had a history of smoking before pregnancy, four had hypertension, and two had diabetes mellitus. Around 75% of women in the AV group had received high school education or below, and 139 women were employed.

Comparison of the demographic and clinical characteristics in the AV group and control group showed significantly more women in the control group had a history of cesarean delivery (20.1% *vs.* 9.9%, P=0.002), while 22.5% of the AV group had a history of vaginal infection, which was much more than the 9.5% in the control group (P<0.001). More women in the AV group received high school education or below compared to the control group (75.8% *vs.* 64.0%, P=0.004), and the proportion of

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Table 1 Demographic and clinical characteristics

Data	Control group (n=503)	AV group (n=182)	P value
Age	27.7±6.0	26.8±5.4	0.072
Body mass index	24.0±4.9	23.9±11.0	0.275
Multifetal pregnancy, n (%)	4 (0.8)	3 (1.6)	0.390
Parity, n (%)			0.283
0	291 (57.9)	117 (64.3)	
1	195 (38.8)	61 (33.5)	
2	17 (3.4)	4 (2.2)	
History of cesarean delivery, n (%)	101 (20.1)	18 (9.9)	0.002
History of vaginal infection, n (%)	48 (9.5)	41 (22.5)	<0.001
History of hypertension, n (%)	15 (3.0)	4 (2.2)	0.793
History of diabetes mellitus, n (%)	8 (1.6)	2 (1.1)	1.000
Level of education, n (%)			0.004
High or below	322 (64.0)	138 (75.8)	
College or above	181 (36.0)	44 (24.2)	
History of smoking, n (%)	40 (8.0)	11 (6.0)	0.401
Occupational status, n (%)			0.039
Unemployed	84 (16.7)	43 (24.7)	
Employed	419 (83.3)	139 (75.3)	

AV, aerobic vaginitis.

Table 2 Distribution of bacterial pathogens in pregnant women with AV

Data	Number (n=182)
Gestational week at diagnosis	22.3±8.6
Pathogens, n (%)	
Escherichia coli	52 (28.6)
Group B *streptococcus*	44 (24.2)
Enterococcus faecalis	32 (17.6)
Enterococcus faecium	15 (8.2)
Coagulase-negative *staphylococci*	13 (7.1)
Staphylococcus aureus	11 (6.0)
Lactobacillus	9 (4.9)
Others	6 (3.3)

AV, aerobic vaginitis.

unemployed women in the AV group was higher than in the control group (24.7% *vs.* 16.7%, P=0.039).

The distribution of bacterial pathogens in pregnant women with AV is summarized in *Table 2*. The mean gestational week at diagnosis of AV was 22.3±8.6 weeks. The most common pathogen was *Escherichia coli* (28.6%), followed by group B *streptococcus* (24.2%), *Enterococcus faecalis* (17.6%), *Enterococcus faecium* (8.2%), coagulase-negative *staphylococci* (7.1%), *staphylococcus aureus* (6.0%), *lactobacillus* (4.9%), and other pathogens (3.3%).

Risk factors of AV were analyzed using logistic regression as shown in *Table 3*. Older age, history of cesarean delivery, history of vaginal infection, college education or above, and employment showed significant effects on the incidence of AV according to univariable logistic regression. However, after adjustment using multivariable logistic regression,

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Table 3 Risk factors of AV in pregnant women

Data	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Older age	0.973 (0.944–1.003)	0.073	–	
History of cesarean delivery	0.437 (0.256–0.745)	0.002	0.429 (0.249–0.739)	0.002
History of vaginal infection	2.756 (1.744–4.356)	<0.001	2.615 (1.639–4.173)	<0.001
Education of college or above	0.567 (0.386–0.834)	0.004	0.577 (0.389–0.855)	0.006
Employment	0.648 (0.428–0.981)	0.040	0.637 (0.415–0.977)	0.039

AV, aerobic vaginitis.

Table 4 Pregnancy outcomes of women with AV

Data	Control group (n=503)	AV group (n=182)	P value
Delivery mode, n (%)			0.095
Vaginal delivery	299 (59.4)	121 (66.5)	
Cesarean section	204 (40.6)	61 (33.5)	
Preterm birth, n (%)	40 (8.0)	35 (19.2)	<0.001
Premature rupture of membranes, n (%)	47 (9.3)	48 (26.4)	<0.001
Birth weight, n (%)			0.572
<2,500	29 (5.8)	13 (7.1)	
2,500–4,000	451 (89.7)	158 (86.8)	
>4,000	23 (4.6)	11 (6.0)	
Apgar score, n (%)			0.613
<7	3 (0.6)	2 (1.1)	
≥7	500 (99.4)	180 (98.9)	
Neonatal jaundice, n (%)	40 (8.0)	27 (14.8)	0.007
Neonatal infection, n (%)	20 (4.0)	15 (8.2)	0.025
Stillbirth, n (%)	0 (0.0)	1 (0.5)	0.266

AV, aerobic vaginitis.

a history of vaginal infection acted as an important risk factor of AV incidence, and a history of cesarean delivery, college education or above, and employment could protect pregnant women from the incidence of AV.

Pregnancy outcomes of pregnant women with AV in both groups are also listed in *Table 4*. Vaginal delivery took place in 299 and 121 women in the control group and AV group, respectively, and preterm birth occurred in 40 women (8.0%) in the control group and 35 women (19.2%) in the AV group, showing significant difference (P<0.001). Similarly, premature rupture of membranes occurred in 47 women (9.3%) in the control group and 48 women (26.4%) in the AV group, showing significant difference (P<0.001). Neonatal jaundice was observed in 40 neonates (8.0%) of the control group and 27 neonates (14.8%) of the AV group, showing a significant difference (P=0.007), and neonatal infection was observed in 20 neonates (4.0%) of the control group and 15 (8.2%) of the AV group, also showing a significant difference (P=0.025). Only one stillbirth was observed in all enrolled women of both groups.

