Microbial Pathogenesis 200 (2025) 107359

Contents lists available at ScienceDirect

Microbial Pathogenesis

journal homepage: www.elsevier.com/locate/micpath

Vulvovaginal candidiasis-an overview of current trends and the latest treatment strategies

Vasundhara B. Bhosale [a,*], Akshada A. Koparde [b], Vandana M. Thorat [c]

[a] Krishna Institute of Pharmacy, Krishna Vishwa Vidyapeeth (Deemed to Be University), Karad, 415539, India
[b] Dean Academics, Krishna Institute of Pharmacy, Krishna Vishwa Vidyapeeth (Deemed to Be University), Karad, 415539, India
[c] Krishna Institute of Medical Science, Krishna Vishwa Vidyapeeth (Deemed to Be University), Karad, 415539, India

ARTICLE INFO

Keywords:
Vulvovaginal candidiasis
VVC
RVVC
Hormonal changes

ABSTRACT

Vulvovaginal candidiasis (VVC) is becoming more common, mostly affecting hospitalized and immunocompromised people. *Candida albicans*, among other species, is a significant causal agent, accounting for 90 % of infections. VVC, which affects up to 75 % of women, causes physical and psychological problems, with *Candida albicans* being associated in 85–95 % of cases(Dantas-Medeiros et al., 2023, Tomas et al., 2021, Dantas-Medeiros et al., 2021). Its physical symptoms include genital discomfort, decreased sexual pleasure, and psychological suffering. According to comparative research, pregnant women had a greater VVC prevalence, which can be ascribed to hormonal changes, poor hygiene, and diabetes. Antifungal medicines, which are widely used for therapy, have resulted in resistance issues, demanding a rethinking of therapeutic techniques. There are still diagnostic hurdles, with symptoms overlapping with other illnesses necessitating rigorous examination and laboratory tests. Recurrent Vulvovaginal Candidiasis (RVVC) affects 138 million women each year, causing morbidity and lowering quality of life. Financial constraints highlight the importance of novel, well-tolerated medicines. Resistance to antifungal drugs, notably azoles, complicates therapy. Probiotics, which focus on vaginal microbiome balance, appear as viable preventative strategies. From menarche to menopause, hormonal changes increase susceptibility to VVC, with estrogen playing a critical role. The growing resistance and limited antifungal alternatives, translating research in to clinical practice is critical. Current care is based on antifungals, but problems continue, necessitating the investigation of new drugs. Oteseconazole and ibrexafungerp show promise and have the potential to change RVVC therapy. While useful, probiotics generally supplement standard antifungal methods. In conclusion, tackling the growing difficulties of VVC necessitates ongoing research, novel therapeutics, and possible vaccine development in order to reduce the significant worldwide burden presented by this common fungal illness.

1. Introduction

In recent decades the incidence of fungal infections has increased, affecting mainly hospitalized and immunocompromised individuals. The fungus of the genus *Candida* is the source of the most clinically significant fungal infection in postmodern times, known as candidiasis. Of these, 90 % of invasive cases are caused by the species *Candida albicans, glabrata, tropicalis, parapsilosis, and krusei* [1]. Vulvovaginal candidiasis (VVC) is a prevalent illness that affects up to 75 % of women at some point in their lives. *Candida albicans* has been shown to be the most prevalent causal pathogen in 85 %–95 % of VVC infections. Non-albicans *Candida* species infections, on the other hand, are becoming more common; according to some research, they account for 10 %–45 % of cases. The illness is mostly caused by the species *C. albicans*, which has become a public health concern because of its virulence characteristics and capacity to build biofilms [2].

Genital pain, diminished sexual pleasure, and psychological suffering are among the physical signs of VVC [3]. The symptoms of vulvovaginal candidiasis include burning, itching, pain, and discomfort in the vagina that results in whitish-yellow discharge that frequently has a curd-like appearance. Depending on the research location, different *Candida* species are more or less common in expectant mothers with VVC [4].

Other species of *Candida* are less commonly identified, certain

* Corresponding author. Krishna Institute of Pharmacy, Krishna Vishwa Vidyapeeth (Deemed to be University), Karad, 415539, India.
E-mail address: vasundharabhosale1997@gmail.com (V.B. Bhosale).

https://doi.org/10.1016/j.micpath.2025.107359
Received 1 August 2024; Received in revised form 27 January 2025; Accepted 30 January 2025
Available online 5 February 2025

publications have shown that *C. albicans* ranged between 80 and 90 % among women with acute VVC caused by *Candida* sp. [5–7].

In adolescent girls and non-pregnant women, especially with a decrease in immunity, vaginitis, including fungal infections, can occur, which clinically manifests as abnormal vaginal discharge, irritation, itching, burning, and discomfort. Sexually transmitted diseases are particularly problematic in women [8].

Epistolar cases of bacterial vaginosis impact 3–7% of non-related sexually active girls and 4–15 % of sexually active girls aged 13–18 years during adolescence [9]. This is a serious issue because the bacteria that cause vaginal flora to develop in bacterial vaginosis are also the cause of pelvic inflammatory disease, cervicitis, and endometritis (often in subclinical forms) [10]. The risk factors for the VVC were mentioned in Fig. 1.

The purpose of this review is to outline the complete details of vulvovaginal candidiasis and discuss how treating and defending VVC may benefit from this association in order to lower treatment costs and unfavourable health outcomes [11].

2. Prevalence of vulvovaginal candidiasis

Multiple studies have carried out a comparative study between non-pregnant and pregnant women and found out that pregnant women have a higher prevalence rate of VVC compared to nonpregnant women [12].

