International Journal of Women's Health

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Changes of Vaginal Microecology of Women with Intrauterine Adhesions

Sidi Dun*, Chunying Liu*, Na Li

Department of Obstetrics and Gynecology, Daqing Oilfield General Hospital, Daqing, Heilongjiang, People's Republic of China

*These authors contributed equally to this work

Correspondence: Sidi Dun, Department of Obstetrics and Gynecology, Daqing Oilfield General Hospital, No. 9, Zhongkang Road, Saertu District, Daqing, Heilongjiang, 163000, People's Republic of China, Email dsd2018123456@163.com

Background: Reproductive tract infection is one of the important causes of intrauterine adhesions (IUA). The evaluation of vaginal microecology could provide significant guidance for the treatment of reproductive tract infection. This study aimed to investigate the correlation between IUA and vaginal microecology.

Methods: Patients who came to the gynecology department of our hospital from March 2020 to February 2022 and were diagnosed with IUA were selected as the research subjects (n=150). Patients with normal uterine cavity were selected as the control group (n=150). All research subjects underwent hysteroscopy and vaginal microecological examination. The vaginal pH, hydrogen peroxide (H_2O_2), leukocyte esterase (LE), sialidase (SNA), 3-glucuronidase (GUS), and acetylglucosidase (NAG) of the participants were recorded and analyzed, respectively. Vulvovaginal candidiasis (VVC), trichomonas vaginitis (TV), and bacterial vaginosis (BV) were evaluated and diagnosed separately.

Results: The incidence of abnormal vaginal microecological morphological and functional indicators in the IUA group was remarkably higher than that in the control group, mainly manifested as relatively high pH value, reduction of Lactobacillus, increased ratio of flora density I, IV and flora diversity I, IV, higher detection rate of TV and BV. In addition, the increase in the positive rate of H_2O_2, LE, SNA, and NAG were observed in IUA patients.

Conclusion: Vaginal microecological imbalance is closely related to the occurrence of IUA, which should cause clinical concern.

Keywords: intrauterine adhesions, vaginal microecology, lactobacilli, reproductive tract infection

Introduction

Intrauterine adhesion (IUA) refers to endometrial basal layer damage caused by various reasons such as miscarriage, postpartum curettage, uterine artery embolism, postpartum uterine hemorrhage, manual placenta retrieval, and infection.[1] During the repair process, the endometrium is prone to form fibrous scar tissue, causing adhesion and occlusion in the uterine cavity and (or) the cervix.[2] As an endometrial injury disease, IUA could cause symptoms such as decreased menstrual flow, amenorrhea, infertility, and repeated miscarriages, which seriously affects women's health.[3] With the change of sexual concept, the increase of uterine cavity operation and the improvement of diagnostic technology, the incidence of IUA in China has been increasing.[4] Mechanical or infectious endometrial injury caused by intrauterine operation is the main cause of IUA, but a small number of women without a history of intrauterine operation may also develop IUA, suggesting that there may be a synergistic effect of other factors in the occurrence of IUA.[5]

The vaginal microbiome of women is an ecosystem composed of vaginal microflora, endocrine regulation system, vaginal anatomy and local mucosal immunity.[6] The balance of vaginal microflora plays an important role in maintaining the stability of vaginal microecology.[7] The vaginal microflora is diverse, with Lactobacillus as the dominant bacteria, and the cytotoxins produced by it can inhibit cervical cancer cells by promoting apoptosis.[8] The reduction of vaginal lactobacilli, the imbalance of flora and the increase of pH value favor the growth of other pathogens and increase the risk of cervical HPV infection.[9]

Received: 2 February 2023
Accepted: 27 April 2023
Published: 31 May 2023

The role of endometritis in the development of IUA is gradually being paid attention to.[10] When the balance of vaginal microbiota is disrupted, conditional pathogens in turn inhibit the growth of lactobacilli, leading to a decrease in vaginal defense ability. In addition, some pathogenic bacteria can also ascend to infect the uterine cavity, causing endometritis.[11] A study has found that there is a certain similarity between the microbiota in the official cavity and the microbiota parasitized in the lower reproductive tract, which further confirms that the bacterial colonies in the official cavity may originate from the lower reproductive tract.[12] Previous studies have found that the incidence of vaginal microbiota imbalance in patients with IUA is significantly higher than that of healthy women, with an increase in the diversity and density of vaginal microbiota.[10] In this study, we speculate that the imbalance of vaginal microecology will lead to the decline of vaginal immunity, which may cause pathogenic bacteria to ascend along the reproductive tract or with the operation of the uterine cavity, resulting in endometrial infection and IUA. Therefore, this work aims to study the changes of vaginal microecology in IUA patients compared with healthy controls.