Finally, the risk factors of premature rupture of

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Table 5 Risk factors of premature rupture of membranes and neonatal infection in pregnant women

Data	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Premature rupture of membranes				
AV	3.475 (2.225–5.428)	<0.001	2.505 (1.537–4.082)	<0.001
Older age	1.131 (1.091–1.171)	<0.001	1.141 (1.099–1.184)	<0.001
Higher body mass index	1.047 (1.005–1.091)	0.028	1.054 (1.010–1.101)	0.016
Parity ≥1	0.607 (0.387–0.953)	0.030	0.652 (0.405–1.050)	0.079
Neonatal infection				
AV	2.169 (1.086–4.334)	0.028	2.384 (1.173–4.845)	0.016
Older age	1.114 (1.058–1.173)	<0.001	1.118 (1.061–1.178)	<0.001

AV, aerobic vaginitis.

membranes and neonatal infection were also analyzed and are shown in *Table 5*. After adjustment using multivariable logistic regression, the incidence of AV, older age, and higher body mass index were identified as important risk factors of premature rupture of membranes. Similarly, the incidence of AV and older age were also important risk factors of neonatal infection.

Discussion

This retrospective cohort study enrolled 685 pregnant women from a single center. We measured the pathogen profile of AV in these pregnancies as well as the gestational week at diagnosis of AV. The risk factors of AV were then identified using multivariable logistic regression, and included history of vaginal infection, history of cesarean delivery, college education or above, and being unemployed. The results of this study may assist in the treatment and prevention of AV in pregnant women.

In recent years, Trichomonas vaginitis has been decreasing while the incidence rate of AV has remained stable. A total of 665 pregnant women in this study suffered from vaginitis, of which 182 had AV, accounting for 27.3%. The proportion of AV was slightly higher than that in previous studies, which ranged from 4.2% to 23.7% (10,12,15,16). Krauss-Silva *et al.* reported a prevalence of 32.5% of bacterial vaginitis in black women and 28.1% in white women, indicating the living environment and race could significantly affect the incidence of bacterial vaginitis (16). Furthermore, some previous studies divided AV patients into a slight AV group and severe group, which may provide more detailed analysis for its risk factors. However, it was difficult to group participants according to the severity of AV in this study due to its retrospective nature. *Escherichia coli* was the most common pathogen of AV in our study, which is consistent with the results of previous studies (10,13,17). This also reveals that one of the main sources of vaginitis is the gastrointestinal tract. It has been reported that both early and late pregnancy had a higher incidence rate of AV (9,10,18,19). The mean gestational week at diagnosis of AV in our study was 22.3±8.6 weeks, which may show that there is no special gestational age with high risk for AV in pregnant women.

We then determined the risk factors of AV according to multivariable logistic regression and found the most important risk factor to be a history of vaginal infection, which increased the risk of AV by 2.6 times and P<0.001. This result aligns with that of Han *et al.*, who reported a history of vaginal infection within 1 year would increase the risk of AV by 3.2 times in pregnant women (10). Previous studies have shown intrauterine device use, external hemorrhoids, long-term antibiotic use, and frequent vaginal douching were independent risk factors for AV (10,13). We found higher educational level and being employed may also help reduce the incidence of AV in pregnant women, which is also similar to previous studies (20,21). Interestingly, we found that a history of cesarean delivery may play a protective role in pregnant women with AV. This may be because vaginal delivery can lead to changes in the vaginal flora and slight structural damage, resulting in the increased risk of AV in future pregnancies. We found that the presence of AV worsened pregnancy outcomes, by increasing the incidence of preterm birth, the premature

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rupture of membranes, neonatal jaundice, and neonatal infection. A Chinese population study also confirmed that AV would increase the incidence of neonatal jaundice and neonatal infection (9), and a systematic review of 12 related studies showed an association between AV and preterm birth and premature rupture of membranes (8). However, it also found that AV would increase the proportion of neonates with low birth weight. Only 42 neonates with low birth weight were delivered in our study and there was no significant difference between the two groups. After adjustment using multivariable logistic regression, older age, especially older than 35 years, was also seen as an important risk factor of adverse pregnant outcomes, which is similar to the results of a previous study (22).

There are some limitations in our study. Firstly, as a retrospective study, the types of data that can be collected are relatively limited. Some other data such as the results of serological and immunological examinations could not be obtained, which may affect the final result. Secondly, follow-up and data collection were performed when women attended hospital for prenatal examination and delivery, and some risk factors of AV and adverse pregnancy outcomes that may have existed out of hospital and after delivery could also not be collected. Thirdly, different pathogens of AV were identified in our study, and it is still unclear what effect each of these pathogens has on pregnancy outcomes. Studies focusing on the effect of a single pathogen may improve the quality of future studies.

Our study enrolled 685 pregnant women including 503 healthy women and 182 with AV and found that the incidence of AV increased the incidence of adverse pregnancy outcomes. To reduce the incidence of AV in pregnancy, more attention should be paid to women with a history of vaginal infection. The results from our study provide some evidence for clinical care and treatment in pregnancy.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-1710

Data Sharing Statement: Available at https://dx.doi.org/10.21037/apm-21-1710

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/apm-21-1710). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was approved by the Ethics Committee of the Affiliated Wuxi Maternity and Child Health Care Hospital of Nanjing Medical University (No. 20200037) and was conducted in compliance with the ethical principles of the Declaration of Helsinki (as revised in 2013). Written informed consent was not required due to the retrospective nature of the study.

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