Vaginitis is a common condition, but it receives disproportionately little attention. The burden of these infections is still unknown in many parts of the world, including the majority of the Asia-Pacific region [13].

Recent years have seen a significant rise in the prevalence of both superficial and deep candidiasis, which is closely linked to several factors, including hormonal changes during pregnancy, the use of oral contraceptives, local factors like poor hygiene, and general factors like diabetes [14]. Thanks to lactobacillus' synthesis of hydrogen peroxide and lactic acid, the flora protects against the growth of pathogenic microorganisms. Because pregnancy raises estrogen levels, which encourage the deposition of glycogen and other substances in the vagina, pregnant women are at risk. Furthermore, it is commonly known that pregnancy is linked to a minor lowering of immunity. Due to the prevalence of these *Candida* infections and the symptoms they produce, antifungal medications have been used extensively, which has led to the development of resistance and the loss of sensitivity in some fungal species to specific antifungal medications (Fig. 2) [15].

3. Host-pathogen interaction

A delicate balance between tolerance and immune resistance toward the opportunistic fungus *Candida albicans*, which is commonly found on human mucosal surfaces, must be maintained in order to regulate inflammation and maintain homeostasis. Vulvovaginal candidiasis (VVC), the most common mucosal fungal infection, significantly lowers quality of life, particularly in chronic and recurrent forms (RVVC) [16].

Through the promotion of NLRP3 (NACHT, LRR, and PYD domains-containing protein) inflammasome activity and MMC (mucosal mast cells) expansion, IL-9 has a pro-inflammatory effect during the early stages of VVC. As a result, early infection-stage IL-9 neutralization reduces inflammation and reinstates epithelial homeostasis, indicating a possible therapeutic application for IL-9 neutralizing antibodies in the

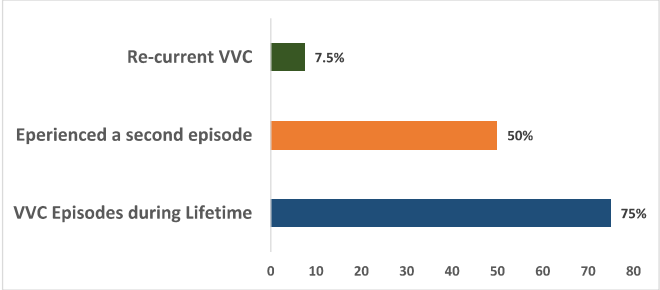

Fig. 2. Prevalence of VVC worldwide.

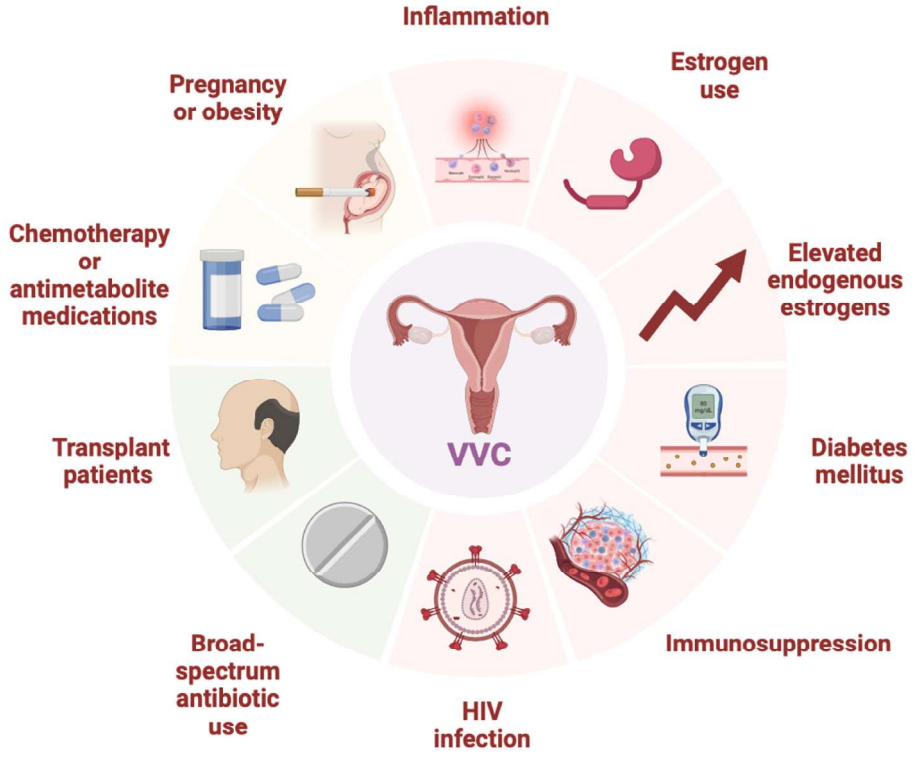

Fig. 1. Risk factors for Vulvovaginal candidiasis.

management of *Candida* infection [17].

4. Diagnostic approaches and challenges

Patients' social and professional lives may suffer as a result of VVC, which can also lead to psychosocial stress. The reduction in quality of life caused by VVC is similar to what people who have chronic obstructive bronchitis or bronchial asthma experience [18]. Itching is the main symptom of VVC in 90 % of the affected women. Given the growing number of women with similar symptoms who self-medicate, anamnesis and a thorough diagnostic work-up are essential for VVC [19]. Despite the fact that many people use over-the-counter medications, research indicates that only 28 % of women who self-treated had VVC [20].