Methods

Study Subjects

Patients with clinical symptoms such as decreased menstrual flow, amenorrhea or infertility and were diagnosed with IUA by hysteroscopy were selected as the research subjects (n=150). Patients with normal uterine cavity who were admitted to hospital for diagnosis and treatment with clinical symptoms such as decreased menstrual flow, amenorrhea or infertility as the main complaints and excluded intrauterine adhesions by hysteroscopy were selected as the control group (n=150). The research method was reviewed by the ethics committee of Daqing Oilfield General Hospital, and all subjects signed the informed consent. This study was performed in strict accordance with the Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects.

Both menstrual regular and irregular menstruation were performed hysteroscopy (Nissan Olympus) 3–7 days after menstruation was clean. The uterine cavity is expanded with a dilatation medium, and a cold light source is introduced into the uterine cavity through a fiber guide beam, a lens, and a hysteroscope. Under the direct vision of hysteroscopy, the cervical canal, internal cervical orifice, endometrium, fallopian tube opening, etc. are examined, and the lesion tissue is sampled and sent for pathological examination. Mild adhesion refers to the presence of slender or thin adhesions in less than 1/4 of the uterine cavity, the upper end of the uterine cavity and the orifice of the fallopian tubes are normal, and the shape of the uterine cavity is normal. Moderate adhesions refer to the presence of adhesions in 1/4–3/4 of the uterine cavity but not progressing to the uterine wall, with atresia at the upper end of the uterine cavity and the orifice of the fallopian tubes, and abnormal shape of the uterine cavity. Severe adhesion refers to the adhesion of more than 3/4 of the uterine cavity, which is relatively hypertrophic and serious, and has progressed to the uterine wall, the upper end of the uterine cavity and the orifice of the fallopian tubes are completely closed, and the shape of the uterine cavity is deformed.

Exclusion criteria include having received vaginal local medication within 1 month, using estrogen and progesterone drugs, suffering from immune diseases or malignant tumors, and suffering from reproductive system diseases such as endometrial polyps, uterine fibroids, and adenomyosis, genital tract malformations, perimenopausal women, previously diagnosed or treated IUA by hysteroscopy.

All research subjects (150 cases in the control group and IUA group) underwent vaginal microecological examination. Routine vaginal secretion smears are dried and fixed for Gram staining, and the vaginal microecology is examined under a microscope. The inspection indicators include the bacterial flora density, bacterial flora diversity, dominant bacterial species, fungi, and trichomonas in the vagina. The detection kits for vaginal pH, hydrogen peroxide (H_2O_2), leukocyte esterase (LE), sialidase (SNA), 3-glucuronidase (GUS) and acetylglucosaminidase (NAG) were purchased from Jiangsu Bioperfectus Technologies Co., Ltd.

Detection of Vaginal Flora Density, Diversity and Dominant Bacteria

The vaginal secretions were made into saline glass slides, and fungal hyphae, trichomonas, etc. were observed under a microscope; after Gram staining, the vaginal flora density, diversity, and dominant bacteria were observed and analyzed under an oil microscope.

Bacterial density index: on average, 1–9 bacteria can be seen in each field of view under the oil microscope, which is "level I"; 10–99 bacteria, which is "level II"; 100–999 bacteria, which is "level III"; ≥ 1000 bacteria, which is "level IV".

Bacterial diversity index: 1 to 3 bacteria can be identified in each field of view under the oil microscope, which is "level I"; 4 to 6 bacteria, which is "level II"; 7 to 9 bacteria, which is "level III"; ≥10 species of bacteria, which is "level IV".

Dominant bacteria: the most common microorganisms seen under the oil microscope.

