REVIEW PAPER

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Candida albicans as the main etiological factor in vulvovaginal candidiasis with consideration of the impact of hormonal contraception. Review

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Abstract

Introduction: Vulvovaginal candidiasis (VVC) is considered the most frequent fungal infection affecting women of reproductive age. In more than 85% cases, the etiological factor is *Candida albicans*, while less frequently other species, such as *C. glabrata* or *C. tropicalis* are involved. The purpose of this article is to present the risk factors for developing VVC, the virulence factors of the pathogen, and an analysis of the impact of hormonal contraception on the incidence of infections. Literature shows that hormones, which are the main component of the contraceptives, significantly affect the vaginal microbiota – leading to a reduction in the population of *Lactobacillus* species and thereby facilitating the colonisation of *C. albicans*. Population studies confirm that a higher incidence of VVC is observed among women using hormonal contraception, compared to those who do not.

Aim: Existing reaserch highlights the necessity of monitoring the vaginal microbiota in female patients using hormonal contraceptives, and for considering prophylaxis when selecting contraceptive methods.

Material and methods: The investigation entails a systematic review executed by exploring primary articles within databases, including PubMed, Semantic Scholar, Medline, Scopus, Science Direct, and EBSCO.

Results and discussion: The confirming articles 17. The denying articles 4.

Conclusions: Women using hormonal contraception should remain alert and seek professional advice if characteristic symptoms occur.

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1. INTRODUCTION

Candida albicans is a pathogen classified as a yeast-like fungus. It is a single-celled organism, round or oval in shape, measuring up to only 10 µm. In addition to existing as single cells, it can also form chains of yeast cells, enabling the creation of pseudomycelium. It is characterised by asexual reproduction, most commonly by budding or division.

Among the many factors predisposing to the development of candidiasis are: immunosuppression, steroid treatment, prolonged vascular cannulation, invasive medical procedures, long-term treatment with broad-spectrum antibiotics, skin damage due to burns, gastrointestinal dysfunction, diabetes, birth weight in premature infants (<2000 g), reduced immune function, and HIV infection. However, in the case of vaginal candidiasis (VC), the key predisposing factors include: gastrointestinal disorders, the use of contraceptives, antibiotics with bactericidal effect on *Lactobacillus* – a bacterium which naturally colonises the vaginal microbiota – reduced immunity, and wearing tight underwear. Excessive intimate hygiene or vaginal douching can also contribute to the development of VC.

The pathogenesis of candidiasis not only depends on patient predisposition, but also on the virulence factors of *C. albicans*, which facilitate colonisation, tissue invasion, and evasion of host immune responses.

Candida albicans is responsible for over 85% of VVC cases. Other species, such as *Candida glabrata* and *Candida tropicalis*, are less commonly invlolved. Vaginal infections affect approximately 75% of all women during pregnancy, and approximately 5%–10% of women develop recurrent VC (VVC). Colonisation of the vagina by the pathogen, may result from reinfection or incomplete treatment of a previous episode. Reinfection occurs when *Candida* cells, after successful therapy, repopulate the vaginal epithelium through sexual transmission or from the digestive tract. In most cases, *Candida* is never completely eliminated from the vagina, partly due to the frequent use of fungistatic rather than fungicidal products. When drug concentrations decrease, the pathogen may resume growth and cause new infection. The disease most often manifests as a white, curd-like discharge, accompanied by vulvovaginal itching. It may also be associated with dysuria. Clinical symptoms typically occur when the number of cells exceeds 10^5 colony-forming units per milliliter of vaginal fluid (cfu/mL). Although superficial candidiasis occurs frequently, it is not life-threatening. It can be classified as sporadic or recurrent, with recurrence defined as four or more episodes per year. In cases of recurrent infection, extended diagnostic evaluation is recommended[1].

