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VULVOVAGINAL CANDIDIASIS: UPDATES ON DIAGNOSTIC AND TREATMENT APPROACHES

CANDIDÍASE VULVOVAGINAL: ATUALIZAÇÕES NAS FORMAS DE DIAGNÓSTICO E TRATAMENTO

CANDIDIASIS VULVOVAGINAL: ACTUALIZACIONES EN LAS FORMAS DE DIAGNÓSTICO Y TRATAMIENTO

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ABSTRACT

Vulvovaginal candidiasis (VVC) is one of the most frequent gynecological infections, affecting approximately 70% of women at some point in their lives and representing the second leading cause of vaginitis. It is mainly caused by Candida albicans; however, non-albicans species, which are more resistant to azoles, have increased in prevalence in recent decades, making clinical management more challenging. Clinically, VVC manifests with intense pruritus, burning sensation, dyspareunia, and thick white vaginal discharge. Despite its typical presentation, these symptoms have low predictive value and may be confused with other forms of vulvovaginitis, highlighting the need for laboratory confirmation. Diagnosis should include direct microscopy and mycological culture (gold standard), especially in recurrent or refractory cases. Molecular methods, such as PCR, have stood out for their high sensitivity and specificity, particularly in detecting non-albicans species, although they still face limitations related to cost and availability. VVC can be classified as uncomplicated (mild, sporadic episodes, usually caused by C. albicans and with good therapeutic response) or complicated, which includes resistant species, severe symptoms, pregnancy, comorbidities, immunosuppression, and recurrent vulvovaginal candidiasis (RVVC), defined as ≥4 episodes within one year. Treatment of uncomplicated VVC may be carried out with topical antifungals or oral fluconazole, both showing similar cure rates. In recurrent cases, prolonged fluconazole therapy is recommended (induction followed by maintenance for six months). The emergence

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of azole resistance has stimulated the development of new antifungal agents, such as ibrexafungerp. Partner treatment is only indicated when symptoms are present. VVC negatively impacts quality of life, affecting self-esteem, sexuality, and mental health, reinforcing the importance of accurate diagnosis, professional guidance, and individualized management. The article concludes that laboratory and therapeutic updates are essential to reduce recurrences and improve treatment effectiveness.

Keywords: *Candida albicans*. Non-albicans Candida. Antifungal Resistance. Updated Therapeutic Review. Advanced Differential Diagnosis.

RESUMO

A candidíase vulvovaginal (CVV) é uma das infecções ginecológicas mais frequentes, afetando cerca de 70% das mulheres em algum momento da vida e representando a segunda maior causa de vaginite. É causada principalmente pela Candida albicans, embora espécies não-albicans, que são mais resistentes aos azólicos, tenham aumentado nas últimas décadas, dificultando o manejo clínico. Clinicamente, manifesta-se por prurido intenso, ardor, dispareunia e corrimento branco espesso. Apesar da apresentação típica, esses sintomas possuem baixo valor preditivo, podendo ser confundidos com outras vulvovaginites, o que mostra a necessidade de confirmação laboratorial. O diagnóstico deve incluir microscopia direta e cultura micológica (padrão-ouro), especialmente nos casos recorrentes ou refratários. Métodos moleculares, como PCR, têm se destacado pela alta sensibilidade e especificidade, sobretudo na detecção de espécies não-albicans, embora ainda tenham limitações relacionadas ao custo e disponibilidade. A CVV pode ser classificada em não complicada (quadros leves, esporádicos, geralmente por C. albicans e com boa resposta terapêutica) ou complicada, incluindo espécies resistentes, sintomas intensos, gestação, comorbidades, imunossupressão e candidíase vulvovaginal recorrente (CVVR), definida como ≥4 episódios em um ano. O tratamento da forma não complicada pode ser feito com antifúngicos tópicos ou fluconazol oral, ambos com taxas de cura semelhantes. Nos casos recorrentes, indica-se terapia prolongada com fluconazol (indução e manutenção por 6 meses). A emergência de resistência aos azólicos tem estimulado o desenvolvimento de novos antifúngicos, como o ibrexafungerp. O tratamento do parceiro só é indicado se houver sintomas. A CVV impacta negativamente a qualidade de vida, afetando autoestima, sexualidade e saúde mental, reforçando a importância de diagnóstico adequado, orientação profissional e manejo individualizado. O artigo conclui que as atualizações laboratoriais e terapêuticas são fundamentais para reduzir recidivas e melhorar a eficácia do tratamento.