Postmenopausal women have candidiasis of the groin and vulvar areas, while premenopausal women have symptoms that start before the menstrual period and are primarily restricted to the vestibule and vulva. Moreover, burning rhagades and edematous labia minora may manifest in RVVC cases. Physicians should keep in mind, though, that only 35–40 % of women who complain of itching are actually suffering from VVC [21].

In order to improve the differential diagnosis, it is important to take into account the fact that VVC does not smell bad and that the vaginal discharge of affected women is typically lumpy and white in color [22].

In addition to the features of the clinical presentation, laboratory techniques should be used in the diagnosis. Phase contrast microscopy should be used to examine the vaginal discharge using saline solution (or alternatively, 10 % KOH solution) at 400-fold magnification after the patient has undergone anamnesis and a gynaecological examination [23].

One of the most important criteria for a proper diagnosis is the obvious presence of hyphae under a microscope, but this observation is only possible in 50–80 % of positive cases [24].

Low germ load can sometimes make microscopic detection more difficult. Particularly, culture tests are necessary in RVVC cases; however, the minimal inhibitory concentration should not be routinely determined in these procedures. The serological assays used to measure *Candida* antibody levels are still deficient in specificity and evidence. In mild or superficial VVC cases, these tests may identify fungal colonization in other body parts, such as the oral cavity [25].

5. Treatment strategy

Clinicians are frequently faced with the dilemma of whether or not to treat patients due to the possible mechanisms that support *Candida* vaginal colonization and the host factors that enhance the diversion to infection [26]. Simple and complex cases are separated out in VVC. Simple ones are irregular bouts of mild *Candida albicans* infections. Severe infections brought on by non-albicans *Candida* species, recurrent VVC, VVC during pregnancy, or VVC connected to additional medical disorders like diabetes or immunosuppression are examples of complicated cases [27].

Although 96 % of women report a better quality of life after starting fluconazole as their first line treatment for VVC, 63 % of them still experience persistent infections even after finishing maintenance therapy [28]. Women with permanent vaginal yeast colonization have experienced discomfort and anxiety from inadequate treatment, and there are significant clinical concerns about the decisions made regarding treatment in the future [29].

VVC continues to be a public health concern due to its high prevalence, vaginal yeast colonization following standard treatment, and negative effects of topical azole antifungal agents. Odeteconazole and Ibrexafungerp, two novel medications with reduced side effect potential and increased effectiveness in treating VVC, have recently come to market [30] (see Table 1).

Table 1
Available drug treatment for VVC and their mechanisms.

Sr. no.	Class and Drugs	Mechanism of Action	Side effects/Adverse effects	Reference
1	Azoles • Fluconazole • Itraconazole • Oteseconazole • Voriconazole • Ketoconazole • Clotrimazole • Miconazole • Terconazole • Butoconazole • Tioconazole • Oteseconazole	Inhibits the fungal lanosterol 14α-Demethylase and inhibits ergosterol biosynthesis.	Anaphylaxis, nausea, gastrointestinal disturbance, phototoxicity, cardiomyopathy, etc.	[60] [61–63]
2	Echinocandin • Caspofungin • Rezafungin • Anidulafungin • Ibrexafungerp • Micafungin	Inhibits the production of 1,3 β-d-glucan through non-competitive inhibition of the 1,3 β-d-glucan synthase complexes.	Hepatic toxicity, etc.	[60,64, 65]
3	Allylamines • Terbinafine • Naftifine • Flunarizine	Inhibition of the ergosterol biosynthesis by inhibition of squalene epoxidase (Erg1)	Rash, photosensitivity, etc.	[9]
4	Polyene • amphotericin B • Nystatin • Natamycin	Inhibition of the ergosterol biosynthesis by inhibition of squalene epoxidase (Erg1)	Nephrotoxicity, hepatic toxicity, etc.	[9]
5	Antimetabolite • Flucytosine • Griseofulvin	Inhibit nucleic acid synthesis, disrupt microtubule functions	Gastrointestinal disturbance, anemia associated with decreased erythropoietin production, etc	[9,60]
6	Tavaborole	Tavaborole is a topical antifungal that works by inhibiting an enzyme called aminoacyl-tRNA synthetase	Local irritation, itching, or redness	[66]

6. Recurrent vulvovaginal candidiasis

According to recent global analyses of RVVC epidemiology, 138 million women are impacted each year [29]. However, their analyses also revealed that there are very few if any, robust global studies that follow women with consistent clinical and microbiological data for at least a year. Based on these data, they conjecture that prevalence and incidence are likely higher than estimated and are likely rising as a result of an expanding population of women who are at risk [31]. RVVC has a substantial negative impact on morbidity and quality of life, causing physical pain and increased anxiety and depression in women, even in between episodes of symptoms [32].

There is also a significant financial impact on individuals and healthcare systems; worldwide productivity losses are estimated to be around $14 billion [20].

The reason behind the successful clearance of the majority of VVC infections following a single medication course remains unknown, but some women experience relapses of symptomatic episodes even after stopping therapy or even during long-term maintenance treatment.

Therapeutic options for RVVC are limited, and novel, innovative approaches are needed to treat this debilitating condition. The therapies need to be well-tolerated and prevent RVVC recurrence [33].

7. VVC impact on quality of life

RVVC significantly affects morbidity and quality of life, with women incurring physical pain and elevated levels of depression and anxiety, including between symptomatic episodes [20]. According to a study conducted on South Asian women in England, even one case of vaginal candidiasis can cause feelings of shame, stigma, and depression [34].

