ORIGINAL ARTICLE

Vaginal microbiota in pregnant women with inflammatory rheumatic and inflammatory bowel disease: A matched case-control study

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Abstract

**Background:** Rheumatic diseases and vaginal infections both increase the risk of preterm birth. It is unclear whether pregnant women with rheumatic disease are more likely to experience vaginal infections, which might potentially accumulate modifiable risk factors.

**Objective:** In this study, we sought to evaluate the vaginal microbiota of pregnant women with inflammatory rheumatic and inflammatory bowel disease.

**Methods:** A total of 539 asymptomatic women with singleton pregnancy were routinely screened for an abnormal vaginal microbiota between 10 + 0 and 16 + 0 gestational weeks. Vaginal smears were Gram-stained and microscopically analysed. Those with inflammatory diseases (with or without immunomodulatory therapy) were assigned to the case group and matched in a 1:3 ratio to healthy pregnant controls.

**Results:** Overall, an abnormal vaginal microbiota occurred more frequently among women of the case group, compared with those of the control group (33.8% vs 15.6%; 95% CI: 1.78–4.27, \( p < .001 \)). In particular, *Candida* colonisation (22.3% vs 9.2%; 95% CI: 1.69–4.75, \( p < .001 \)), but also bacterial vaginosis (14.9% vs 7.2%; 95% CI: 1.25–4.1, \( p = .006 \)), occurred more often in the case than in the control group. No significant difference was found with regard to the occurrence of an abnormal vaginal microbiota between subgroups with and without immunomodulatory therapy (37.0% vs 27.1%; 95% CI: 0.29–1.35, \( p = .232 \)).

**Conclusion:** Pregnant women with inflammatory rheumatic and inflammatory bowel disease are at risk for bacterial vaginosis and *Candida* colonisation, which might pose a risk for preterm birth. Prospective studies are needed to further evaluate the influence of autoimmune conditions and immunosuppressive therapy on the vaginal microbiota.

**Keywords**
*Candida albicans*, candidosis, immunomodulatory therapy, inflammatory bowel disease, inflammatory rheumatic disease, microbiota, preterm birth, vulvovaginal infection

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1 | INTRODUCTION

Pregnant women with systemic inflammatory autoimmune diseases are known to have an increased risk of adverse pregnancy outcomes, both of the mother and the offspring. In particular, those with high activity of the underlying inflammatory autoimmune disease have a higher risk for miscarriage, preterm birth (PTB), stillbirth, low birthweight, as well as caesarean section, preeclampsia and gestational diabetes.\(^1-3\) Pregnancy outcomes of women with stable disease are similar to those of the general obstetric population, but adequate treatment with immunomodulatory agents is often required to manage disease activity during pregnancy.\(^1,3,4\)

Apart from the risk for the pregnancy itself, inflammatory autoimmune disease poses a risk for various infectious conditions, such as pneumonia, influenza, fungal diseases, as well as infections with human papillomavirus (HPV) and herpes simplex.\(^5\) The fact that these women have an a priori increased risk to experience PTB when being compared to healthy women,\(^1-4\) is even aggravated by the altered hormonal and immune situation during pregnancy which might, at least in part, increase their likelihood for infections.\(^6\) According to our previous work, 28% of pregnant women showed asymptomatic vaginal infections at antenatal screening smear, whereof candidosis was found in 13.2%, bacterial vaginosis (BV) in 8.7% and trichomoniasis in 0.7% of the cases.\(^7\) This is of particular importance, considering the fact that vaginal infections are responsible for up to 40% of PTB, which is still the leading cause of neonatal mortality and morbidity.\(^8,9\)

Little is yet known about the vaginal microbiota of women with inflammatory autoimmune conditions. Only, a few studies have investigated their vaginal microbiota; some have reported a link between immunosuppression, autoimmune disease and vaginal infections,\(^10-13\) and others have demonstrated contradictory results.\(^14\) However, no data yet exist about the incidence of vaginal infections in rheumatic patients during pregnancy. In order to avoid infection-related complications and prevent an accumulation of risk factors for PTB, it is indeed important to further evaluate the comparative risk of an abnormal vaginal microbiota that could lead to vaginal infections in these women.