Detection of Pathogenic Microorganisms

Vulvovaginal candidiasis (VVC) detection: vaginal secretions were collected using the hanging drop method, and spores and hyphae were observed under a microscope.

Trichomonas vaginitis (TV) detection: leukocytosis and trichomonas with wave-like movement can be seen under the microscope. Bacterial vaginosis (BV) test: the dominant bacteria are *Vibrio* or *Gram-negative bacilli*, and the sialidase is positive. A Nugent score ≥ 7 is diagnosed as BV.

Microecological Evaluation

"Normal microecology" means that the density and diversity of vaginal flora are both II to III, the dominant bacteria are Lactobacillus, white blood cells or pus cells can be seen under a 0–5 magnification microscope, and the pH value is less than or equal to 4.5 and the H_2O_2 level is greater than 2 μmol/L. "Microecological imbalance" refers to any abnormality in vaginal flora density, diversity, dominant bacteria, H_2O_2 level and pH value.

Statistical methods

SPSS 23.0 statistical software was used. The data presented are mean ± SD or n (percentage). The comparisons of data between the two group were done by Mann–Whitney test, Chi-square test or Fisher's exact test. Binary logistic regression analysis was applied for multivariable logistic analysis. $P<0.05$ was considered statistically significant.

Results

Clinical Characteristics of Patients with IUA

A total of 150 patients with decreased menstrual flow, amenorrhea, or infertility who were diagnosed with IUA after hysteroscopy were included in the study. The clinical characteristics of 150 participants and 150 healthy control volunteers are shown in Table 1. There were no significant differences in BMI and age between IUA patients and healthy controls. The number of pregnancies and abortions and the number of uterine evacuations in IUA patients were

Table 1 Clinical Characteristics of Women with Intrauterine Adhesions (IUA) and Control

Characteristics	Control (n=150)	IUA (n=150)	p value
Age (years)	34.5 ± 4.9	35.2 ± 5.6	0.481
BMI (kg/m^2)	22.6 ± 4.8	23.1 ± 4.4	0.296
Gravidity, %			
0	48 (32%)	15 (10%)	< 0.001
1	69 (46%)	58 (38.7%)	
2	24 (16%)	56 (37.3%)	
> 2	9 (6%)	21 (14%)	

(*Continued*)

Table 1 (Continued).

Characteristics	Control (n=150)	IUA (n=150)	p value
Abortion, %			
0	97 (64.7%)	32 (21.3%)	< 0.001
1	38 (25.3%)	68 (45.3%)	
2	11 (7.3%)	37 (24.7%)	
> 2	4 (2.7%)	13 (8.7%)	
Uterine curettage, %			
0	111 (74%)	48 (32%)	< 0.001
1	29 (19.3%)	56 (37.3%)	
2	7 (4.7%)	34 (22.7%)	
> 2	3 (2%)	12 (8%)	
Severity, %			
Mild	–	64 (42.7%)	–
Moderate		47 (31.3%)	
Severe		39 (26%)	

Notes: The data presented are mean ± SD or n (percentage). The comparisons of data between the two group were done by Mann–Whitney test or Chi-square test.
Abbreviation: BMI, body mass index.

all significantly higher than those in the control group. IUA patients were divided into mild (64, 42.7%), moderate (47, 31.3%) and severe (39, 26%) according to the severity of the disease.

Comparisons of Vaginal Microecology Between the Women with IUA and Controls

To assess the vaginal microenvironment of IUA patients, we took intravaginal samples from IUA patients and healthy controls and analyzed vaginal pH and multiple microbes in Table 2. The number of IUA patients with vaginal pH value less than 4.5 (89, 59.3%) was significantly lower than that of the control group (123, 82%), suggesting that the vaginal pH value of IUA patients was increased. Lactobacillus is a common vaginal dominant bacterium in ordinary people.

Table 2 Comparisons of Vaginal pH Value and Vaginal Microecology Between the Women with Intrauterine Adhesions (IUA) and Control

Variables	Control (n=150)	IUA (n=150)	p value
Vaginal PH values			
≤ 4.5	123 (82%)	89 (59.3%)	< 0.001
> 4.5	27 (18%)	61 (40.7%)	
Dominant bacteria			
Lactobacillus	119 (79.3%)	96 (64%)	0.005
Not lactobacillus	31 (20.7%)	54 (36%)	

(*Continued*)

Table 2 (Continued).