The use of oral hormonal contraception increases the risk of both the onset and recurrence of VC. This risk depends on the type of contraceptive and individual susceptibility. Long-term use of hormonal contraception may lead to changes in the vaginal microflora. The hormones that constitute the main ingredient in contraceptives indirectly reduce the population of *Lactobacillus spp.*, which are essential for maintaining a low vaginal pH. A decrease in *Lactobacillus* levels increases the pH and disrupts the balance of the vaginal microbiota, creating conditions favourable for the growth of *C. albicans*. Estrogen plays a key role in the development of the infection. Exogenous hormones does not compensate for the physiological decline in ovarian estrogen secretion. As a result, the vaginal mucosa becomes thinner, vaginal secretions decrease, and overall moisture levels drop. Vaginal dryness lowers local immunity and increases susceptibility to infection. Therefore, vaginal candidiasis is recognised as one of the possible side effects of hormonal contraception.

2. AIM

The aim of this review was to assess the effect of oral hormone therapy in women on the risk of developing genital yeast infections.

3. MATERIAL AND METHODS

The investigation entails a systematic review executed by exploring primary articles within databases, including PubMed, Semantic Scholar, Medline, Scopus, Science Direct, and EBSCO. Search strategies varied for each database to account for different search capabilities. Additional articles were obtained from a list of references in published reviews. The reference lists of retrieved articles and grey literature were searched to detect studies potentially eligible for inclusion (Tables 1 and 2).

4. RESULTS

4.1. THE CONFIRMING ARTICLES:

Jasim ST. *The relationship between Vulvovaginal Candidiasis and Some Predisposing Factors in Prevalence among Baghdad women*[2] (Google Scholar, ResearchGate)

The research involved 195 women, aged 20–55 years, of whom 127 were classified as users of hormonal contraception. Vaginal swabs were cultivated on Sabouraud Dextrose Agar and later inspected for yeast colonies. The results showed that 106 women, tested positive

Table 1. The number of articles found, along with the name of the sources.

Source	Number of articles found
PubMed	11
ResearchGate	9
Google Scholar	8
ScienceDirect	5

Table 2. The number of articles found, along with the name of the sources, after removing duplicate publications.

Source	Number of articles found
PubMed	4
ResearchGate	5
Google Scholar	3
ScienceDirect	2

for VVC. Moreover, among contraceptive users, *Candida* species were isolated in 83 cases (65.3%), compared with 23 cases (39.7%) among non-users. Of all the *Candida* isolates, *C. albicans* was the most prevalent species with 50.6% of isolates in contraception users, and 43.5% in non-users. The highest infection rate was observed among oral contraceptive pill users – 82.2%, in comparison, the IUCD presented much lower rate – at only 17.8%. Finally, the highest prevalence of VC was found in the 23– 6 age group – 37.3%. These findings indicate a strong link between hormonal contraceptive use – especially oral contraceptive pills – and an increased prevalence of VVC, especially in women at reproductive age.

Pereira LC, Correia AF, da Silva ZDL, et al. Vulvovaginal candidiasis and current perspectives; new risk factors and laboratory diagnosis by using MALDI TOF for identifying species in primary infection and recurrence[3] (PubMed, Google Scholar)

This study analysed 278 patients (173 symptomatic, 105 asymptomatic) to evaluate VVC, using phenotypic and presumptive methods, all confirmed by MALDI TOF. Only 50.3% of patients reported the classic symptoms (discharge, itching, burning), with a positive predictive value of 67.8%. Species analysis showed the primary prevalence of 80.9% *C. albicans*, 15.2% non-*albicans*, 1% *Rhodotorula mucilaginosa*, 1.9% unidentified species. In recurrence form of the disease, the prevalence of *C. albicans* was 66.7%. Finally, there also was a statistical correlation between candidiasis and certain risk factors, including contraceptive use. To summarise, the study highlights the low predictive value of symptoms, the prominent impact of risk factors and emphasises laboratory identification for effective treatment and prevention of antifungal resistance.