In the present study, we sought to evaluate the vaginal microbiota of pregnant women with inflammatory rheumatic and inflammatory bowel disease, comparing it to a group of matched healthy controls. Our aim was to assess whether pregnant women with inflammatory rheumatic or inflammatory bowel diseases are at risk for an abnormal vaginal microbiota, including both bacterial and fungal diseases. Since infections are a modifiable risk factor for PTB, their early detection through consequent screening and treatment might be recommended for these women.

2 | PATIENTS AND METHODS

2.1 | Patients and groups

This study was approved by the ethical review committee of the Medical University of Vienna (No: EK 1128/2018). We included retrospectively collected data from all women with inflammatory rheumatic diseases (ie systemic lupus erythematosus, rheumatoid arthritis, juvenile idiopathic arthritis, seronegative spondyloarthritis, mixed connective tissue disease, undifferentiated connective tissue disease, Sjögren’s syndrome, etc) and inflammatory bowel diseases (ie ulcerative colitis, Crohn’s disease), who routinely presented with singleton pregnancy at the Department of Obstetrics and Gynecology, Medical University of Vienna (Vienna, Austria), between January 2004 and November 2017. Data of these women were assigned to the case group and stratified between women who received immunomodulatory therapy during pregnancy (DWT) and those who did not receive any immunomodulatory therapy (DNT). The control group consisted of healthy women with singleton pregnancies without any chronic maternal conditions (eg diabetes mellitus, multiple sclerosis, neoplasms, etc). Inclusion criteria for cases and controls were as follows: registration for a planned delivery between 10 + 0 and 16 + 0 gestational weeks, maternal age ≥18 years, singleton pregnancy. The diagnosis of an autoimmune disease through a specialist (ie rheumatologist or gastroenterologist) was considered mandatory for all women who were assigned to the case group; those with missing or inconclusive data were excluded. Cases and controls were matched in a 1:3 ratio, according to maternal age at delivery and body mass index (BMI).

2.2 | Outcome measures

The vaginal microbiota at routine infection screening served as the primary outcome variable. The null hypothesis stated that there was no difference in the occurrence of an abnormal vaginal microbiota (AVM) between pregnant women with inflammatory rheumatic diseases and/or inflammatory bowel disease and healthy controls. AVM was defined as the occurrence of BV with a Nugent score of 7-10,\(^15\) and/or the occurrence of Candida species, and/or Trichomonas vaginalis on the vaginal screening smear. Women with a normal or intermediate microbiota (ie Nugent scores 0-3 or 4-6) with the absence of Candida spp. and Trichomonas vaginalis were considered as normal. Secondary outcome variables included gestational age at delivery, maternal BMI, neonatal birthweight, mode of delivery, Apgar score and umbilical cord arterial pH value. In addition, we assessed foetal and maternal outcomes, as well as pregnancy complications among different inflammatory disorders. Immunomodulatory therapy was defined as treatment with corticosteroids, biologic disease-modifying antirheumatic drugs (DMARDS) and/or non-biologic DMARDS, given for a minimum of four weeks throughout the pregnancy. PTB was defined as delivery prior to 36 + 6 weeks of gestation. Stillbirth was defined as the delivery of an infant with an Apgar score of 0/0/0 or an infant that had died in utero.