Palavras-chave: *Candida albicans*. Candida Não-Albicans. Resistência Antifúngica. Revisão Terapêutica Atualizada. Diagnóstico Diferencial Avançado

RESUMEN

La candidiasis vulvovaginal (CVV) es una de las infecciones ginecológicas más frecuentes, afectando aproximadamente al 70% de las mujeres en algún momento de su vida y representando la segunda causa principal de vaginitis. Está causada principalmente por Candida albicans; sin embargo, las especies no-albicans, que presentan mayor resistencia a los azoles, han aumentado en las últimas décadas, dificultando el manejo clínico. Clínicamente, se manifiesta por prurito intenso, ardor, dispareunia y flujo vaginal blanco espeso. A pesar de su presentación típica, estos síntomas tienen bajo valor predictivo y pueden confundirse con otras vulvovaginitis, lo que pone de manifiesto la necesidad de confirmación de laboratorio. El diagnóstico debe incluir microscopía directa y cultivo micológico (patrón oro), especialmente en los casos recurrentes o refractarios. Los métodos moleculares, como la PCR, se han destacado por su alta sensibilidad y especificidad, sobre todo en la detección de especies no-albicans, aunque aún presentan limitaciones

relacionadas con el costo y la disponibilidad. La CVV puede clasificarse en no complicada (cuadros leves, esporádicos, generalmente causados por C. albicans y con buena respuesta terapéutica) o complicada, que incluye especies resistentes, síntomas intensos, embarazo, comorbilidades, inmunosupresión y candidiasis vulvovaginal recurrente (CVVR), definida como ≥4 episodios en un año. El tratamiento de la forma no complicada puede realizarse con antifúngicos tópicos o fluconazol oral, ambos con tasas de curación similares. En los casos recurrentes, se indica terapia prolongada con fluconazol (inducción y mantenimiento durante seis meses). La aparición de resistencia a los azoles ha estimulado el desarrollo de nuevos antifúngicos, como el ibrexafungerp. El tratamiento de la pareja solo está indicado si presenta síntomas. La CVV impacta negativamente la calidad de vida, afectando la autoestima, la sexualidad y la salud mental, lo que refuerza la importancia de un diagnóstico adecuado, orientación profesional y manejo individualizado. El artículo concluye que las actualizaciones laboratoriales y terapéuticas son fundamentales para reducir las recurrencias y mejorar la eficacia del tratamiento.

Palabras clave: *Candida albicans*. Candida no-albicans. Resistencia Antifúngica. Revisión Terapéutica Actualizada. Diagnóstico Diferencial Avanzado.

1 INTRODUCTION

Vulvovaginal candidiasis is one of the most common gynecological infections, observed among women around the world, where about 70% of the entire female population will have at least one episode of the disease during their reproductive life, which is why it is considered the second leading cause of vaginitis. Its pathology is characterized by an acute inflammatory condition of the vulva and vaginal mucosa, induced by the overgrowth of yeasts of the genus Candida, especially the species Candida albicans (CRUZ *et al.*, 2020). Although CVV is not considered a condition of clinical severity, its impact on women's well-being and quality of life is significant, due to the discomfort generated by the symptoms (ELIAS *et al.*, 2023). Clinically, it is manifested by intense vulvar itching, burning, thick white discharge and dyspareunia, and can cause important physical and psychological repercussions.