Rabi Salih S, Ali Haddad R, Abid Hassan S. Prevalence of vulvovaginal candidiasis and its association with Contraceptives[4] (Google Scholar)

In 2021, a study was conducted to investigate the relationship between the use of hormonal contraceptives and the development of vaginal yeast infections. Vaginal swabs were taken from 270 women, 202 of whom were using contraceptives. The results showed that candidiasis was more prevalent among women using the pill compared to women who were not taking any form of contraception (84.1% vs 15.9%). All *Candida* species were more prevalent among contraceptive users, with *C. albicans* being the dominant species (71.7%). Among the contraceptive methods studied, it was concluded that oral hormonal contraception is the method most predisposing to the development of VC.

Arechavala A, Negroni R, Santiso G, Depardo R, Bonvehí P. Chronic recurrent vulvovaginitis is not only due to Candida[5] (PubMed, ScienceDirect)

This investigation analysed the medical records of 316 adult patients (age between 16–45 years) who had consulted for vulvovaginitis. Yeasts were isolated from 211 (66.8%) patients, but only 166 samples (52.5%) exhibited pseudo-hyphae – a virulence factor that enables penetration in vaginal epithelial cells. Furthermore, predisposing risk factors were identified, among which, the use of contraceptives. Nearly 90% of patients received antifungal treatment, with or without microbiological confirmation. Among the isolates, *C. albicans* was the most common species, detected in 187 (88.6%) patients, followed by *C. glabrata*. Taken together, the microbiological analysis is essential to confirm VVC. Identifying isolated species, awarness of predisposing risk factors and determination of antifungal susceptibility are particularly crucial.

Wei T, Wang H, Wen B. Comparison of copper IUDs and hormonal IUDs in prevalence of Candida species in cervicovaginal smears[6] (PubMed)

The study investigated the prevalence of *Candida* species in 160 women, before and 3 months after intrauterine device (IUD) insertion. It also aimed to compare copper IUDs and hormonal IUDs. Patients were divided into two separate groups – the first group received copper IUDs, and the second hormonal IUDs. After three months, candidiasis was detected in 29.57%

of copper IUD users, with the predominance of *C. albicans*. Furthermore, other species of *Candida* were observed in 22.95% of hormonal IUD users. The result suggests that IUD, described as one of the most influential and long-lasting methods of contraception – either hormonal or not, may increase the risk of VVC.

Fernandes A, Azevedo N, Valente A, et al. Vulvovaginal candidiasis and asymptomatic vaginal colonization in Portugal: Epidemiology, risk factors and antifungal pattern[7] (PubMed, Google Scholar)

This research aimed to reveal the incidence, microbiology, antifungal pattern and risk factors of VVC in Portugal. It was based on collecting vaginal samples from 470 women – both symptomatic and asymptomatic. The results presented VVC occurance of 74.4% in women with vulvovaginitis. Moreover, 63.7% of asymptomatic women were colonised with *Candida spp. – C. albicans* being the most common species (59%). Importantly, participants with factors such as usage of oral contraceptive pills and non-cotton underwear were found to be at significantly higher risk of developing VVC. Finally, the study focused on the susceptibility of the species towards different antibiotics – fluconazole and caspofungin, highlighting the conclusion that, identifying the *Candida* species and their antifungal susceptibility is essential for effective treatment, same as avoiding certain risk factors may help prevent VVC.

Alsudani A, Al-Awsi A. Detection of *Candida* spp. That causes vulvovaginitis in women that use contraceptive methods[8] (PubMed, ResearchGate, Google Scholar)

The aim of following the study was to determine the distribution of *Candida* spp. in 98 women, aged 18 to 50 with vulvovaginitis, and varying contraceptive use. The study also assessed the *Candidas*' sensitivity to some antifungals. The results showed that 43.87% women used IUD, 15.30% used birth control pills, 7.14% used an injection of contraceptives, 5.10% used contraceptive suppositories and 28.57% did not use any contraceptives.