Variables	Control (n=150)	IUA (n=150)	p value
Vaginal flora density			
II, III	127 (84.7%)	102 (68%)	0.001
I, IV	23 (15.3%)	48 (32%)	
Vaginal flora diversity			
II, III	126 (84%)	94 (62.7%)	< 0.001
I, IV	24 (16%)	56 (37.3%)	
Vulvovaginal candidiasis (VVC)			
Yes	4 (2.7%)	12 (8%)	0.069
No	146 (97.3%)	138 (92%)	
Trichomonas vaginitis (TV)			
Yes	6 (4%)	18 (12%)	0.018
No	144 (96%)	132 (88%)	
Bacterial vaginosis (BV)			
Yes	8 (5.3%)	23 (15.3%)	0.007
No	142 (94.7%)	127 (84.7%)	
Vaginal microecology assessment			
Normal	112 (74.7%)	77 (51.3%)	< 0.001
Imbalance	38 (25.3%)	73 (48.7%)	

Notes: The data are presented as n (percentage, %). The comparison of data between the two groups was done by Fisher's exact test.

Among 150 healthy volunteers, the predominant vaginal species in 119 patients was Lactobacillus. However, only 96 people had Lactobacillus as the predominant vaginal species, which was significantly lower than the control group. In addition, the bacterial species diversity and distribution density in the vagina of IUA patients were significantly lower than those of healthy individuals. The incidence of TV and BV were significantly higher in IUA patients than in controls. Overall, the vaginal microecology assessment indicated that the vaginal microecological imbalance accounted for 25.3% in the control group and 48.7% in the IUA group, with a statistically significant difference.

Comparisons of Vaginal Functions Between the Women with IUA and Controls

To further analyze the vaginal microenvironment of IUA patients, we compared the vaginal function of IUA patients with healthy controls and presented the results in Table 3. Test contents included H_2O_2, LE, SNA, GUS and NAG. The number of patients with intravaginal hydrogen peroxide levels greater than 2 was significantly lower in the IUA group relative to the healthy controls. However, both intravaginal IE and SNA levels were significantly higher in IUA patients than in healthy controls. In addition, the number of positive vaginal NAG in IUA patients was also significantly higher than that in healthy controls.

Multivariable Logistic Analysis of IUA

To analyze the risk factors of IUA, we performed multivariable logistic regression analysis on IUA patients. We took the occurrence of IUA (0=no, 1=yes) as the dependent variable, and selected patient age, BMI, Gravidity ≥ 2, Abortion ≥ 2,

Table 3 Comparisons of Vaginal Functions Between the Women with Intrauterine Adhesions (IUA) and Control

Variables	Control (n=150)	IUA (n=150)	p value
H_2O_2 (μmol/L)			
≤ 2	29 (19.3%)	61 (40.7%)	< 0.001
> 2	121 (80.7%)	89 (59.3%)	
LE (U/L)			
≥ 9	24 (16%)	43 (28.7%)	0.012
< 9	126 (84%)	107 (71.3%)	
SNA (U/L)			
≥ 7	30 (20%)	53 (35.3%)	0.004
< 7	120 (80%)	97 (64.7%)	
GUS (g/L)			
≥ 0.5	17 (11.3%)	28 (18.7%)	0.105
< 0.5	133 (88.7%)	122 (81.3%)	
NAG (U/mL)			
≥ 0.1	37 (24.7%)	65 (43.3%)	0.001
< 0.1	113 (75.3%)	85 (56.7%)	

Notes: The data are presented as n (percentage, %). The comparison of data between the two groups was done by Fisher's exact test.