A cross-sectional study of women in the US and five European countries found that RVVC was linked to depressive symptoms, anxiety, and decreased productivity. Subsequent investigations of women in China [35] and Australia ([36] found that RVVC had a similar detrimental impact on mental health difficulties [37].

8. Antifungal drug resistance in VVC

Even though azole agents are the preferred medications for treating VVC, some species of *Candida* have developed resistance to them through distinct mechanisms, most likely because of their fungistatic properties, which has led to treatment failures [38].

C. albicans possesses a plethora of virulence factors, and several studies have found that azole resistance could be linked to these factors [39]. 30.4 %, 17.6 %, 11.3 %, and 6.4 % of the 204 isolates of *Candida albicans* were resistant to voriconazole, itraconazole, fluconazole, and econazole, respectively. Previous reports of *C. albicans* have indicated varying degrees of azole resistance. It has been demonstrated that this depends on the kind and location of the infection as well as the history of prior or extended exposure to these substances, especially when fluconazole is used [40].

It has been demonstrated that *C. albicans* cells grow primarily in biofilms on biotic and abiotic surfaces. These biofilms give the fungus ecological advantages and also serve as a source of resistant infections. Biofilm formation has a strong correlation with antifungal resistance, albeit its exact nature remains unclear. Numerous mechanisms have been proposed to explain this intricate phenomenon; however, due to its sponge-like ability to sequester azole agents, the composition of the biofilm matrix is likely the most significant [41].

Other researchers, however, did not report a significant correlation between biofilm formation and antifungal drug resistance in *C. albicans* isolated from VVC and bloodstream infection.

Additionally, in *C. albicans* clones isolated successively from an HIV-positive patient who received gradually higher dosages of fluconazole over a two-year period, the in vivo capacity to form biofilm was not correlated with the degree of fluconazole resistance [42].

9. Probiotics and preventive measures for VVC

Originally derived from the Greek and Latin words "pro: for, bios: life," probiotics are referred to as the "good" bacteria. It was first described as microorganisms and/or materials secreted from living microorganisms in 1965 with the intention of improving health either directly or indirectly or promoting the growth of others [43].

Nowadays, Lactobacillus, Bifidobacterium, Saccharomyces, Enterococcus, Streptococcus, Escherichia, and Bacillus are the prevalent probiotics. Probiotics have been shown to be beneficial microorganisms that restore physiological homeostasis and host function, reducing harmful bacteria, regulating immunity, preventing infection, and promoting overall gastrointestinal tract health. This growing body of evidence has led to the widespread recommendation of probiotics by doctors, particularly gastroenterologists, and has made them one of the most widely consumed food supplements globally. The probiotic industry is constantly expanding, with sales reaching billions of dollars annually [44].

Probiotics have also been used to prevent diseases related to female reproduction by preserving the equilibrium of the vaginal microbiota. As is well known, maintaining a healthy vaginal environment is essential for managing vulvovaginal candidiasis VVC and bacterial vaginosis (BV). This is made possible by a robust host-microbial relationship [45].

Research on probiotic bacteria has focused largely on *Lactobacillus* species thus far. Probiotics have been seen as potentially beneficial for safeguarding the vaginal environment in VVC patients. Production of lactic acid, which provides pathogenic exclusion ability by lowering pH to 3.5–4.5 and contributes to indirect pathogenic inhibition by efficient acid cervicovaginal human mucus; production of bacteriocins, which are AMPs and proteins produced as a response to vaginal microbiome imbalance, to protect the host against microbial invasion by blocking vaginal pathogen colonization as a result of displacement and exclusion competition by Lactobacillus [46].

10. Impact of hormonal changes from menarche to menopause

Clinical data reveal that VVC most commonly occurs in women during the luteal phase of the menstrual cycle when estrogen and progesterone levels are increased. In contrast, premenarchal and postmenopausal women not receiving HRT rarely suffer from VVC [37].

While it has long been known that *C. albicans* vaginal infections are frequently reliant on the presence of reproductive hormones. The precise functions of estrogen and progesterone remain unknown. Although experimental *C. albicans* vaginal infections in animals are dependent on a state of pseudoestrus, no formal research on the limitations of estrogen and the role progesterone may play in the infection has been done [47].

Estrogen is important in predisposing women to VVC, although the specific processes are unclear. Estrogen stimulates glycogen formation in the vaginal mucosa, creating a nutrient-rich environment for *C. albicans* growth [48]. Women with low circulatory estrogen levels (i.e., postmenopausal women) have a low risk of developing VVC, whereas women with high estrogen levels (i.e., during pregnancy or women taking high-estrogen-containing oral contraceptives) have a high risk of developing VVC. Elevated estrogen levels promote infection by increasing glycogen at the vaginal mucosa, decreasing leukocyte infiltration, and decreasing epithelial cell antifungal activity [49].

11. Translating candidiasis research into clinical practices: from bench to bedside

Until recently, the antifungal arsenal was highly restricted, with just four antifungal classes (polyenes, azoles, echinocandins, and flucytosine), each having restrictions such as toxicities, method of administration, and rising resistance [50,51]. The pace of antifungal drug development has slowed until the approval stage due to fundamental scientific, economic, and regulatory challenges ranging from the identification of target structures that are non-toxic in humans to obstacles in clinical trial design and approval agency demands. However, tremendous progress has been achieved in recent years through innovative approaches to chemical screening and the facilitation of regulatory processes. Antifungal resistance in *Candida* spp. is increasing globally, necessitating the development of new or repurposed therapies, including those with novel modes of action.