Candida spp. was detected in 57.83% of specimens from contraceptive users, compered to 39.29% in non-users. Moreover, a total of 59 women were tested positive for candidiasis, with *C. albicans* (47.46%) being the predominant species. The 26–35 age group, presented almost 40 women with vulvovaginitis symptoms. Notably, nystatin was found to be the most effective treatment for *Candida* spp. These findings emphasise that the use of contraceptive methods, especially an IUD, increases the risk of VVC.

Pizga Kumwenda A, Cottier F, Hendry AC, et al. Estrogen promotes innate immune evasion of *Candida albicans* through inactivation of the alternative complement system[4] (ScienceDirect)

The study mentioned above focused on the correlation between the level of estrogen and the occurrence of VVC, as well as its impact on the host innate immune system. The results demonstrate that one of the major risk factors associated with the development of VVC is an elevated estrogen level, which naturally occurs during pregnancy, and is also induced by the use of high – estrogen – containing oral contraceptives. Consequently, VVC occurs less frequently in postmenopausal women, highlighting the significant role of estrogen in promoting the virulence of *C. albicans*. Estrogen promotes glycogen production in the vaginal mucosa, establishing a favourable environment for *C. albicans*. One of the forms of the estrogen – 17α-ethynylestradiol, is a synthetic compound used in oral contraceptives. To determine whether *C. albicans* adaptation to estrogen affects the host-pathogen interactions, research assessed fungal growth in the presence of physiological (0.0001 μM) and super-physiological (0.1 μM, 10 μM) concentrations of 17β-estradiol, estriol, or 17α-ethynylestradiol, and quantified the phagocytosis rates. The findings revealed that all three forms of estrogen significantly inhibited macrophage and neutrophil phagocytosis of *C. albicans*. Furthermore, the fungus demonstrated an ability to recruit Factor H – which helps to avoid opsonophagocytosis, thus facilitating the avoidance of immune system reactions. Collectively, these observations indicate that estrogen–induced immune evasion is a general trait of clinically relevant and estrogen-adapted *C. albicans*. Estrogen-driven modulation of innate immunity, contributes to an increased susceptibility of women to VVC, particularly during period of elevated estrogen levels, happening, for instance, on oral contraceptives.

Lillian A, Chuku A, Joseph N, Ajide B, Reuben R, Akwashiki O. Phylogenetic Diveristy and Susceptibility of Candida Species from Women using Contraceptive Devices in Central Nigeria[9] (ScienceDirect)

This research begins with a strong assertion 'that the use of contraceptive devices predisposes women to VVC globally.' Therefore, it aimed to characterise and determine the phylogenetic diversity and susceptibility of *Candida* spp. among 1,600 women using contraceptive devices in central Nigeria. The results revealed that five *Candida* species were identified among 710 contraceptive users with VVC. *Candida albicans* was the predominant species (43.23%), while non-*albicans Candida*

spp. was also present: *C. glabrata* (19.01%), *C.* tropicalis (15.77%), *C. akabanensis* (13.09%) and *C. parapsilosis* (8.87%). All pathogens showed varying degrees of susceptibilities to antifungals, with *C. akabanensis* exhibiting 100% resistance to both voriconazole and fluconazole. These outcomes demonstrate that women using contraceptive devices in Nigeria harbour a phylogenetically diverse range of *Candida* spp., including the rare and highly resistant *C. akabanensis*, indicating the need for targeted antifungal strategies.