2.3 | Infection screening

Asymptomatic women who presented for a planned delivery at our centre were routinely screened at their first visit as part of our routine protocol. Vaginal smears were assessed with sterile swabs from the posterior vaginal fornix and lateral vaginal wall, then applied on
a microscope slide for direct visualisation, Gram-stained and analysed in our in-house laboratory by trained and experienced staff. The vaginal microbiota was graded using the Nugent scoring system, differentiating between (a) Gram-positive rods (*Lactobacillus* spp.), (b) small Gram-negative rods (*Bacteroides* spp.), small Gram-variable rods (*Gardnerella vaginalis*) and (c) curved rods (*Mobiluncus* spp.). The Nugent score was then calculated by the sum of a + b + c, whereas a score of 0–3 was considered as normal, 4–6 as intermediate and 7–10 as BV.15 For internal validation, the vaginal microbiota was also determined by the degrees of purity, as described and modified by Robert Schroeder in 1921.16 The presence or absence of *Candida* spp. (ie hyphes, blastospores or chlamydospores) and *Trichomonas vaginalis* was assessed independently from the Nugent scoring system. All women who were screened were asymptomatic without clinical signs and symptoms that are pathognomic for ongoing vaginal infections. Those with BV on Gram-stained smears received 2% clindamycin vaginal cream for 6 days, or oral clindamycin (0.3 g) twice daily for 7 days in case of a recurrent disease. Women with *Candida* colonisation received local clotrimazole (0.1 g) for 6 days, and those with trichomoniasis received local metronidazole (0.5 g) for 7 days. Antibiotic treatments were always followed by supplementation of vaginally applied lactobacilli for 6 days to rebuild the microbiota, as well as by consequent follow-up smears.

**2.4 | Data collection**

Eligible cases with inflammatory rheumatic or inflammatory bowel diseases were identified using the obstetric documentation software (ViewPoint® Fetal Database, version 5.6.9.17) using the following search terms in the diagnosis field for ambulatory visits: “rheu”*, “rheuma”, “rheumatoid arthritis”, “arthritis”, “SLE”, “lupus”, “Morbus Still”, “colitis ulcerosa” and “crohn”. In addition, we searched for specific medications, such as synthetic and biological disease-modifying antirheumatic drugs, glucocorticoids. The selection of cases, as described by the inclusion criteria, as well as the manual search for detailed demographic and clinical data, was performed by VM. Data search and quality were reviewed by KR. For data protection, patients were given consecutive study numbers and data were anonymised.

**2.5 | Statistical analysis**

Graphs, diagrams and univariate statistical analyses were performed using the SPSS statistical software package version 23.0 (IBM). For metric variables, we used mean ± standard deviation (M ± SD). Categorical variables are presented as numbers (absolute frequencies and percentages). Significance (*p* < .05) was tested using a two-sided chi-squared test. We accounted for multiplicity by applying the Bonferroni correction to the resulting *p*-values when appropriate. Multivariate logistic regression was tested to assess relative independent associations of AVM on the dependent outcome of preterm birth.

### RESULTS

#### 3.1 | Study population and demographic data

The data of 539 women were eligible for the analyses, whereof 148 were considered as cases with inflammatory rheumatic or inflammatory bowel diseases, being matched in a 1:3 ratio to 391 healthy controls. The 148 cases consisted of 100 cases (67.6%) with immunomodulatory therapy during pregnancy (DWT) and 48 cases (32.4%) without immunomodulatory therapy during pregnancy
**TABLE 2** Vaginal microbiota among 539 cases and controls

| Variable                                      | Case group | Control group | Total   | OR   | 95% CI  | p-value |
|-----------------------------------------------|------------|---------------|---------|------|---------|---------|
| Participants                                  | 148 (27.5) | 391 (72.5)    | 539 (100) |      |         |         |
| Normal/intermediate microbiota^a              | 98 (66.2)  | 330 (84.4)    | 428 (79.4) | 0.36 | 0.23–0.56 | <.001   |
| Normal microbiota^b                           | 89 (60.1)  | 303 (77.4)    | 394 (70.1) | 0.45 | 0.30–0.67 | <.001   |
| Intermediate microbiota^a                     | 9 (6.1)    | 27 (6.9)      | 34 (6.3) | 0.67 | 0.28–1.57 | .36     |
| Abnormal vaginal microbiota (any)^b           | 50 (33.8)  | 61 (15.6)     | 111 (20.6) | 2.76 | 1.78–4.27 | <.001   |
| Bacterial vaginosis (total)                   | 22 (14.9)  | 28 (7.2)      | 50 (9.3) | 2.26 | 1.25–4.1  | .06     |
| Bacterial vaginosis without Candida           | 15 (10.1)  | 25 (6.5)      | 40 (7.4) | 1.65 | 0.85–3.23 | .139    |
| Bacterial vaginosis with Candida              | 7 (4.7)    | 3 (0.8)       | 10 (1.9) | 6.4  | 1.64–24.17| .002    |
| Candida colonisation (total)                  | 33 (22.3)  | 36 (9.2)      | 69 (12.8) | 2.83 | 1.69–4.75 | <.001   |
| Normal/intermediate microbiota with Candida   | 26 (17.6)  | 33 (8.4)      | 59 (10.9) | 2.31 | 1.33–4.02 | .002    |
| Trichomoniasis ^c                             | 2 (1.4)    | 0 (0.0)       | 2 (0.4)  | -    | -       | .021    |