The species Candida albicans is the main responsible for vulvovaginal candidiasis, corresponding to more than 90% of acute episodes, and most strains are sensitive to azole antifungals. However, other species, such as *Candida glabrata, C. tropicalis, C. krusei, and C. parapsilosi,* which emerged in the last two decades, have been increasingly associated with infection, showing greater resistance to azoles and contributing to the difficulty in clinical management (AMORIM, 2024). Thus, the growing resistance among non-albicans species has resulted in therapeutic failures and the need for longer treatments. In this context, laboratory diagnosis becomes essential for the precise identification of the species involved and for the rational choice of antifungal therapy.

CVV has a high prevalence and is one of the most frequent reasons for gynecological consultations, so that it affects approximately 138 million women annually and that about 500 million women have at least one episode throughout their lives, with an annual global prevalence of 3,871 cases per 100,000 women (RÓSATE *et al.*, 2020). According to Lírio et al. (2022), when three or more episodes of CVV occur in a period of 1 year, the condition is classified as recurrent vulvovaginal candidiasis (CVVR), which falls within the complicated form of the disease. Several factors are implicated in the predisposition and recurrence of the infection, including pregnancy, prolonged use of antibiotics, inadequate eating habits, intestinal colonization by *Candida*, use of tight underwear or synthetic material, inadequate hygiene practices, and immunological alterations. In addition to these, in recurrent vulvovaginal candidiasis, a history of bacterial vaginosis, corticosteroid therapy, diabetes mellitus (DM), and the use of hormonal contraceptives also stand out as additional risk factors (PEREIRA EPR, et al., 2022).

In view of this, CVV remains a relevant clinical challenge, especially in the face of changes in epidemiological patterns and the emergence of strains resistant to conventional

antifungals. Understanding the new diagnostic and therapeutic approaches is essential for the proper management of the disease and for the reduction of recurrences. In recent decades, there has been a significant advance in laboratory techniques, favoring more targeted therapeutic approaches (AMORIM, 2024; LÍRIO et al., 2022). At the same time, new pharmacological options, such as combined topical formulations and long-acting antifungals, have been investigated for cases of resistance or recurrence (PEREIRA et al., 2022). In view of this scenario, the constant updating of health professionals is indispensable, since knowledge about the etiological agents, resistance mechanisms, and therapeutic alternatives is essential to ensure the accurate diagnosis and effective treatment of this prevalent infection.

Thus, this study aimed to perform a narrative review of the latest updates on the diagnosis and current treatment of vulvovaginal candidiasis.

2 CLINICAL ASPECTS

The classic clinical picture of vulvovaginal candidiasis is marked by an important local inflammatory symptomatology of intense pruritus, dysuria and dyspareunia associated with white, thick, lumpy, non-foul-smelling leucorrhoea. (WILLEMS et al., 2020; BALAKRISHNAN et al., 2022; VAN RIEL et al., 2021). Clinical signs can commonly include vulvar edema, hyperemia, and fissures (CRUZ G et al., 2020). It is often observed that the symptoms of CVV, especially itching and burning, tend to intensify in the premenstrual period, probably due to hormonal fluctuations and temporary changes in the vaginal microbiota associated with the menstrual cycle. (Nyirjesy et al., 2022; Sun et al., 2023; Oerlemans et al., 2022). A recent study showed that even considering the classic triad of itching, burning, and discharge, the presence of these signs has a low positive predictive value for vulvovaginal candidiasis (PEREIRA et al., 2021). Thus, the described clinical condition may be present in a similar way in other causes of vulvovaginitis, such as bacterial vaginosis and non-infectious etiologies such as vulvar dermatitis and hypersensitivity reactions, which reinforces the need for complementary tests to confirm the diagnosis (CRUZ G et al., 2020).