Irene VR, Sajeeth CI, Karthikeyan V, Sabitha J. Assessments of Risk Factors for Developing Vulvovaginal Candidiasis Among Women at Various Age Groups[10] (GoogleScholar)

This study included 90 women aged from 18 to 65 years, with the objective of identifying risk factors responsible for developing VVC across reproductive, pregnant, and postmenopausal age groups. Oral contraceptive use and hormonal replacement therapy, were considered the main factors contributing to VVC. The results showed that among the collected data, VVC was most prevalent among women of reproductive age (18–35 years), affecting 40% of participants. Furthermore, prevalence was higher among women with BMI of 25.0–29.9 (54.4%), suggesting overweight as another reason for infection development. Martial status was also associated with VVC: 97% of cases (88 patients) occurred among married participants, while only 3% (2 patients) were reported among unmarried women. Past medical history like diabetes mellitus (27.7%) or hypothyroidism (24.5%), as well as past medication use, including antibiotics (23.3%), steroids and oral contraceptives (1.1%) were identified as major risk factors for VVC. In addition, personal hygiene, clothing and sexual practices appeared to influence the risk of infection. To summarise, VVC is more common in women of reproductive age, due to their hormonal influences, sexual behaviour, and intimate hygiene. Awarness of these risks is essential, as not only do they may predispose women to disease, but also potentially worsen its clinical course.

Subedi A, Upreti MK, Rana JC, Sapkota RP, Thapa Shrestha U. Vulvovaginal candidiasis, an increasing burden to women in the tropical regions attending Bharatpur Hospital, Chitwan[11] (PubMed, ScienceDirect)

This article investigated the prevalence of VVC, identified *Candida* species, and assessed their antifungal susceptibility. It was said that this infection is becoming a great burden among married women, and is even more challenging with antifungal–resistant *Candida* species. A total of 300 sympotomatic married women were enrolled, showing a 37.3% (112/300) prevalence of VVC. *Candida albicans* was the most predominant species (52.6%), followed by *C. glabrata* (29.3%), among non–*albicans* isolates. Women aged 25–35 years, were the most infected (47.3%), and a significant relationship was observed between contraceptive use and VVC ($P < 0.05$). Finally, the highest susceptibility was shown against Amphotericin – B (68.1%), presenting *C. albicans* more susceptible to antifungals than non–*albicans* species. To conclude, VVC represent a considerable burden for women of reproductive age. Detecting risk factors, *Candida* species distribution, and antifungal resistance is essential for effective management.

Bahat AA, Murtiastutik D, Setyaningrum T, Listiawan MY, Sawitri, Utomo B. The association between vulvovaginal candidiasis and hormonal contraceptive use in the outpatient clinic of Dr Soetomo Hospital, Surabaya in 2017–2020: A retrospective study[12] (Google Scholar)

This study explored the association between hormonal contraceptive use and vulvovaginal candidiasis (VVC) among 308 patients – of whom 132 (42.9%) were diagnosed with VVC and 84 (27.3%) reported hormonal contraceptive use. Findings indictated that hormonal contraceptive use - independent of sexually transmitted infection (STI) history and immunodeficiency disorders – was associated with 3.4-fold increase in the odds of developing VVC. Specifically, oral contraceptive pills (OCPs) were linked to a 2.3-fold increase, whereas other forms of contraception, such as injectables and implants, were associated with a 8.7-fold increase. The probability of developing VVC in OCP users was 49.5%, while users of other hormonal contraceptives had a higher probability of 78.6%. These findings suggest that hormonal contraceptives pose a significant risk factor for the occurance of VVC.

Hussen I, Aliyo A, Abbai MK, Dedecha W. Vaginal candidiasis prevalence, associated factors, and antifungal susceptibility patterns among pregnant women attending antenatal care at bule hora university teaching hospital, Southern Ethiopia[13] (PubMed)

This research aimed to determine the prevalence, associated factors, and antifungal susceptibility patterns of VVC among 317 pregnant women. Sabourouda Dextrose Agar and Chromogenic *Candida* Differential Agar were used for isolation and identification of *Candida* species. The overall prevalence of VVC was 26.8%. Several risk factors were found to be significantly associated with infection, including contraceptive use (AOR

= 5.03) and a history of previous vaginal candidiasis (AOR = 6.95). Antifungal susceptibility testing revealed that itraconazole, amphotericin B, and miconazole were the most effective against all *Candida* isolates. In contrast, resistance was observed against fluconazole, ketoconazole and clotrimazole. To conclude, study indicates the need to raise awarness of the risk factors and antifungal resistance of *Candida* infections among pregnant women to effectively cure the infection.