Abbreviations: OR, odds ratio; CI, confidence interval; N, number; N/A, not available.

^a Without Candida colonisation or Trichomonas vaginalis.

^b Including bacterial vaginosis, trichomoniasis and/or Candida colonization.

^c Trichomoniasis was not documented in the control group, which did not allow calculation of odds for this parameter.
(DNT). Disease distribution and immunomodulatory therapy are shown in Table S1. The most frequent disease diagnosis was systemic lupus erythematosus (SLE), followed by Crohn’s disease, ulcerative colitis, rheumatoid arthritis and Sjögren’s syndrome. Maternal characteristics of the cases and controls are shown in Table 1.

3.2 | Vaginal microbiota

Evaluation of the routine antenatal screening smears showed that 50/148 (33.8%) women in the case group, and 61/391 (15.6%) women in the control group had an AVM. Out of the case group, we found that 13/48 (27.1%) women in the DNT subgroup, and 37/100 (37.0%) women in the control group had an AVM. Out of the case group, we found 50/148 (33.8%) women in the case group, and 61/391 (15.6%) women in the control group. Rates of trichomoniasis were higher in the DNT subgroup compared with the DWT subgroup, although the numbers were small (1.0% vs 2.1%; p = .593), as shown in Table 3.

3.3 | Obstetrical outcomes

Obstetrical outcomes are reported in Table S2. We found that 530/534 (99.3%) women experienced live birth, whereas 4/534 (0.7%) experienced stillbirth, whereof 2/148 (1.4%) occurred in the case group (one case in the DWT and in the DNT subgroup, each) and 2/386 (0.5%) in the control group. Data were missing for five infants in the control group.

Overall, the mean gestational age at delivery was 38.6 ± 2.6 weeks, with a mean of 38.7 ± 2.5 weeks in the case group and 38.5 ± 2.5 weeks in the controls. Women of the DWT subgroup delivered at a mean of 38.9 ± 2.7 weeks, compared to 38.4 ± 3.6 in the DNT subgroup. We found no significant difference with regard to the gestational age between cases and controls (p = .416), as well as between cases of the DWT vs the DNT subgroup (p = .376).

Overall, PTB was reported in 94/532 (17.7%) women, whereof 26/141 (18.4%) were cases, and 68/391 (17.4%) were controls (no data available for 7 cases; p = .780). The difference between the 94/45 (20.0%) cases with PTB in the DNT subgroup, and 17/96 (17.7%) in the DWT subgroup was not statistically significant (p = .774). We found no correlation between an AVM and PTB in our cohort, as shown in Table S3. Overall, the mean neonatal birthweight was 3216 ± 669 g, with a mean of 2961 ± 744 g in the case and