Uterine curettage ≥ 2, PH value> 4.5, non-Lactobacillus dominant bacteria, vaginal flora diversity (grade I, IV), density (grade I, IV), VVC positive, TV positive, BV positive, H_2O_2 positive (< 2 μmol/L), LE ≥ 9 U/L, SNA ≥ 7 U/L, GUS≥ 0.5 g/L, and NAG ≥ 0.1 U/mL as independent variables. We used a stepwise method to exclude irrelevant items. Finally, statistically significant IUA related factors were presented in Table 4. Related factors for IUA include gravidity ≥ 2,

Table 4 Multivariable Logistic Analysis of Intrauterine Adhesions (IUA)

	OR	95% CI
Gravidity ≥ 2	3.85	3.42 to 4.29
Abortion ≥ 2	3.47	2.86 to 3.95
Uterine curettage ≥ 2	4.28	3.92 to 4.51
Vaginal PH values > 4.5	1.12	0.90 to 1.53
Dominant bacteria are not lactobacillus	1.21	0.99 to 1.81
Vaginal flora density I, IV	1.44	1.03 to 1.92
Vaginal flora diversity I, IV	1.78	1.29 to 2.46
Vulvovaginal candidiasis positive	1.07	0.86 to 1.13
Trichomonas vaginitis positive	1.09	0.84 to 1.17
Bacterial vaginosis	2.16	1.34 to 3.62

(*Continued*)

Table 4 (Continued).

	OR	95% CI
H_2O_2 ≤ 2 μmol/L	1.79	1.26 to 2.49
LE ≥ 9 U/L	1.11	0.82 to 1.24
SNA ≥ 7 U/L	1.03	0.92 to 1.09
GUS ≥ 0.5 g/L	1.05	0.89 to 1.18
NAG ≥ 0.1 U/mL	2.23	1.37 to 3.19

Abbreviations: OR, Odds Ratio; CI, confidence interval.

abortion ≥ 2, uterine curettage ≥ 2, pH > 4.5, non-Lactobacillus dominant bacteria, vaginal flora diversity (grade I, IV), density (grade I, IV), BV positive, H_2O_2 positive and NAG positive.

Comparisons of Vaginal pH Value, Microecology and Functions Between the Women with Mild to Moderate IUA and Severe IUA

IUA patients were divided into mild (64, 42.7%), moderate (47, 31.3%) and severe (39, 26%) according to the severity of the disease. We further analyzed vaginal pH value, microecology and functions between the women with mild to moderate IUA and severe IUA in Table 5. The proportion of vaginal pH greater than 4.5 was significantly higher in patients with more severe IUA than in patients with mild to moderate IUA. Patients with more severe IUA had a higher proportion of vaginal primary flora that were not Lactobacilli compared with patients with mild to moderate IUA. The

Table 5 Comparisons of Vaginal pH Value, Microecology and Functions Between the Women with Mild to Moderate Intrauterine Adhesions (IUA) and Severe IUA

Variables	Mild to Moderate (n=111)	Severe (n=39)	p value
Vaginal PH values			
≤ 4.5	79 (71.2%)	10 (25.6%)	< 0.001
> 4.5	32 (28.8%)	29 (74.4%)	
Dominant bacteria			
Lactobacillus	80 (72.1%)	16 (41%)	< 0.001
Not lactobacillus	31 (27.9%)	23 (59%)	
Vaginal flora density			
II, III	84 (75.7%)	18 (46.2%)	0.001
I, IV	27 (24.3%)	21 (53.8%)	
Vaginal flora diversity			
II, III	76 (68.5%)	18 (46.2%)	0.020
I, IV	35 (31.5%)	21 (53.8%)	
Vulvovaginal candidiasis (VVC)			
Yes	6 (5.4%)	6 (15.4%)	0.079
No	105 (94.6%)	33 (84.6%)	

(*Continued*)

Table 5 (Continued).

Variables	Mild to Moderate (n=111)	Severe (n=39)	p value
Trichomonas vaginitis (TV)			
Yes	8 (7.2%)	10 (25.6%)	0.007
No	103 (92.8%)	29 (74.4%)	
Bacterial vaginosis (BV)			
Yes	12 (10.8%)	11 (28.2%)	0.018
No	99 (89.2%)	28 (71.8%)	
Vaginal microecology assessment			
Normal	72 (64.9%)	5 (12.8%)	< 0.001
Imbalance	39 (35.1%)	34 (87.2%)	
H_2O_2 (μmol/L)			
≤ 2	33 (29.7%)	28 (71.8%)	< 0.001
> 2	78 (70.3%)	11 (28.2%)	
LE (U/L)			
≥ 9	24 (21.6%)	19 (48.7%)	0.002
< 9	87 (78.4%)	20 (51.3%)	
SNA (U/L)			
≥ 7	35 (31.5%)	18 (46.2%)	0.120
< 7	76 (68.5%)	21 (53.8%)	
GUS (g/L)			
≥ 0.5	18 (16.2%)	10 (25.6%)	0.233
< 0.5	93 (83.8%)	29 (74.4%)	
NAG (U/mL)			
≥ 0.1	41 (36.9%)	24 (61.5%)	0.009
< 0.1	70 (63.1%)	15 (38.5%)	