Aklilu A, Woldemariam M, Manilal A, et al. Aerobic vaginitis, bacterial vaginosis, and vaginal cadidiasis among women of reproductive age in Arba Minch, southern Ethiopia[14] (PubMed)

In 2024, a cross-sectional study was conducted among 398 women of reproductive age to investigate the prevalence of reproductive tract infections (RTIs), their drug resistance, and associated risk factors. Vaginal and/or cervical swabs were collected to diagnose bacterial vaginosis (BV) and aerobic vaginitis (AV), while microbiological culture techniques were used to detect isolates responsible for AV and VC. The findings revealed AV in 122 (30.7%) participants, making it the predominant RTI. It was followed by BV in 117 (29.4%), and VC in 111 (27.9%) women. Among bacterial isolates linked to AV, *Escherichia coli* (34.2%) and *Klebsiella pneumoniae* (28.5%) were the most common. Unfortunately, multidrug-resistance (MDR) was identified in 69 patients (65.71%). Analysis of risk factors indicated that history of abortion (AOR = 4.0%) and the use of contraceptives (AOR = 4.7%) carried the greates odds of predisposing women to RTIs. The high prevalence of RTIs, together with the burden of MDR and existing risk agents, highlights the urgent need for effective interventions and continuous surveillance to reduce long-term complications.

M'Mebwa Mtende L, Kasujja M, Simba LM, Tabu GB. Factors associated with vulvovaginal candidiasis and antifungal susceptibility patterns among nonpregnant women attending the gynecology clinic at Hoima Regional Referral Hospital: A cross-sectional study[15] (ResearchGate)

This research investigated the prevalence, assosiacted factors, and antifungal sensitivity patterns of VVC among 278 non-pregnant women, aged 15–50 years who attended the Gynecology Clinic of HRRH with clinical features of vulvovaginitis. The prevalence of VVC was 27.7%, with the significant associations observed between VVC and age, HIV status, hormonal contraceptive use (AOR = 0.96%), and prior VVC occurance. Multivariate analysis revealed that participants aged 20–34 years were more likely to present VVC (AOR = 7.87%). Additionally, HIV-positive patients (7.01%), and those with a history of previous VVC episodes (AOR = 10.48%) were also at greater risk. *Candida albicans* – the predominant pathogen, responsible for over 85%–90% of cases, presented the highest susceptibility to amphotericin B (97.4%), followed by ketoconaloze (79.22%). The prevalence rate in this study, was comparable with the findings from Uganda, where 27.5% of pregnant women were affected. To summarise, not only does this study propose a significant factors for VVC, contraceptives included, but also provides insights into the antifungal susceptibility patterns of *Candida* species, guiding an effective treatment strategies.

Karam KBS, Arceneaux ABS, Vincent KL, Pyles R. Risks of Infections With Contraceptive Vaginals Rings Compared to No Hormone Use[16] (ResearchGate)

This investigation aimed to explore the outcomes of combined contraceptive vaginal rings (CCVRs) on vaginal health and infection risk, compared to non-contraceptive useres. The results showed that CCVR usage was associated with an increased risk of gonorrhea (22.1%) HSV-2 (22.9%), acute vaginitis (31.4%), subacute/chronic vaginitis (70.8%), acute vulvitis (70.8%), subacute/chronic vulvitis (72.2%), pelvic inflammatory disease (31.4%), and candidiasis (40.2%), compared to non-users. Additionally, CCVR showed significant decreased risk of chlamydia (78.6%), syphilis (49.3%) and HIV (43.4%). To conclude, CCVR use appears to increase the risk of certain vaginal infection while reducing the risk of others, highlighting the need for careful monitoring and further research.