The clinical presentation of CVV can vary between two main classifications, namely: uncomplicated CVV, with C. albicans as the etiological agent, with typical, mild to moderate symptoms in isolated or infrequent episodes, and with good response to treatment, in the absence of comorbidities; and complicated CVV, with non-albicans etiological agent, intense symptoms, or in the presence of comorbidities, immunosuppression, or pregnancy, which tend to evolve with recurrence, defined by the occurrence of 4 or more episodes in a 12-month period (CARVALHO et al., 2021). Most cases encompass the concept of

uncomplicated CVV, while the complicated form covers 10 to 20% of complaints, and today recurrent vulvovaginal candidiasis (CVVR) is considered a significant health problem among women of reproductive age, with a prevalence of 7% for women aged 15 to 54 years, specified at 5.4% for the age group of 15 to 24 years, with the highest prevalence (9%) observed for the 25-34 age group. The data obtained point to estimates that the number of women affected annually exceeds 130 million worldwide, with a projection that this population will reach approximately 158 million by 2030 (Balakrishnan et al., 2022; Dermendzhiev et al., 2022; Van Riel et al., 2021).

The inaccurate clinical diagnosis of CVV, without confirmation by laboratory tests, has been pointed out as one of the main factors that contribute to the persistence and recurrence of the disease. Recent studies show that empirical management, based only on symptoms, often results in diagnostic errors and inadequate treatments, which makes it difficult to control the infection and favors its chronicity (Benedict *et al.*, 2022). According to Donders *et al.* (2022), the absence of confirmatory methods, such as microscopy, culture, and species identification, compromises therapeutic effectiveness and increases the risk of treatment failures, especially in cases involving *non-albicans* species or antifungal resistance. In consonance, the recommendations of the International Society for the Study of Vulvovaginal Disease (ISSVD, 2023) emphasize that diagnostic confirmation is essential before initiating therapy, in order to avoid inappropriate use of antifungals and reduce the recurrence of infection.

Current evidence points to the factor of self-medication as a phenomenon that is also common and relevant because it contributes to a greater probability of recurrence or evolution to a chronic condition. In a recent review on rapid molecular diagnosis, Donders et al. (2022) observed that only 11% of women were able to correctly identify the infection, and even among those with previous episodes, the success rate did not exceed 35%, demonstrating the low reliability of self-diagnosis. These findings show that the self-diagnosis of vulvovaginal candidiasis has very limited accuracy and is an important factor for the inappropriate use of antifungals and consequent therapeutic failures. Corroborating this perspective, recent epidemiological studies show that a significant portion of women resort to over-the-counter antifungals without a medical prescription, reinforcing the need for professional guidance for the proper management of the infection (Benedict et al., 2022; Andrade et al., 2025).

Given its epidemiological and clinical relevance, it is also important to highlight that the impact of candidiasis extends to the physical, psychological, and social spheres, with damage to self-esteem, intimate relationships, and the ability to perform daily activities with confidence. A profound effect on the quality of life of affected women with additional systemic

symptoms, such as clinical worsening of depression and anxiety, was also evidenced (WILLEMS et al., 2020; BALAKRISHNAN et al., 2022; VAN RIEL et al., 2021).

3 DIAGNOSIS

According to Neal and Martens (2022), the diagnosis of vulvovaginal candidiasis is initially based on the clinical evaluation of symptoms and physical examination. Typical clinical manifestations with pruritus and vaginal discharge, dysuria, burning and dyspareunia associated with a compatible gynecological examination, showing the presence of white, milky plaques in the vaginal cavity are frequently observed. (VIEIRA-BAPTISTA; STOCKDALE; SOBEL, 2023). However, these manifestations are nonspecific and may overlap with other forms of vulvovaginitis and infectious vaginosis, such as bacterial vaginosis and trichomoniasis, which makes the exclusively clinical evaluation insufficient for a definitive diagnosis (DIAS; CASTRO; NUNES MOSQUE; VITÓRIA, 2025). This symptomatic similarity may result in underdiagnosis or overdiagnosis, negatively impacting therapeutic management. Therefore, laboratory confirmation is recommended, especially in recurrent, refractory, or atypical cases, through tests such as microscopy and fungal culture, which allow the identification of the species involved and the detection of strains resistant to azole antifungals. These tests are essential, since women with recurrent CVV are more likely to be infected by non-albicans species. (NEAL; MARTENS, 2022)