Note: The data are presented as n (percentage, %). The comparison of data between the two groups was done by Fisher's exact test.

diversity and density of vaginal flora in patients with more severe IUA were significantly different from those with mild to moderate IUA. In addition, the severe IUA patient group had more TV and BV positive patients. However, the proportion of SNA and GUS positivity in the severe IUA group was not significantly different from that in the mild to moderate IUA group.

Discussion

At present, it is believed that the occurrence of IUA is mainly related to the uterine cavity injury after intrauterine operation, but there are still many other factors that play an important role in the occurrence and development of IUA, such as infection, congenital developmental abnormalities, and genetic factors.[13] Long-standing chronic endometritis is a high-risk factor for the formation of intrauterine adhesions.[14] Some studies have reported that women of childbearing age who suffer from chronic genital tract inflammation before abortion have a relatively high probability of intrauterine

adhesions, which may be related to the fact that bacteria and various other pathogens are easily brought into the uterine cavity during uterine cavity operations and lead to infection.[15] Inflammation can inhibit endometrial hyperplasia, induce fibrosis between the basal layers of the endometrium, and lead to the occurrence of IUA.[16]

The vagina of women is a micro-ecosystem of the human body.[17] There are a variety of microbial flora in the vagina, and the flora is coordinated with each other to maintain the balance of the vaginal flora.[18] Due to the interaction of vaginal anatomical structure, vaginal microflora, local immunity of vaginal mucosa, and the endocrine state of the human body, the vaginal microecological system is maintained in a dynamic and stable state.[19] Vaginal microecological system is closely related to reproductive tract infection and other diseases, which is a research hotspot in recent years.[20] Vaginal microecological disorders will cause changes in the cleanliness and pH of the vagina, which will easily induce vaginitis, and also create favorable conditions for the ascending infection of endogenous and exogenous pathogens, leading to the occurrence of pelvic inflammatory disease and further leading to IUA.[21] Some studies have found that[15] the microbes in the uterine cavity are similar to the flora parasitic in the lower genital tract, which further confirms that the colonies of the uterine cavity may originate from the lower genital tract.[22] In order to explore the changes of vaginal microecology in IUA patients and improve the accuracy of the research conclusions, the subjects of this study were all women with IUA or normal uterine cavity confirmed by endoscopy. In this study, we found that the proportion of vaginal microecological imbalance in the control group was 25.3%, and the proportion of vaginal microecological imbalance in the IUA group was 48.7%, with a statistical difference. The incidence of abnormal vaginal microecological morphological and functional indicators in the IUA group was remarkably higher than that in the control group, mainly manifested as relatively high pH value, reduction of Lactobacillus, increased ratio of flora density I, IV and flora diversity I, IV, and higher detection rate of TV and BV.