Wood S, Traub CW, Karam K, Golovko G. Risks of Vaginal and Sexually Transmitted Infections With Copper Intrauterine Devices Compared to Oral Contraceptives[17] (ResearchGate)

Copper IUDs (Cu-IUDs) have been reported to induce na inflammatory response and alter the vaginal microbiome. For this reason, this retrospective chart aimed to asses the relative risk of vaginal infections associated with Cu-IUD use, compared to oral contraceptive (OC) use in 73,123 women. Cu-IUDs were associated with an increased risk of acute vulvitis (+88%), subacute/chronic vulvitis (+91%), acute vaginitis (+72%), subacute/chronic vaginitis (+88%), gonorrhea (+153%), syphilis (+132%), trichomoniasis (+114%), chlamydia (+100%), candidiasis (+52%), HIV (+96%), anogenital warts (+38%), HSV-2 (+22%), and pelvic inflammatory disease (+36%). In addition, Cu-IUDs did not show a decreased risk for any of the analysed infections, compared to OCs. This study indicates that Cu-IUD users are at higher risk of vaginal infections, including candidiasis, compared to

OC useres. Nevertheless, OC use may still contribute to certain vaginal diseases, representing a relevant risk factor.

4.2. The denying articles

Omran EA, Youssef NES, Abdelfattah AH, Esmail SA, Fouad AM. Copper IUD increases virulence of non-albicans Candida species isolated from women with vulvovaginal candidiasis[18] (PubMed)

The aim of this study was to examine the impact of copper IUD use on *Candida* species, in women with VVC. It focused on pathogens' ability to produce proteinase and phospholipase enzymes, as well as their antifungal susceptibility. Among 132 women, 65 used a copper IUD and 67 did not. Results showed that in IUD users, non-*albicans Candida* (NAC) isolates, produced more proteinase and exhibited higher antifungal resistance to fluconazole and nystatin. Contradistinctively, *Candida albicans* in IUD users, produced less proteinase and showed no change in drug resistance. In conclusion, copper IUD, a non-hormonal type of contraception, may worsen existing VVC, by increasing the virulence factors and antifungal resistance, mainly in non-*albicans Candida* (NAC).

Bakus C, Budge KL, Feigenblum N, Figueroa M, Francis AP. The impact of contraceptives on the vaginal microbiome in the non-pregnant state[19] (Google Scholar, ResearchGate)

This study examined the impact of different contraceptive methods - both hormonal and non-hormonal – on the vaginal microbiome. The vaginal ecosystem might be influenced by numerous factors, including pregnancy, age, douching, menstruation and contraceptive use. Since nearly all sexually active women in the United States have used some form of contraception during their reproductive years, it is crucial to understand its influence on vaginal health. Evidence show that douching decreases hydrogen peroxide production by *Lactobacillus*, leading to an increase in vaginal pH and higher susceptibility to infection. In contrast, most forms of hormonal contraception - such as combined oral contraceptives (COC), etonogestrel implant or depot medroxyprogesterone - are associated with promoting a more stable microbiome. Although concerns have been raised regarding the potential of COCs to increase the risk of VVC, the majority of evidence support otherwise. The exception are progesterone-only-pills (POPs), which have been linked to increased rates of aerobic vaginitis and vaginal atrophy. In conclusion, the high rate of contraceptive use demands a development in understanding of how different methods influence vaginal microbiome, and may lead to less or more serious infections. This study proves that a significant proportion of contraceptive methods do not adversely affect the vagina, stabilising its microbiota.