| Variable                                      | DWT subgroup | DNT subgroup | Total (N) | OR    | 95% CI          | p-value |
|------------------------------------------------|--------------|--------------|-----------|-------|-----------------|---------|
| Participants                                   | 100 (67.6)   | 48 (32.4)    | 148 (100) | 0.63 | 0.29-1.35       | .232    |
| Normal/intermediate microbiota^a               | 63 (63.0)    | 35 (72.9)    | 98 (66.2) | 0.98 | 0.49-1.99       | .96     |
| Normal microbiota^b                            | 60 (60.0)    | 29 (60.4)    | 89 (60.1) | 0.61 | 0.25-1.53       | .292    |
| Intermediate microbiota^a                      | 3 (3.0)      | 6 (12.5)     | 9 (6.1)   | 0.21 | 0.05-0.91       | .036    |
| Abnormal vaginal microbiota (any)^b            | 37 (37.0)    | 13 (27.1)    | 50 (33.8) | 1.58 | 0.74-3.36       | .232    |
| Bacterial vaginosis (total)                    | 17 (17.0)    | 5 (10.4)     | 22 (14.9) | 1.76 | 0.61-5.09       | .292    |
| Bacterial vaginosis without Candida            | 12 (12.0)    | 3 (6.2)      | 15 (10.1) | 2.05 | 0.55-7.62       | .278    |
| Bacterial vaginosis with Candida               | 5 (5.0)      | 2 (4.2)      | 7 (4.7)   | 1.21 | 0.23-6.48       | .823    |
| Candidosis (total)                             | 24 (24.0)    | 9 (18.8)     | 33 (22.3) | 1.37 | 0.58-3.23       | .473    |
| Normal/intermediate with Candida               | 19 (19.0)    | 7 (14.6)     | 26 (17.6) | 1.37 | 0.53-3.53       | .509    |
| Trichomoniasis                                | 1 (1.0)      | 1 (2.1)      | 2 (1.4)   | 0.46 | 0.03-7.76       | .593    |

Abbreviations: OR, odds ratio; CI, confidence interval; DNT, disease without therapy; DWT, disease with therapy; N, number.
^aWithout Candida colonisation or Trichomonas vaginalis.
^bIncluding bacterial vaginosis, trichomoniasis and/or Candida colonisation.
^cTrichomoniasis was not documented in the control group, which did not allow calculation of odds for this parameter.
Autoimmune diseases and immunomodulatory therapies both alter the balance among the key players in our immune system, and therefore, potentially contribute to vaginal dysbiosis and infection. Pregnant women with inflammatory autoimmune diseases have an a priori increased risk for PTB, and it is, therefore, important to define, prevent and modify further risk factors for this multifactorial event. To the best of our knowledge, our study is the first evaluating the vaginal microbiota. The increased risk of women with autoimmune conditions for an AVM might theoretically be attributed to an inappropriate immune response on the basis of the pathogenic mechanism of autoimmunity itself. Although we observed a trend towards an increased risk of AVM in women who received immunosuppressive treatment, compared with those who did not, this finding was not statistically significant.

In our study, vaginal colonisation with *Candida* spp. was increased among pregnant women with inflammatory autoimmune disease. Previously published studies of healthy pregnant women reported *Candida* colonisation rates of 11%-14% at early gestation, which are comparable to our findings in the control group. With regard to the prevalence of *Candida* among healthy pregnant women, significantly higher rates have been reported in a study from Papua New Guinea, which might reflect the importance of genetic factors influencing susceptibility for infections. Indeed, it is well known that *Candida* occurs more frequently in patients under immunosuppression. In animal models, prednisolone and cyclophosphamide were the most potent factors for high fungal burden and long-lasting infections in association with immunosuppression. To the contrary, Aikawa et al found a very low prevalence of *Candida* in patients with rheumatic diseases who received anti-TNF-therapy. In their study, only one out of 194 patients (0.5%) had *Candida*, and none of them experienced systemic candidosis. Interestingly, the authors only evaluated cases with symptomatic infection among women with autoimmune disorders, while all women in our study were asymptomatic at the time of screening.

