Vulvovaginitis in pregnant women: A systematic review from 2018 to 2023

https://doi.org/10.56238/levv15n40-030

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ABSTRACT

Objective: To evaluate the prevalence of vulvovaginitis in pregnant women through a comprehensive review of the existing literature. Methodology: A systematic review was carried out based on the question: "What is the prevalence of vulvovaginitis in pregnant women?" Original and quantitative studies addressing vulvovaginitis in pregnant women, published between 2018 and 2023, in English, complete and free of charge, were included. The search was performed in the PubMed database in July 2023, using the terms: Vulvovaginitis AND pregnant women. Results: A total of 62 articles were identified, of which 57 were excluded because they did not meet the inclusion criteria: 36 did not have vulvovaginitis as the main focus, 14 were not related to pregnant women, and 7 did not provide relevant data. After screening, 11 articles were read in full and 5 were selected for the systematic review. Conclusion: Despite existing guidelines for the diagnosis and treatment of vulvovaginitis, it is essential to strengthen prevention among pregnant women by raising awareness about the most prevalent diseases, signs, symptoms, and risk factors.

Keywords: Pregnancy, Vulvovaginitis, Pregnancy complications.

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INTRODUCTION

The changes in a woman's body during pregnancy are caused by a series of hormonal and mechanical factors and can be generalized or localized in the genital area (Gonçalves AK, et al., 2014).

For Giraldo PC, et al. (2014), color changes, edema, and vulvovaginal softening of the genital area can be observed due to increased vascularization of the uterus, vagina, and vulva, as well as venous vasodilation, resulting in more exudate in the vaginal cavity. These modifications favor the maintenance of vulvar moisture and promote changes in the ecosystem of the reproductive tract. The growth of the uterus can prevent venous drainage in the lower part of the body, leading to increased accumulation of oxygenated blood in the genital area.

Pregnancy is characterized by important changes that favor full fetal growth, such as hormonal, immunological and metabolic changes (CLEMENTE *et al*., 2012). According to Gonçalves *et al*. (2014), several changes that occur in a woman's body during pregnancy, combined with changes in the genital organs, favor the development of vulvovaginitis.

As corroborated by Cardoso RM, et al. (2017), vulvovaginitis, characterized by infection or inflammation of the vaginal canal, can directly lead to pregnancy complications, such as premature labor, premature rupture of membranes, low birth weight, miscarriage, neonatal death, inflammation of the fetal membrane, in addition to increasing the risk of transmission of acquired immunodeficiency virus (HIV) and other sexually transmitted infections (STIs). The main pathogens that can cause such inflammatory/infectious processes are fungi, bacteria, and protozoa. Among the most common types of vulvovaginitis during pregnancy, bacterial vaginosis, candidiasis, and trichomoniasis stand out (FEBRASCO, 2010).

The infectious process caused by vulvovaginitis is one of the public health diseases that affect women due to the ease of transmission and negative impact on women's health (CARDOSO RM, et al., 2017).

According to the studies by Gigi RMS, et al. (2023), microorganisms in the female genital tract can have a direct pathogenic effect on pregnancy through intra-amniotic infection and/or stimulation of the inflammatory cascade. In addition to prostaglandins, chemokines and pro-inflammatory cytokines can also mature the cervix and induce contractions. These pathways can be activated by infection during pregnancy and lead to preterm birth. Fungal infections in the female genital tract cause inflammation that increases pro-inflammatory mediators in vaginal fluid, such as interleukin 8, which has been linked to preterm birth.

For Nunes RD, et al. (2018), genital discomfort during pregnancy is not uncommon. Almost all pregnant women experience vaginal discharge, odor and/or itching, burning and pain during sexual intercourse.

Taking into account these factors and knowing the factors that favor the development of vulvovaginitis during pregnancy, this study aims to determine the prevalence of vulvovaginitis in pregnant women based on existing studies through a comprehensive evaluation.

METHODS

This is a systematic review that seeks to describe and synthesize the existing evidence on vulvovaginitis in pregnant women, using retrospective studies. For the development of this research, a guiding question was elaborated through the PVO (population, variable and objective) strategy: "What is the prevalence and factors associated with vulvovaginitis in pregnant women?"

The searches were carried out in July 2023, using the PubMed database. Two descriptors were used in combination with the Boolean term "AND": Vulvovaginitis and Pregnant Women. The search strategy used was: Vulvovaginitis AND Pregnant Women. From this search, 62 articles were found, which were subsequently submitted to the selection criteria. The inclusion criteria were: (1) original and quantitative articles, excluding editorials, letters to the editor, theoretical articles, case studies, and qualitative studies; (2) the research subjects were pregnant women with vulvovaginitis; (3) complete and freely available articles; (4) published between 2018 and 2023 in English.