Wrønding T, Mollerup S, Troen Lundsgaard A, et al. Exploring the relationship between the vaginal microbiota and vaginal symptoms[20] (ResearchGate)

This research, conducted as a part of a double-blinded randomized controlled trial (RTC) evaluating vaginal microbiota transplantation (VMT) in 263 women aged 18–40 years, explored the relationship between vaginal symptoms and microbiome composition. A vaginal dysbiosis (VD) defined by the absence of beneficial *Lactobacillus* species and increased pathogens, often results with vaginal discharge and malodour, although many women remain asymptomatic. Among participants, 65% exhibited eubiotic microbiomes, 23% dysbiotic microbiomes, and 12% intermediate microbiomes, while 33% reported symptoms. *Lactobacillus crispatus* was the predominant species (40%), followed by *L. iners* (30%). and *Gardnerella vaginalis* (9.1%). Both *L. iners* and *L. crispatus* were found in symptomatic and asymptomatic women. Dysbiotic profiles were more strongly associated with increased discharge and malodour, whereas stinging and itching were more prevalent in eubiotic samples. Finally, as for external factors, contraceptive use showed only weak associations with microbial changes, while sexual behaviour patterns, particularly the number of sexual male partners, significantly influenced microbiome composition. These findings highlight the complex interplay between vaginal microbiota, symptoms and external factors. These outcomes demonstrate that contraceptive use showed no clear effect on the vaginal microbiome, whereas sexual habits were more influential in shaping microbial patterns.

Rosati D, Ponce IR, Omosa-Manyonyi GS. Plasma Inflammatory Proteome Profile in a Cohort of Patients with Recurrent Vulvovaginal Candidiasis in Kenya[21] (PubMed, ResearchGate)

VVC affects approximately 75% of women at least once in their lifetime, and around 8% of them suffer form recurrent episodes of VVC. The study aimed to investigate the systematic inflammatory protein profile in 158 (63%) symptomatic women with RVVC within an African population, while also considering the potential influence of hormonal contraceptive on systemic inflammation. The study also included a control group of 92 (37%) asymptomatic women. Among all participants, 136 women (54%) used hormonal contraceptives. The findings showed no notable correlation between hormonal contraceptive

use and systemic inflammatory protein profiles, in either RVVC patients or the controls. Nevertheless, RVVC women using hormonal contraceptives exhibited lower concentrations of four inflammatory proteins: TNF-related activation-included cytokines (TRANCE), transforming growth factor alpha (TGF-Alpha), TNF-related wiek inducer of apoptosis (TWEAK), and neutrophin 3 (NT-3), and a higher concentration of chemokine ligand 28 (CCL28). Despite these observations, the differences were no statistically significant, as well as contraceptives impact. Furthermore, women with RVVC had lower circulating fibroblast growth factor 21 (FGF-21) compared with healthy controls, which may be linked to the immune dysregulation observed in recurrent VVC cases. Last of all, hormonal contraceptive use did not significantly affect systemic inflammation. The altered protein profile among women with RVVC, suggest an underlying immune component in the pathophysiology of recurrent VVC, without the influence of contraception.

5. Conclusions

Candida albicans is the primary etiological agent of VVC. Owing to its high colonisation capacity and multiple virulence factors, elimination remains difficult. Despite the superficial nature of the infection, VVC can result in significant clinical symptoms, particularly in recurrent cases. A thorough understanding of the pathogenic mechanisms of *C. albicans*, as well as the factors contributing to its overgrowth, is crucial for the development of effective preventive and therapeutic strategies. The findings support hormonal contraception as a substantial risk factor for VVC. Most studies highlight this correlation, emphasising the importance of contraceptive use in the etiology of the disease, with only 4 (17.4%) studies (compared with 19; 82.6%), failing to demonstrate such association.

Taken together, VVC remains a challenging infection. It requires proper microbiological assessment to ensure faster recovery. Women using hormonal contraception should remain alert and seek professional advice if characteristic symptoms occur.

CONFLICT OF INTEREST

No conflict of interest have been implied. Every information written above is based on the sources stated in the references.

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