Our findings support the hypothesis that inflammatory autoimmune disease in pregnant women might influence local immune mechanisms and thus increase the individual susceptibility for fungal infections. The role of the adaptive immunity in *Candida*-specific defence mechanisms was investigated in several immune-compromised pathologies, such as HIV infection, previous organ transplantation, glucocorticoid therapy or antineoplastic chemotherapy. In this immunocompromised group of patients, the decreased T-cell-mediated immune response seems to be associated

### TABLE 4 Maternal and foetal complications among 148 cases in the DWT and DNT subgroups

| Variable                          | DWT subgroup N (%) | DNT subgroup N (%) | p-value |
|-----------------------------------|--------------------|--------------------|---------|
| Participants                      | 100 (18.6)         | 48 (8.9)           |         |
| Maternal complications            |                    |                    |         |
| Pregnancy-induced hypertension    | 6 (6.1)            | 2 (4.3)            | .654    |
| Preeclampsia                      | 2 (2.0)            | 2 (4.3)            | .44     |
| Gestational diabetes              | 9 (9.0)            | 4 (8.5)            | .922    |
| Foetal complications              |                    |                    |         |
| IUGR                              | 2 (2.0)            | 1 (2.1)            | .966    |
| Death within first week of life   | 1 (1.0)            | 0 (0.0)            | .496    |
| NICU admission                    | 13 (13.7)          | 8 (17.8)           | .526    |
| Foetal lung maturation            | 9 (9.4)            | 5 (11.1)           | .748    |
| Tocolysis                         | 9 (9.4)            | 4 (8.9)            | .926    |

Abbreviations: DNT, disease without therapy; DWT, disease with therapy; IUGR, intrauterine growth restriction; N, number; NICU, neonatal intensive care unit.
with increased susceptibility to vulvovaginal candidiasis. However, this theory needs to be further investigated. In contrast to fungal infections, where the risk of PTB is yet under debate, BV is clearly known to be a risk factor for this multifactorial event. Gardnerella vaginalis is the predominant microbe in women with BV and is, therefore, of particular interest. In 2014, Schilling et al. described an urogenital G. vaginalis biofilm in women with inflammatory bowel disease. The urine of these women was frequently colonised with Gardnerella, and women who received steroid therapy were more often colonised. The authors attributed their findings to an epithelial barrier dysfunction of the genital tract. We were unable to compare our findings with those of our study, as we did not analyse urine samples. Donmez et al. also linked BV to autoimmune antibody positivity. In their study, women with antibody positivity showed BV rates of 13.8%, compared to 2.4% in the antibody-negative group. Still, it is not clear whether BV induces autoantibody production or whether autoimmunity increases the risk of BV. Based on our findings, we cannot confirm either of these hypotheses, as we did not find significant differences in BV rates among our case groups. However, the BV rates that we found in our cohort were comparable to those of previously published studies. The risk of infections in patients on immunotherapy is well known. Unfortunately, the scarcity of data on vaginal infections related to immunotherapy in inflammatory rheumatic or bowel diseases in pregnancy does not allow extensive comparisons. Further studies are needed to evaluate whether DMARDs or steroid therapy pose an additional risk for vaginal infections.

The primary reasons why we aimed to identify whether or not women with inflammatory rheumatic diseases are at risk of AVM was to avoid a potential accumulation of additional risk factors for PTB among high-risk pregnant women. With regard to PTB, we found no significant differences between cases and controls, as well as between cases with and without an immunosuppressive therapy. Notably, the PTB rate among our cohort is significantly higher than the overall PTB rate in the country, as we only observed high-risk women at our tertiary referral centre. Austrian perinatal registry data suggest an average PTB rate that ranges from 7.3% in 2018 to 8.7% in 2014, with a lower rate in 2014 and 11.1% in 2008. Dominitz et al. described a lower PTB rate than we found in our study, along with the findings of Smith et al., who described PTB rates of 10.9% in women with ankylosing spondylitis, and of 13.7% in those with psoriatic arthritis; all of which are considerably lower than in our study. In women with SLE who are known to experience more complicated pregnancies than women with other autoimmune disorders, reported PTB rates are considerably higher, ranging from 20% to 54%. We suggest that the high PTB rate in our study is likely due to the tertiary study setting. Overall, the PTB rate of 18.4% among women in our case group is still considered to be satisfactory and comparable with the available literature.