After applying the inclusion and exclusion criteria, 57 articles were eliminated: 36 because they did not have vulvovaginitis as the main subject, 14 because they were not related to pregnant women, and 7 because they did not provide relevant data for the study. After careful reading of the remaining 11 articles, 5 were selected to compose the systematic review.

RESULTS

Chart 1 presents the results of a systematic review of five articles selected to better present the data and answer the central question. The articles will be presented in chronological order.

1. In 2023, authors Ranjana M S Gigi, Diana Buitrago-Garcia,Katayoun Taghavi, Cara-Mia Dunaiski, Janneke H H M van de Wijgert, Remco P H Peters, Nicola Low, investigated the associations between symptomatic and asymptomatic vulvovaginal fungal

infections in pregnancy and perinatal outcomes. 3909 references were selected and 57 studies were included. Only 22/57 studies reported information about the participant's vulvovaginal symptoms. Preterm birth was an outcome in 35/57 studies (49,161 women). There was no strong statistical evidence of an increased risk of preterm birth or other adverse perinatal outcomes in pregnant women with symptomatic or asymptomatic vulvovaginal yeast infection.

2. The researchers, Cara Mulinganya, Annelies de Vulder, Ghislain Bisimwa, Jerina Boelens, Geert Claeys, Karen de Keyser, Daniel De Vos, Erick Hendwa, Freddy Kampara, Yvette Kujirakwinja, Jules Mongane, Mubalama Inocente, Mario Vaneechoutte, Steven Callens, Piet Esfresque (2021), investigated the prevalence of bacterial vaginosis (BV), risk factors, and the association between bacterial vaginosis and adverse pregnancy outcomes in a population of pregnant women from Bukavu, DRC. The prevalence of BV was 26.3% and approximately half of the women were asymptomatic. The prevalence of BV in Bukavu is high, but according to the global average, it was associated with adverse pregnancy outcomes in the study population.

3. Nahed Ghaddar, Elie Anastasiadis, Rawad Halimeh, Ali Ghaddar, Rita Dhar, Wadha AlFouzan, Hoda Yusef, Mira El Chaar in 2020, determined the prevalence of candida species in symptomatic pregnant women and evaluated the antifungal susceptibility profile of isolated Candida strains. Among 258 women tested, 100 (39%) were positive for Candida species. C. albicans, C. glabrata and C. krusei were isolated from 42, 41 and 17% of the women, respectively. The current study revealed a high incidence of C. albicans and non-C strains. Candida albicans causing vulvovaginitis among pregnant women in Beirut, Lebanon.

4. According to the study by authors Dennis Gyasi Konadu, Alex Owusu-Ofori, Zuwera Yidana, Farrid Boadu, Louisa Fatahiya Iddrisu, Dennis Adu-Gyasi, David Dosoo, Robert Lartey Awuley, Seth Owusu-Agyei, Kwaku Poku Asante (2019), determined the prevalence of vulvovaginal candidiasis (CVV), bacterial vaginosis (BV), and trichomoniasis (VT) in pregnant women attending the antenatal clinic at the Kintampo Municipal Hospital. The prevalence of vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis was 36.5, 30.9, and 1.4%, respectively. Women with more than four previous pregnancies (OR: 0.27, 95% CI: 0.13-0.58) and those in the third trimester of pregnancy (OR: 0.54, CI: 0.30-0.96) were associated with a lower risk of bacterial vaginosis. The prevalence of vaginal infections was high among pregnant women in the Kintampo area. There is a need for interventions such as proper investigations and early treatment of vaginal infections to reduce the burden of disease and prevent associated complications.

5. As for the study by Nahed Ghaddar, Ali El Roz, Ghassan Ghssein, José-Noel Ibrahim (2019), determined the prevalence and risk factors of vulvovaginal candidiasis (CVV) in pregnant women at 35-37 weeks gestation. VVC was detected in 44.8% of the samples, with *C. glabrata* (44.4%) and *C. albicans* (43.4%) being the most isolated species. Approximately, half of the pregnant women (57.7%) were co-infected with *Candida* and bacterial vaginosis, while 26% of them were simultaneously carrying *Candida* spp. In contrast, participants with previous miscarriages and those hospitalized during the past 12 months were more susceptible to developing vaginal C*. krusei* infection compared to other *Candida* species(p=0.316 and p=0.0042, respectively). Routine medical examination and regular screening for candidiasis in the antenatal care program are highly recommended to manage the disease and its complications.