Fosmanogepix has been given fast-track status by the US Food and Drug Administration (FDA) for the treatment of invasive candidiasis. Its broad range of *in-vitro* and *in-vivo* action against most *Candida* , including *C. auris*, is promising, and clinical trials will help to establish the function of Fosmanogepix in the treatment of invasive candidiasis/candidemia, including infections caused by antifungal-resistant strains [52]. Despite the promise of recently licensed and experimental antifungal medications, there are still unmet needs in the treatment of invasive candidiasis. Even with these new and growing possibilities, there are still far too few antifungals that can be administered orally or penetrate the CNS. There is an urgent need for clinical data on

experimental medications, particularly given the present trend of azole-resistant and multi-drug-resistant *Candida* spp., such as *C. auris, C. glabrata, and C. parapsilosis*. Despite the potential of these new antifungal choices, continuous research and development into additional options, including medicines from newer antifungal families, will help refill the present antifungal arsenal.

12. The current recommended management strategy for VVC

VVC is a serious issue that impacts the quality and comfort of patients' daily functioning. Although oral fluconazole is the first-line therapy for uncomplicated VVC, it appears to be ineffective against VVC caused by species other than *Candida albicans* [53].

Because both oral and topical fluconazole usage may cause adverse effects in patients, new medications such as Oteseconazole and Ibrexafungerp are being researched. According to studies, these medicines are effective against treatment-resistant *Candida* species and have a shorter treatment period than fluconazole. Sobel et al. showed in 2021 that oteseconazole reduces VVC symptoms up to 50 % quicker than fluconazole [54].

Furthermore, the researchers demonstrated that oteseconazole might prevent vaginal recolonization for up to 12 months. Further research into this concept might lead to a significant shift in the treatment of individuals with RVVC and comorbidities like diabetes or HIV, which are linked to an elevated risk of VVC morbidity [55]. Preclinical investigations have revealed that Ibrexafungerp has the same or even higher *in-vitro* activity as echinocandins in the treatment of VVC caused by treatment-resistant species. Both Oteseconazole and Ibrexafungerp appear to be promising treatments for RVVC [56].

Ibrexafungerp is a valuable addition to the antifungal arsenal, offering strong bioavailability and a distinct spectrum of activity, particularly against azole-resistant *Candida* species. While it is currently approved for the treatment of vulvovaginal candidiasis (VVC), Phase III clinical trials are actively exploring its efficacy in patients with candidemia and invasive candidiasis [57].

Although the existing studies found no negative effects from the use of probiotics, their use in the therapy of VVC appears irrational. Probiotics may be beneficial as a complement to basic treatment in women with VVC. A comprehensive analysis of the use of probiotics in VVC patients found that adding probiotics can increase the efficiency and impact of traditional antifungal medicines in terms of short-term cure rates. However, probiotics alone have little influence on long-term cure rate improvement [58].

In the past decade, only one new azole and two pharmaceutical products containing posaconazole as the active ingredient have been introduced to the market [50,59].

13. Conclusion

According to a review of the present literature, there is a significant need for the treatment of VVC infections, particularly those caused by yeasts other than *C. albicans*. The primary objective of this review is to provide an updated understanding of VVC, emphasizing the challenges posed by recurrent vulvovaginal candidiasis and infections caused by non-albicans *Candida* species. By evaluating current treatment options, including emerging therapies like Oteseconazole and Ibrexafungerp, as well as exploring the potential of VVC vaccines, we aim to highlight the gaps in current clinical practices and encourage further research to develop effective, long-term therapeutic strategies.

CRediT authorship contribution statement

Vasundhara B. Bhosale: Writing – original draft, Conceptualization. **Akshada A. Koparde:** Visualization, Supervision, Mr. Shekhar Laxman Junghare, Writing – review & editing. **Vandana M. Thorat:** Visualization, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ms. Vasundhara Bhosale reports writing assistance was provided by Krishna Vishwa Vidyapeeth (Deemed to be University) Krishna Institute of Pharmacy. Ms. Vasundhara Bhosale reports a relationship with Krishna Vishwa Vidyapeeth (Deemed to be University) Krishna Institute of Pharmacy that includes: employment. Ms. Vasundhara Bhosale has patent pending to -. - If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

None.

Data availability

The authors are unable or have chosen not to specify which data has been used.

References

[1] M. Da Silva Campelo, E.O. Melo, S.P. Arrais, F.B.S.A. Do Nascimento, N. V. Gramosa, S. De Aguiar Soares, M.E.N.P. Ribeiro, C.R. Da Silva, H.V.N. Júnior, N. M.P.S. Ricardo, Clove essential oil encapsulated on nanocarrier based on polysaccharide: a strategy for the treatment of vaginal candidiasis, Colloids Surf. A Physicochem. Eng. Asp. 610 (2021) 125732.

[2] A.M.Z. Vinueza, Probiotics for the prevention of vaginal infections: a systematic review, Cureus 16 (2024) e64473.

[3] M.G. Martens, B. Maximos, T. Degenhardt, K. Person, S. Curelop, M. Ghannoum, A. Flynt, S.R. Brand, Phase 3 study evaluating the safety and efficacy of oteseconazole in the treatment of recurrent vulvovaginal candidiasis and acute vulvovaginal candidiasis infections, Am. J. Obstet. Gynecol. 227 (2022) 880, e1-880. e11.

[4] L. Li, X. Zhang, Q. Li, W. Zhong, H. Zou, The increasing trend of triazole-resistant *Candida* from vulvovaginal candidiasis, Infect. Drug Resist. (2024) 4301–4310.

[5] A. Ben-Haroush, Y. Yogev, B. Kaplan, The importance of diagnostic work-up in the management of candidal vulvovaginitis. A prospective study, Clin. Exp. Obstet. Gynecol. 31 (2004) 113–116.