Direct microscopy, a direct mycological examination, is a simple, fast and low-cost method, widely used in the laboratory screening of vulvovaginal candidiasis. By observing samples collected from the vaginal walls with an Ayre spatula or SWAB, prepared with saline solution and 10% potassium hydroxide (KOH), it is possible to visualize characteristic fungal structures, such as blastoconidia and pseudohyphae (ESPINHEIRO et al., 2022). However, its sensitivity is limited, ranging between 40% and 70% and can be reduced especially in the presence of non-albican species, such as *Candida glabrata*, which do not form hyphae or pseudohyphae (NEAL; MARTENS, 2022). For diagnostic confirmation and identification of the species involved, mycological culture is recommended, considered the gold standard among traditional methods, and is commonly performed in Sabouraud medium or in CHROMagar Candida, which allows the differentiation of species by the coloration pattern of the colonies (SATORA et al., 2023). Such testing is especially important in cases of recurrent CVV, treatment failure, or suspected non-albican species, as it enables accurate identification and directs appropriate antifungal treatment. However, this method has limitations, such as prolonged processing time (usually 48 to 72 hours) and laboratory

costs, which can delay the start of therapy and restrict its use in some health services (SATORA et al., 2023).

In recent years, there has been a significant growth in the use of molecular techniques as an alternative to traditional methods of mycological diagnosis. Polymerase chain reaction (PCR) is an example of this, presenting itself as a method of greater sensitivity and specificity, allowing the rapid and simultaneous detection of multiple pathogens, which is especially advantageous in cases of co-infection and infections caused by non-albicans species (SATORA et al., 2023). In a recent study, CRP demonstrated a sensitivity of 90.9% and specificity of 94.1% for detecting CVV, while for C. glabrata these values were 75.9% and 99.7%, evidencing its enhanced diagnostic potential (SATORA et al., 2023). Even so, this technique faces limitations related to cost and availability, factors that restrict its routine application. Despite this, the incorporation of molecular methods represents an advance for the rapid and accurate diagnosis of Candida vulvovaginitis, contributing to the appropriate therapeutic choice and to reducing the risk of antifungal resistance, in this sense, it is important that future studies focus on improving these tests (SATORA et al., 2023).

The interpretation of test results should be performed in correlation with the clinical symptoms presented (NEAL; MARTENS, 2022). In addition, it is critical to consider the most common differential diagnoses, including bacterial vaginosis, contact dermatitis, infectious virus-induced vulvovaginitis (KYEI; MARFO; BOAKYE, 2021), atrophic vaginitis, trichomoniasis, psoriasis, and lichen sclerosus, among other inflammatory vaginitis (HEINONEN et al., 2021). Recent research has explored preventive strategies such as the development of targeted vaccines against hyphal virulence factors of Candida albicans, which have shown promising results in early studies (DONDERS et al., 2022). This shows that continuous advances in research and constant updating of clinical practices are essential to improve the management of vulvovaginal candidiasis.

4 TREATMENT

The management of vulvovaginal candidiasis has three central goals: rapid relief of symptoms (itching, burning, discharge), eradication of the causative agent, and prevention of clinically significant recurrences. Therapeutic selection should be individualized according to the severity of the condition, the frequency of episodes, and the patient's profile (comorbidities, medication use, preference) (Denison *et al*., 2020). In uncomplicated infections, evidence from systematic reviews and meta-analyses shows that both topical (intravaginal) and oral therapies achieve high clinical and mycological cure rates, with no consistent difference in main outcomes, which allows the route to be chosen according to

availability, tolerability, and patient preference. In addition, it is mandatory to identify and correct predisposing factors (recent use of antibiotics, uncontrolled diabetes, synthetic/tight clothing, aggressive intimate hygiene, hormonal changes) to reduce the risk of recurrence. (Sun *et al*., 2023; Elias *et al.*, 2023).