Lactobacilli are the most important flora for maintaining the balance of the vaginal microbiome, producing lactic acid and bacteriocins that help prevent bacterial growth.[23] Lactobacilli adhere to the surface of vaginal or cervical epithelial cells and can prevent bacterial adhesion to infected epithelial cells or facilitate the clearance of cells infected by microorganisms such as bacteria and viruses.[24] The reduction or disappearance of the number of lactobacilli can lead to a series of microbial imbalances such as the alkaline pH of the vagina, the growth of miscellaneous bacteria, the increase of white blood cell count, and the increase of cleanliness level.[25] The anatomical position of the vagina and cervix is adjacent to the vagina, and the external orifice of the cervix also has normal vaginal flora growth.[26] Therefore, the state of the cervix has a certain correlation with the microecology in the vagina. In the present study, we found that Lactobacilli were significantly reduced in IUA patients. In addition, the increase in the positive rate of H_2O_2 further demonstrated the reduction of vaginal lactobacilli, and the increase in the positive rate of NAG and SNA revealed that the enhanced probability of anaerobic infection. Further analysis found that gravidity ≥ 2, abortion ≥ 2, uterine curettage ≥ 2, pH > 4.5, non-Lactobacillus dominant bacteria, vaginal flora diversity (grade I, IV), density (grade I, IV), BV positive, H_2O_2 positive and NAG positive were risk factors for IUA. In addition, this paper found that there were also differences in vaginal microecological flora among patients with different adhesions. Patients with severe adhesions had the most abnormal degree of vaginal microecological flora, and the dysbacteriosis was more obvious. Lactobacillus was the predominant bacterium in 72.1% of mild to moderate IUA patients, but only 41% in severe IUA patients, suggesting that Lactobacillus is crucial to the occurrence of IUA. In addition, recurrence after IUA treatment is also a difficult clinical problem. Therefore, we plan to elucidate in future studies whether IUA recurrence is related to the vaginal microbiota status before and after treatment.

Conclusion

In this study, we reported that vaginal microecological imbalance is a risk factor for synergistic formation of IUA. Gravidity ≥ 2, abortion ≥ 2, uterine curettage ≥ 2, pH value>4.5, dominant bacteria not Lactobacillus, diversity of vaginal microbiota (grade I, IV), density (grade I, IV), BV positive H2O2<2 μ mol/L and NAG ≥ 0.1 U/mL are risk factors for IUA.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the corresponding author (Sidi Dun), without undue reservation.

Funding

There is no funding to report.