[6] F. Boselli, G. Chiossi, P. Garutti, A. Matteelli, M. Montagna, A. Spinillo, Preliminary results of the Italian epidemiological study on vulvo-vaginitis, Minerva Ginecol. 56 (2004) 149–153.

[7] M. Babić, M. Hukić, *Candida albicans* and non-albicans species as etiological agent of vaginitis in pregnant and nonpregnant women, Bosn. J. Basic Med. Sci. 10 (2010) 89.

[8] G. Jarząbek-Bielecka, M. Pawlaczyk, M. Pawlaczyk, M. Pawlaczyk, M. Pisarska-Krawczyk, P. Wojtyła-Buciora, M. Mizgier, J. Boroch, W. Kędzia, The problem of inflammation of the female genital system–assessment of girls' knowledge about prevention and treatment, Medycyna Rodzinna 1 (2018) 29–36.

[9] C.M. Neal, M.G. Martens, Clinical Challenges in Diagnosis and Treatment of Recurrent Vulvovaginal Candidiasis, vol. 10, SAGE Open Medicine, 2022 20503121221115201.

[10] M. Mizgier, G. Jarzabek-Bielecka, K. Mruczyk, W. Kedzia, The role of diet and probiotics in prevention and treatment of bacterial vaginosis and vulvovaginal candidiasis in adolescent girls and non-pregnant women, Ginekol. Pol. 91 (2020) 412–416.

[11] Z. Xiao, Y. Liang, X. Zhang, Y. Zhu, L. Huang, S. Fan, Three-dose antifungal treatment improves the efficacy for severe vulvovaginal candidiasis, Mycopathologia 189 (2024) 93.

[12] T. Disha, F. Haque, Prevalence and risk factors of vulvovaginal candidosis during pregnancy: a review. Infectious Diseases in Obstetrics and Gynecology, 2022, p. 2022.

[13] S.-H. Huang, H.-C. Hsu, T.-F. Lee, H.-M. Fan, C.-W. Tseng, I.-H. Chen, H. Shen, C.-Y. Lee, H.-T. Tai, H.-M. Hsu, Prevalence, associated factors, and appropriateness of empirical treatment of trichomoniasis, bacterial vaginosis, and vulvovaginal candidiasis among women with vaginitis, Microbiol. Spectr. 23 (2023) e00161.

[14] F. Chassot, M.F. Negri, A.E. Svidzinski, L. Donatti, R.M. Peralta, T.I. Svidzinski, M. E. Consolaro, Can intrauterine contraceptive devices be a *Candida albicans* reservoir? Contraception 77 (2008) 355–359.

[15] M. Benchellal, K. Guelzim, Z. Lemkhente, H. Jamili, M. Dehainy, D.R. Moussaoui, W. El Mellouki, K.S. Idrissi, B. Lmimouni, La candidose vulvo-vaginale à l'hôpital militaire d'instruction Mohammed V (Maroc), J. Mycolog. Med. 21 (2011) 106–112.

[16] I.D. Jacobsen, The role of host and fungal factors in the commensal-to-pathogen transition of *Candida albicans*, Curr. Clin. Microbiol. Rep. 10 (2023) 55–65.

[17] R. Gaziano, S. Sabbatini, C. Monari, The interplay between *Candida albicans*, vaginal mucosa, host Immunity and resident microbiota in health and disease: an overview and future perspectives, Microorganisms 11 (2023) 1211.

[18] H. Meyer, S. Goettlicher, W. Mendling, Stress as a cause of chronic recurrent vulvovaginal candidosis and the effectiveness of the conventional antimycotic therapy, Mycoses 49 (2006) 202–209.

[19] J.D. Sobel, Y.S. Vempati, Bacterial vaginosis and vulvovaginal candidiasis pathophysiologic interrelationship, Microorganisms 12 (2024) 108.

[20] S. Aballéa, F. Guelfucci, J. Wagner, A. Khemiri, J.-P. Dietz, J. Sobel, M. Toumi, Subjective health status and health-related quality of life among women with recurrent vulvovaginal candidosis (RVVC) in Europe and the USA, Health Qual. Life Outcome 11 (2013) 1–13.

[21] A. Unnikrishnan, S. Kalra, V. Purandare, H. Vasnawala, Genital infections with sodium glucose cotransporter-2 inhibitors: occurrence and management in patients with type 2 diabetes mellitus, Indian journal of endocrinology and metabolism 22 (2018) 837.

[22] J. Jayatilake, Y. Samaranayake, L. Cheung, L. Samaranayake, Quantitative evaluation of tissue invasion by wild type, hyphal and SAP mutants of *Candida albicans*, and non-albicans *Candida* species in reconstituted human oral epithelium, J. Oral Pathol. Med. 35 (2006) 484–491.

[23] K. Akinosoglou, G. Schinas, D. Papageorgiou, E. Polyzou, Z. Massie, S. Ozcelik, F. Donders, G. Donders, Rapid molecular diagnostics in vulvovaginal candidosis, Diagnostics 14 (2024) 2313.

[24] J.D. Sobel, Vulvovaginal candidosis, Lancet 369 (2007) 1961–1971.

[25] V.D. Valeriano, E. Lahtinen, I.-C. Hwang, Y. Zhang, J. Du, I. Schuppe-Koistinen, Vaginal dysbiosis and the potential of vaginal microbiome-directed therapeutics, Frontiers in Microbiomes 3 (2024) 1363089.