Even in women who are not sexually active, vulvovaginal candidiasis can occur as a result of imbalances in the vaginal microbiota and hormonal or metabolic changes that modify the pH and local microbial composition. The vaginal microbiome varies between individuals, and these differences are influenced by factors such as menstrual hygiene habits, douching use, chronic stress, and socioeconomic conditions, regardless of sexual activity (Frontiers in Cellular and Infection Microbiology, 2023). In these cases, topical therapy with azole antifungals (clotrimazole, miconazole) or nystatin, in short regimens of 3 to 7 days, is generally effective and well tolerated, with a lower risk of systemic effects and drug interactions (Satora, 2023). In addition to drug treatment, it is recommended to investigate and correct possible predisposing factors, such as diabetes mellitus, recent use of antibiotics, clothing that is too tight, and excessive intimate hygiene, also providing guidance on self-care and prevention of recurrences (CDC, 2021; Frontiers in Cellular and Infection Microbiology, 2023).

In sexually active women with uncomplicated acute vulvovaginal candidiasis, oral regimens of single-dose fluconazole 150 mg have demonstrated slightly superior efficacy to multi-day topical therapy in early clinical cure (Gardella et al, 2025). Alternatively, topical antifungals such as clotrimazole 500 mg as a single dose may be used. In cases of recurrent vulvovaginal candidiasis, an induction regimen with fluconazole 150 mg on days 1, 4, and 7 is recommended, followed by weekly maintenance for 6 months, with adjustments depending on the species of Candida and susceptibility to azoles (Neal et al, 2022). It is important to emphasize that the treatment of the partner is not routinely indicated, being recommended only when the partner has symptoms compatible with balanitis or symptomatic candidiasis. (CDC, 2021).

Recently, ibrexafungerp, a novel non-azole oral antifungal, was approved by the FDA for the treatment of CVVR, showing clinical and mycological cure rates superior to placebo, with single monthly administration to reduce the incidence of recurrent episodes, offering an oral alternative for severe or resistant cases (Phillips et al, 2023).

In pregnancy, the approach of choice for vulvovaginal candidiasis is topical azole therapy (e.g., clotrimazole, miconazole) for 7 days, as it has proven efficacy and adequate placental safety; systemic oral therapies such as fluconazole are avoided in pregnancy due to potential fetal risks reported in epidemiological studies and should therefore only be

considered in exceptional situations under expert evaluation (CDC, 2021). Completion of the prescribed regimen is essential to reduce the chance of persistence or recurrence and to minimize possible obstetric complications associated with vaginal infection.

5 CONCLUSION

CVV remains one of the most relevant gynecological infections in gynecological practice, both due to its prevalence and the diagnostic and therapeutic challenges that still persist, especially due to the increase in non-albicans species and the growing resistance to azoles. Improving the understanding of the pathogenesis, the behavior of the vaginal microbiome, and the predisposing factors have allowed a more targeted approach, but diagnostic errors resulting from exclusively clinical evaluation are still frequent. In this scenario, laboratory methods, especially microscopy, culture, and molecular techniques, are consolidated as fundamental tools for accurate diagnosis, especially in recurrent, refractory, or atopic cases.

At the same time, the developments of new therapeutic strategies, such as non-azole antifungals, prolonged regimens, and emerging vaccine research, offer promising prospects for the management of complicated and recurrent forms. The integration between assertive diagnosis, individualized therapies, and continuous updating of professionals is essential to reduce recurrences, improve clinical outcomes, and mitigate the physical and psychosocial impact of the disease. Thus, understanding and incorporating these advances is crucial to ensure more effective and evidence-based care for women affected by this prevalent infection.

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