Table 1. Main results of the included studies

Authors	Country	Title	Objectives	Methods	Results
Gigi RMS, et al. (2023).	Switzerland	Vulvovaginal yeast infections during pregnancy and perinatal outcomes: systematic review and meta-analysis	To investigate associations between symptomatic and asymptomatic vulvovaginal fungal infections in pregnancy and perinatal outcomes	We conducted a systematic review and searched eight databases up to July 1, 2022. We included studies reporting pregnant women with and without laboratory-confirmed vulvovaginal yeast infection and preterm birth or eight other perinatal outcomes.	Preterm birth was an outcome in 35/57 studies (49,161 women). In 32/35 studies with available data, the OR of univariate analyses was 1.01 (95% CI 0.84-1.21, I2 60%, prediction range 0.45-2.23).
Mulingany a G, et al. (2021).	Democratic Republic of the Congo	Prevalence, risk factors, and adverse pregnancy outcomes of second-trimester bacterial vaginosis among pregnant women in Bukavu, Democratic Republic of the Congo.	To investigate BV prevalence, risk factors, and the association between BV and adverse pregnancy outcomes in a population of pregnant women from Bukavu, DRC	A total of 533 pregnant women in the second trimester of pregnancy were recruited from the Provincial Referral Hospital of Bukavu, DRC, between January and October 2017, and followed until delivery.	The prevalence of BV was 26.3% and approximately half of the women with BV were asymptomatic.
Ghaddar N, et al. (2020).	Lebanon	Prevalence and antifungal susceptibility of Candida albicans causing vaginal discharge among pregnant women in Lebanon.	It determined the prevalence of candida species in symptomatic pregnant women and assessed the antifungal susceptibility profile of isolated Candida strains, and explored whether Candida species	A total of 258 pregnant women with vaginal discharge at 35 to 37 weeks of gestation participated in this study. The vaginal swabs of these patients were collected from various obstetrics and gynecology	Among 258 women tested, 100 (39%) were positive for Candida species. C. albicans, C. glabrata and C. krusei were isolated from 42, 41 and 17% of the women, respectively.

			predict gestational complications and adverse neonatal outcomes.	clinics in Lebanon over a period of 14 months.	
Konadu DG, et al. (2019).	Ghana	Prevalence of vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis in pregnant women attending antenatal clinic in Ghana's mid-belt.	To determine the prevalence of vulvovaginal candidiasis (VVC), bacterial vaginosis (BV), and trichomoniasis (VT) in pregnant women attending the antenatal clinic at the Municipal Hospital of Kintampo.	The study adopted a cross-sectional design and recruited 589 pregnant women after seeking their informed consent from September 2014 to March 2015. A semi-structured questionnaire was administered to the participants and vaginal swabs were collected.	The overall prevalence of at least one vaginal infection was 56.4%. The prevalence of vulvovaginal candidiasis, bacterial vaginosis, and trichomoniasis was 36.5, 30.9, and 1.4%, respectively.
Ghaddar N, et al. (2019).	Lebanon	Emergence of Vulvovaginal Candidiasis Among Lebanese Pregnant Women: Prevalence, Risk Factors, and Species Distribution.	To determine the prevalence and risk factors of vulvovaginal candidiasis (VVC) in pregnant women at 35-37 weeks' gestation.	Over a period of one year, tall vaginal swabs were collected from pregnant women during their regular antenatal check-up at different polyclinics in Beirut and southern Lebanon.	Half of the pregnant women (57.7%) were co-infected with *Candida* and bacterial vaginosis, while 26% of them simultaneously carried *Candida* spp. and GBS.

Source: Prepared by the authors

DISCUSSION

Vulvovaginitis and vaginosis are disorders of the stratified epithelium of the vulva and/or vagina, whose most common etiology, in addition to the protozoan *Trichomonas*, also involves a high number of fungi and anaerobic bacteria (FEBRASGO, 2010). The common signs and symptoms of these conditions are vaginal discharge, which can vary in number, color, and appearance; itching; tingling and/or burning; and, depending on the cause, dysuria and dyspareunia (LINHARES IM, et al., 2018).

Mulinganya G, et al. (2021) report that genital infection has become a frequent concern during pregnancy because it may be associated with an increased risk of adverse obstetric and perinatal outcomes. Preterm birth (PTP) accounts for 60% to 80% of newborn deaths, and survivors may develop sequelae during development. The risk of PPT increases by 30% to 50% if there is a genital infection.