[26] K.O. Cheng, D.E. Montano, T. Zelante, A. Dietschmann, M.S. Gresnigt, Inflammatory cytokine signalling in vulvovaginal candidiasis: a hot mess driving immunopathology, Oxford Open Immunology 5 (2024) iqae010.

[27] P. Nyirjesy, J.D. Sobel, Vulvovaginal candidiasis, Obstetrics and Gynecology Clinics 30 (2003) 671–684.

[28] T. Crouss, J.D. Sobel, K. Smith, P. Nyirjesy, Long-term outcomes of women with recurrent vulvovaginal candidiasis after a course of maintenance antifungal therapy, J. Low. Genit. Tract Dis. 22 (2018) 382–386.

[29] D.W. Denning, M. Kneale, J.D. Sobel, R. Rautemaa-Richardson, Global burden of recurrent vulvovaginal candidiasis: a systematic review, Lancet Infect. Dis. 18 (2018) e339–e347.

[30] E. Larkin, L. Long, N. Isham, K. Borroto-Esoda, S. Barat, D. Angulo, S. Wring, M. Ghannoum, A novel 1, 3-beta-d-glucan inhibitor, ibrexafungerp (formerly SCY-078), shows potent activity in the lower pH environment of vulvovaginitis, Antimicrob. Agents Chemother. 63 (2019), https://doi.org/10.1128/aac.02611-18.

[31] S.D. Rathod, P.A. Buffler, Highly-cited estimates of the cumulative incidence and recurrence of vulvovaginal candidiasis are inadequately documented, BMC Womens Health 14 (2014) 1–4.

[32] A.K. Sarpong, H. Odoi, Y.D. Boakye, V.E. Boamah, C. Agyare, C. Resistant, Albicans implicated in recurrent vulvovaginal candidiasis (RVVC) among women in a tertiary healthcare facility in Kumasi, Ghana, BMC Womens Health 24 (2024) 412.

[33] E. Otoo-Annan, V.E. Senoo-Dogbey, Recurrent Vulvovaginal Candidiasis: assessing the relationship between feminine/vaginal washes and other factors among Ghanaian women, BMC Public Health 24 (2024) 100.

[34] A. Chapple, Vaginal thrush: perceptions and experiences of women of South Asian descent, Health Educ. Res. 16 (2001) 9–19.

[35] Y.-X. Zhu, T. Li, S.-R. Fan, X.-P. Liu, Y.-H. Liang, P. Liu, Health-related quality of life as measured with the Short-Form 36 (SF-36) questionnaire in patients with recurrent vulvovaginal candidiasis, Health Qual. Life Outcome 14 (2016) 1–6.

[36] Y. Nguyen, A. Lee, G. Fischer, Quality of life in patients with chronic vulvovaginal candidiasis: a before and after study on the impact of oral fluconazole therapy, Australas. J. Dermatol. 58 (2017) e176–e181.

[37] M. Valentine, P. Rudolph, A. Dietschmann, A. Tsavou, S. Mogavero, S. Lee, E. L. Priest, G. Zhurgenbayeva, N. Jablonowski, S. Timme, Nanobody-mediated neutralization of candidalysin prevents epithelial damage and inflammatory responses that drive vulvovaginal candidiasis pathogenesis, mBio 15 (2024) e03409–e03423.

[38] J. Sobel, R. Sobel, Current treatment options for vulvovaginal candidiasis caused by azole-resistant *Candida* species, Expet Opin. Pharmacother. 19 (2018) 971–977.

[39] H.H. El-Houssaini, O.M. Elnabawy, H.A. Nasser, W.F. Elkhatib, Correlation between antifungal resistance and virulence factors in *Candida albicans* recovered from vaginal specimens, Microb. Pathog. 128 (2019) 13–19.

[40] C. Popp, B. Ramírez-Zavala, S. Schwanfelder, I. Krüger, J. Morschhäuser, Evolution of fluconazole-resistant *Candida albicans* strains by drug-induced mating competence and parasexual recombination, mBio 10 (2019), https://doi.org/10.1128/mbio.02740-18.

[41] S. Silva, C.F. Rodrigues, D. Araújo, M.E. Rodrigues, M. Henriques, *Candida* species biofilms' antifungal resistance, Journal of Fungi 3 (2017) 8.

[42] N.-N. Song, G.-Y. Qian, H.-L. Zheng, X.-W. Zhou, H. Mei, D.-M. Li, X.-F. Li, W.-D. Liu, Biofilm alterations on the stepwise acquisition of fluconazole-resistant *Candida albicans* isolates, International Journal of Dermatology and Venereology 5 (2022) 132–139.

[43] D.M. Lilly, R.H. Stillwell, Probiotics: growth-promoting factors produced by microorganisms, Science 147 (1965) 747–748.

[44] J. Suez, N. Zmora, E. Segal, E. Elinav, The pros, cons, and many unknowns of probiotics, Nat. Med. 25 (2019) 716–729.

[45] D. Wang, J. Yu, X. Lu, F. Dufaux, H. Guo, H. Guo, C. Zhu, Fast coding mode prediction for intra prediction in VVC SCC. International Conference on Image Processing (ICIP'2024), 2024.

[46] K.C. Anukam, E. Osazuwa, G.I. Osemene, F. Ehigiagbe, A.W. Bruce, G. Reid, Clinical study comparing probiotic Lactobacillus GR-1 and RC-14 with metronidazole vaginal gel to treat symptomatic bacterial vaginosis, Microb. Infect. 8 (2006) 2772–2776.

