



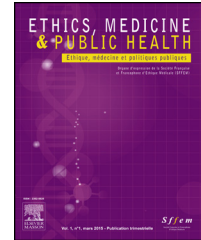
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## LETTER TO THE EDITOR

### Vulvodynia associated with vulvovaginal microbiome: Neglected due to the COVID-19 pandemic?



**Keywords** COVID-19; Microbiome; Pandemic; Vulvodynia

Dear Editor,

The COVID-19 pandemic has posed significant obstacles to clinical practice, oftentimes delaying the management of patients with curable conditions, including urogynecological conditions. Fears of contracting SARS-CoV-2 while visiting healthcare facilities have emerged because of this health crisis [1] in combination with the disruption of outpatient services have resulted in benign yet recurrent conditions such as vulvodynia remaining undiagnosed and untreated for a long time [2].

A rapid literature search on PubMed/Medline, Scopus, reveals that research – and presumably clinical practice – related to vulvodynia, has been neglected since March 2020. Vulvodynia is chronic pain or discomfort of vulva and the pelvic floor for which there is no identifiable cause, its epidemiology and burden is about 16% of the female population [3] and it seems to be associated with the vaginal microbiome. The low number of relevant publications ( $n=4$ ) in comparison to the previous years ( $n=137$ ) is alarming. The limited available evidence is presented below.

Mitchell et al. (2020) compared premenopausal women with vulvodynia to a healthy control group with regard to their vaginal microbiome. The microbiome of most the participants included bacteria such as *Lactobacillus crispatus*, *L. jensenii*, *L. gasseri*, and *L. iners*. *Gardnerella vaginalis* was less prevalent in the patients with vulvodynia. Regarding the vulvovaginal fungal load, yeast sequences were detected in only 5 participants (2 controls, 2 with vulvodynia, 1 with idiopathic vaginitis) with *C. albicans* and/or *C. lusitanae*. Differences in vaginal microbiota and inflammatory markers among women with vulvodynia or those in the control group appear minimal or of no association between vaginal microbiome, inflammation and diagnosis [4].

Van Thiel et al. (2020) provided more evidence about the potential involvement of vaginal microbiome in chronic vulvodynia. Repeated vulvovaginal fungal or vaginal bacterial infections are associated with vulvodynia. Similarly, interstitial cystitis, or bladder pain syndrome, are linked to past urinary tract infections (UTI). Past infections or mere exposures to certain bacterial or fungal species seem to have an important impact on chronic pain conditions such as IBS, interstitial cystitis, and vulvodynia [5].

In 2020, Bedford and colleagues reported that culture-based analyses of the vaginal microbiome showed no differences between cases and controls, based on 16S rRNA sequencing. The increasing number of yeast infections and vulvodynia were strongly correlated. After vaginal smear examinations, participants in both groups had similar polymorphonuclear values of neutrophils and Nugent score and showed no difference regarding H<sub>2</sub>O<sub>2</sub>-negative or positive *Lactobacillus* species, *Gardnerella vaginalis*, *Enterococcus*, *Escherichia coli*, Viridans-group or Group B Streptococci and a number of anaerobic organisms. Female participants with low-diversity microbiomes had a history of childhood abuse, anxiety, depression and high levels of rumination and vulvodynia. Bedford et al. also highlighted that vaginal microbiome differences among female participants strongly correlated to environmental/psychosocial risk factors and vulvodynia [6].

Park et al. (2021) have analyzed the microbial composition of both the vestibule and vagina among female patients with clinically investigated vulvodynia and age-matched healthy controls group participants without vulvodynia. The compositions of bacterial microbiomes were compared by 16S rRNA pyrosequencing. *Lactobacillus* was more commonly detected in both groups. *Streptococcus*, *Gardnerella*, *Prevotella*, *Anaerococcus*, *Corynebacterium*, and *Bacteroides* were also detected. Symptoms of vulvodynia occur in women regardless of whether *Lactobacilli* are prominent or not. Additionally, bacterial loads were similar between the two groups. *Gardnerella* and *L. helveticus* were predominant in patients, whereas *L. iners* and *L. gasseri* were predominant in control groups. Therefore, differences in vaginal microbiome in association with vulvodynia were also reported [7].

The results of the existing studies have shed light to the involvement of the microbiome in the condition and provide a basis for research assessing COVID-19 related microbiome alterations and hygienic or nutritional interventions promoting symbiosis and therefore preventing the development of infections. Furthermore, the significant deficit in the literature in the last two years of the pandemic (2020–2021) testifies to the magnitude of the problem and highlights the need for further studies assessing the impact of the pandemic on the management, the epidemiology and the burden of this condition.

At health systems' level, in order to overcome this diagnostic and therapeutic barrier posed by the pandemic, the authors recommend self-care-education for female patients and the continuous care and follow-up of the disease by the healthcare workers. The use of telemedical health systems and applications, not only for the diagnosis of vulvodynia,

but also for the monitoring of the condition and its potential recurrence, would be of great importance, for the effective treatment of the condition, the improvement of patients' quality of life and the decongestion of overwhelmed health-care systems.

#### Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

#### Informed consent and patient details

The authors declare that the work described does not involve patients or volunteers.

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#### Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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#### Disclosure of interest

The authors declare that they have no competing interest.

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