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Healy MW, Schexnayder B, Connell MT, et al. Intrauterine adhesion prevention after hysteroscopy: a systematic review and meta-analysis. *Am J Obstet Gynecol*. 2016;215:267–275 e267. doi:10.1016/j.ajog.2016.05.001
2. Leung RK, Lin Y, Liu Y. Recent advances in understandings towards pathogenesis and treatment for intrauterine adhesion and disruptive insights from single-cell analysis. *Reprod Sci*. 2021;28:1812–1826. doi:10.1007/s43032-020-00343-y
3. Kou L, Jiang X, Xiao S, Zhao YZ, Yao Q, Chen R. Therapeutic options and drug delivery strategies for the prevention of intrauterine adhesions. *J Control Release*. 2020;318:25–37. doi:10.1016/j.jconrel.2019.12.007
4. Zhang LP, Wang M, Shang X, et al. The incidence of placenta related disease after the hysteroscopic adhesiolysis in patients with intrauterine adhesions. *Taiwan J Obstet Gynecol*. 2020;59:575–579. doi:10.1016/j.tjog.2020.05.018
5. Liu Z, Kong Y, Gao Y, et al. Revealing the interaction between intrauterine adhesion and vaginal microbiota using highthroughput sequencing. *Mol Med Rep*. 2019;19:4167–4174. doi:10.3892/mmr.2019.10092
6. Buchta V. Vaginal microbiome. *Ceska Gynekologie*. 2018;83:371–379.
7. Buggio L, Somigliana E, Borghi A, Vercellini P. Probiotics and vaginal microecology: fact or fancy? *BMC Womens Health*. 2019;19:25. doi:10.1186/s12905-019-0723-4
8. Nami Y, Abdullah N, Haghshenas B, Radiah D, Rosli R, Khosroushahi AY. Assessment of probiotic potential and anticancer activity of newly isolated vaginal bacterium Lactobacillus plantarum 5BL. *Microbiol Immunol*. 2014;58:492–502. doi:10.1111/1348-0421.12175
9. Wu X, Wang L, Xing Z. Impact of HPV infection on vaginal microecology and maternal and neonatal outcomes. *Zhong Nan Da Xue Xue Bao Yi Xue Ban*. 2021;46:497–502. doi:10.11817/j.issn.1672-7347.2021.200066
10. Kuroda K, Yamanaka A, Takamizawa S, et al. Prevalence of and risk factors for chronic endometritis in patients with intrauterine disorders after hysteroscopic surgery. *Fertil Steril*. 2022;118:568–575. doi:10.1016/j.fertnstert.2022.05.029
11. Chen Y, Liu L, Luo Y, Chen M, Huan Y, Fang R. Prevalence and impact of chronic endometritis in patients with intrauterine adhesions: a prospective cohort study. *J Minim Invasive Gynecol*. 2017;24:74–79. doi:10.1016/j.jmig.2016.09.022
12. Wen Y, Wu Q, Zhang L, et al. Association of intrauterine microbes with endometrial factors in intrauterine adhesion formation and after medicine treatment. *Pathogens*. 2022;11:784. doi:10.3390/pathogens11070784
13. Evans-Hoeker EA, Young SL. Endometrial receptivity and intrauterine adhesive disease. *Semin Reprod Med*. 2014;32:392–401. doi:10.1055/s-0034-1376358
14. Chen L, Xiao S, He S, Tian Q, Xue M. Factors that impact fertility after hysteroscopic adhesiolysis for intrauterine adhesions and amenorrhea: a retrospective cohort study. *J Minim Invasive Gynecol*. 2020;27:54–59. doi:10.1016/j.jmig.2018.12.023
15. Mo X, Qin G, Zhou Z, Jiang X. Assessment of risk factors of intrauterine adhesions in patients with induced abortion and the curative effect of hysteroscopic surgery. *J Investig Surg*. 2019;32:85–89. doi:10.1080/08941939.2017.1376130
16. Di Spiezio Sardo A, Calagna G, Scognamiglio M, O'Donovan P, Campo R, De Wilde RL. Prevention of intrauterine post-surgical adhesions in hysteroscopy. A systematic review. *Eur J Obstet Gynecol Reprod Biol*. 2016;203:182–192. doi:10.1016/j.ejogrb.2016.05.050
17. Sjoberg I. Vagina - en ekologisk enhet [Vagina–an ecological entity]. *Lakartidningen*. 1996;93:3796–3798. Swedish.
18. Saraf VS, Sheikh SA, Ahmad A, Gillevet PM, Bokhari H, Javed S. Vaginal microbiome: normalcy vs dysbiosis. *Arch Microbiol*. 2021;203:3793–3802. doi:10.1007/s00203-021-02414-3
19. Larsen B. Vaginal flora in health and disease. *Clin Obstet Gynecol*. 1993;36:107–121. doi:10.1097/00003081-199303000-00016
20. Xiao BB, Liu ZH, Liao QP. 妇科门诊不同阴道症状就诊者阴道微生态状况调查 [Microecological investigation of vaginal microflora in women with varying degree gynecologic symptoms in clinics]. *Zhonghua Fu Chan Ke Za Zhi*. 2009;44:6–8. Chinese.
21. Paavonen J, Brunham RC. Bacterial vaginosis and desquamative inflammatory vaginitis. *N Engl J Med*. 2018;379:2246–2254. doi:10.1056/NEJMra1808418
22. Zheng JJ, Song JH, Yu CX, Wang F, Wang PC, Meng JW. Difference in vaginal microecology, local immunity and HPV infection among childbearing-age women with different degrees of cervical lesions in Inner Mongolia. *BMC Womens Health*. 2019;19:109. doi:10.1186/s12905-019-0806-2
23. Borges S, Silva J, Teixeira P. The role of lactobacilli and probiotics in maintaining vaginal health. *Arch Gynecol Obstet*. 2014;289:479–489. doi:10.1007/s00404-013-3064-9
24. van de Wijgert J, Verwijs MC. Lactobacilli-containing vaginal probiotics to cure or prevent bacterial or fungal vaginal dysbiosis: a systematic review and recommendations for future trial designs. *BJOG*. 2020;127:287–299. doi:10.1111/1471-0528.15870
25. Chee WJY, Chew SY, Than LTL. Vaginal microbiota and the potential of lactobacillus derivatives in maintaining vaginal health. *Microb Cell Fact*. 2020;19:203. doi:10.1186/s12934-020-01464-4
26. Lacroix G, Gouyer V, Gottrand F, Desseyn JL. The cervicovaginal mucus barrier. *Int J Mol Sci*. 2020;21:8266. doi:10.3390/ijms21218266