[47] J.D. Sobel, Pathogenesis and epidemiology of vulvovaginal candidiasis, Ann. N. Y. Acad. Sci. 544 (1988) 547–557.

[48] G. He, K. Xu, C. Wu, Z. Ma, X. Wen, M. Sun, Hybrid video coding scheme based on VVC and spatio-temporal attention convolution neural network. Proceedings of the IEEE/CVF Conference on Computer Vision and Pattern Recognition, 2022, pp. 1791–1794.

[49] L. Salinas-Muñoz, R. Campos-Fernández, E. Mercader, I. Olivera-Valle, C. Fernández-Pacheco, L. Matilla, J. García-Bordas, J.C. Brazil, C.A. Parkos, F. Asensio, Estrogen receptor-alpha (ESR1) governs the lower female reproductive tract vulnerability to *Candida* albicans, Front. Immunol. 9 (2018) 1033.

[50] R. Dantas-Medeiros, G.D. Marena, V.H.S. Araújo, F.D.a.B. Neto, A.C. Zanatta, N. P. Lopes, P. Bermejo, J.A. Guerra, L.M. Bedoya, B. Fonseca-Santos, A new hydrogel containing a proanthocyanidin polymer-rich extract of Commiphora leptophloeos for treating vulvovaginal candidiasis: preclinical results using the alternative model of Galleria mellonella, J. Drug Deliv. Sci. Technol. 85 (2023) 104531.

[51] S. Kaur, S. Kaur, Recent advances in vaginal delivery for the treatment of vulvovaginal candidiasis, Curr. Mol. Pharmacol. 14 (2021) 281–291.

[52] B. Gardela, C. Cassani, M. Dominoni, M.F. Pasquali, A. Spinillo, Maintenance pharmacological therapy of recurrent vulvovaginal candidiasis. A Bayesian network meta-analysis of randomized studies, Eur. J. Obstet. Gynecol. Reprod. Biol. 302 (2024) 310–316.

[53] R. Jeanmonod, V. Chippa, D. Jeanmonod, Vaginal Candidiasis. StatPearls [Internet], StatPearls Publishing, 2024.

[54] J.D. Sobel, P. Nyirjesy, Oteseconazole: an advance in treatment of recurrent vulvovaginal candidiasis, Future Microbiol. 16 (2021) 1453–1461.

[55] G.M. Dixon, J.S. Lewis, G.R. Thompson Iii, Pharmacokinetic evaluation of ibrexafungerp for the treatment of vulvovaginal candidiasis and beyond, Expet Opin. Drug Metabol. Toxicol. 20 (2024) 713–718.

[56] A. Gamal, S. Chu, T.S. Mccormick, K. Borroto-Esoda, D. Angulo, M.A. Ghannoum, Ibrexafungerp, a novel oral triterpenoid antifungal in development: overview of antifungal activity against *Candida glabrata*, Front. Cell. Infect. Microbiol. 11 (2021) 642358.

[57] J. Raposa, J.A. Vazquez, New pharmacotherapeutic strategies for drug-resistant *candida* infections: a review, Expet Opin. Pharmacother. 1–11 (2025).

[58] H.Y. Xie, D. Feng, D.M. Wei, L. Mei, H. Chen, X. Wang, F. Fang, Probiotics for vulvovaginal candidiasis in non-pregnant women, Cochrane Database Syst. Rev. 11 (2017) CD010496.

[59] R. Van Daele, I. Spriet, J. Wauters, J. Maertens, T. Mercier, S. Van Hecke, R. Brüggemann, Antifungal drugs: what brings the future? Med. Mycol. 57 (2019) S328–S343.

[60] S. Bhattacharya, S. Sae-Tia, B.C. Fries, Candidiasis and mechanisms of antifungal resistance, Antibiotics 9 (2020) 312.

[61] M. Satora, A. Grunwald, B. Zaremba, K. Frankowska, K. Żak, R. Tarkowski, K. Kułak, Treatment of vulvovaginal candidiasis—an overview of guidelines and the latest treatment methods, J. Clin. Med. 12 (2023) 5376.

[62] E.E. Ordaya, J. Clement, P. Vergidis, The role of novel antifungals in the management of Candidiasis: a clinical perspective, Mycopathologia 1–12 (2023).

[63] A. Gamal, A. Kadry, M. Elshaer, M.A. Ghannoum, Novel Antifungals for the Treatment of Vulvovaginal Candidiasis: where Are We?, 2022.

[64] N. Pérez-González, N. Bozal-De Febrer, A.C. Calpena-Campmany, A. Nardi-Ricart, M.J. Rodríguez-Lagunas, J.A. Morales-Molina, J.L. Soriano-Ruiz, F. Fernández-Campos, B. Clares-Naveros, New formulations loading caspofungin for topical therapy of vulvovaginal candidiasis, Gels 7 (2021) 259.

[65] P.G. Pappas, C.M. Rotstein, R.F. Betts, M. Nucci, D. Talwar, J.J. De Waele, J. A. Vazquez, B.F. Dupont, D.L. Horn, L. Ostrosky-Zeichner, Micafungin versus caspofungin for treatment of candidemia and other forms of invasive candidiasis, Clin. Infect. Dis. 45 (2007) 883–893.

[66] S.M.S. Ng, J.M. Yap, Q.Y. Lau, F.M. Ng, E.H.Q. Ong, T. Barkham, J.W.P. Teo, M. Alfatah, K.W. Kong, S. Hoon, Structure-activity relationship studies of ultra-short peptides with potent activities against fluconazole-resistant *Candida albicans*, Eur. J. Med. Chem. 150 (2018) 479–490.