The lower mean birthweight that we found among the case group, could theoretically be attributed to impaired placental function in women with inflammatory rheumatic diseases. It is well known that disease activity is an important risk factor for adverse obstetric outcomes, including PTB and intrauterine growth restriction (IUGR). Unfortunately, we did not routinely record disease activity in our study, and this prevents us from further analysing this point. Our findings are in line with available literature, which suggests that inflammatory rheumatic or bowel disease might lead to IUGR through endothelial damage from circulating antiangiogenic factors and other inflammatory molecules in combination with pre-existing maternal vascular risk factors.

The caesarean section rate that we found was significantly higher among women with autoimmune conditions (Table S2). Increased rates of caesarean section have already been reported for women with autoimmune diseases. Chakravarty et al reported that 39.4% of pregnant women suffering from SLE, and 37.2% with rheumatoid arthritis required a caesarean section. The recently published study by Smith et al reported a caesarean section rate of 33.3% in women with ankylosing spondylitis and 48.7% in women with psoriatic arthritis. Again, we assume that the reason for the high caesarean section rate that we observed was attributed to the fact that we solely care for high-risk pregnancies at our centre. Moreover, the decision-making regarding the mode of delivery is often compromised from fear of complications in late pregnancy or peripartum, which poses a bias to clinical decision-making towards the operative mode of delivery. In addition, the higher caesarean section rate among the case group might also be attributed to the increased rate of primiparous women in this group, who are known to have an increased likelihood for caesarean section, compared with multiparous women.

We are aware that our study has several limitations, above all due to its retrospective character. First and foremost is the fact that inflammatory rheumatic and inflammatory bowel diseases are rare conditions; although we analysed our in-house data for a long time period, the number of eligible cases remained relatively small. Moreover, there are several risk factors that might have been associated with vaginal infections (eg stress, pre-existing comorbidities, antibiotic or probiotic treatment) that were not considered, since these data were not part of our database. As it is known that complication rates vary between different inflammatory disorders, with the highest complication rates among women with SLE, it is difficult to compare our results to that of previously published studies, as most of them referred to particular diseases. Finally, we were unable to report maternal comorbidities and disease activity during pregnancy, even though these factors are known to increase the risk for adverse obstetrical outcomes.

5 | CONCLUSIONS

Our findings indicate that pregnant women with inflammatory rheumatic and inflammatory bowel diseases are at increased risk for an abnormal vaginal microbiota, including BV and the colonisation with Candida species. Considering the risk that autoimmune conditions pose on obstetrical outcomes and complications that may arise from consecutive vaginal dysbiosis and infection, we suggest that affected
women need to be consequentially screened and treated during pregnancy. Further prospective studies are needed to confirm our findings, as well as to evaluate whether there is an influence of autoimmune diseases and immunosuppressive treatments on the vaginal microbiota.

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None.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Klara Rosta: Data curation (equal); Investigation (equal); Conceptualization (equal); Writing - original draft (lead). Antonia Mazzucato-Puchner: Data curation (equal); Investigation (equal); Project administration (equal); Resources (supporting); Writing-review & editing (equal). Herbert Kiss: Resources (equal); Supervision (equal); Writing-review & editing (equal). Veronika Malik: Data curation (supporting); Formal analysis (supporting); Investigation (supporting); Writing - review & editing (supporting). Peter Mandl: Formal analysis (supporting); Investigation (equal); Methodology (supporting); Supervision (supporting); Writing - review & editing (supporting). Inbal Shafran: Data curation (supporting); Resources (supporting); Writing-review & editing (supporting). Ljubomir Petricevic: Conceptualization (supporting); Supervision (equal); Validation (equal); Writing-review & editing (supporting). Philipp Foessleitner: Data curation (supporting); Resources (supporting); Writing-review & editing (supporting). Wilhelm Temsch: Formal analysis (lead); Software (lead); Validation (lead). Alex Farr: Conceptualization (lead); Investigation (lead); Methodology (lead); Project administration (lead); Supervision (lead); Writing - original draft (supporting); Writing - review & editing (lead).

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**SUPPORTING INFORMATION**

Additional supporting information may be found online in the Supporting Information section.

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