The female genital area has its own characteristics in terms of immune response because, if it had oral or intestinal mechanisms, there would be no conception. Thus, the cervicovaginal canal is more tolerant to foreign proteins and more dependent on the balance of the ecosystem to maintain the homeostasis of the environment. During pregnancy, there is marked immunological regulation that can favor receptive conception,

but can also predispose the maternal body to viral and fungal infections. There seem to be four hypotheses for fetal non-rejection (WITKIN SS, 2019):

1. Neutral fetus.
2. The placenta acts as a barrier that separates the mother from the fetus.
3. Privileged immune uterus.
4. Physiological immunosuppressive status in pregnant women.

Vulvovaginal fungal infections are common during pregnancy and can cause widespread inflammation that can lead to poor perinatal outcomes. Preterm birth is the most common cause of neonatal death worldwide. Causes of preterm birth include socioeconomic factors, underlying maternal conditions, fetal status, and infectious causes (Gigi RMS, et al., 2023). Infectious causes include upper genital tract infection and possibly lower genital tract infection, and some evidence suggests that early preterm birth is more commonly associated with infection than late preterm birth. Vulvovaginal yeast infections caused by Candida are more common in pregnant women than in non-pregnant women, possibly due to hormonal and immune changes that occur during pregnancy. It is unclear whether yeast burden is higher in pregnant women than in non-pregnant women, or whether they are related to inflammation levels or adverse perinatal outcomes (Chatzivasileiou P, Vyzantiadis TA, 2019).

BACTERIAL VAGINOSIS (VB) AND PREGNANCY

BV is a polymicrobial syndrome that occurs due to a reduction in Lactobacillus species and is associated with an overgrowth of facultative anaerobic bacteria; it is characterized by fishy-smelling vaginal discharge when 10% potassium hydroxide (KOH) is added to the presence of *clue cells*, little or no lactobacillus present, and little or no polymorphonuclear leukocyte (KAMGA, et al., 2019).

According to FEBRASGO (2010), the clinical and microbiological diagnostic criteria are the same for pregnant and non-pregnant women, following the Amsel criteria adopted since 1983, which consider the presence of at least three of the following signs: pH greater than 4.5, the Whiff test is positive, uniform whitish vaginal discharge adhered to the upper vaginal wall, and *Clue cells* are present in more than 20% of the area in bacterioscopy/microscopy.

In addition to the standard clinical methods of Amsel, there is the Nugent score, which consists of methods adopted for laboratory diagnosis and is considered the gold standard. Lactobacillus morphotype, Gardnerella using Gram staining. and Mobiluncus spp.

appears on the blade and gets points for it. If this score is equal to or greater than 7, consider the diagnosis of BV (CAMPOS *et al*., 2012).

Imidazole derivatives are first-line drugs for the treatment of bacterial vaginosis. Another treatment option is clindamycin 300 mg or 2% cream orally every 12 hours every night for 3 days (CAMPOS *et al*., 2012).

According to the studies by Larsson PG, et al. (2007), bacterial vaginosis is associated with increased risks for mother and child, such as miscarriage, premature birth, premature rupture of membranes, and puerperal infection. However, the effectiveness of bacterial vaginosis treatments in reducing these outcomes remains conflicting.

TRICHOMONIASES AND GESTURES

Trichomonas vaginalis (VT) is a sexually transmitted protozoan with genitourinary tendencies. An estimated 120 million cases occur in women each year. During pregnancy, it is the third most common cause of vulvovaginitis, with a prevalence of 4% in asymptomatic pregnant women in the second trimester (BRASIL, 2015).

Vaginal colonization by Trichomonas may be asymptomatic but usually presents as severe symptomatic vaginitis with yellowish-green discharge, vulvar and urethral irritation, and severe dyspareunia. The diagnosis is easily made by identifying motile and flagellated parasites on recent slides. The amine test may be positive and the pH may reach more than 4.5. More sensitive techniques (such as culture, immunofluorescence, or immunoassays) are no longer effective due to the cost and time required to perform them (PARVEEN N, et al., 2008).

The drug of choice for the treatment of trichomoniasis is metronidazole, which must first be administered orally. There was no difference in the therapeutic efficiency of metronidazole compared to the single-dose or seven-day regimen (GONÇALVES AK, et al., 2014).

For Parveen N, et al. (2008), trichomoniasis is associated with preterm birth and low birth weight, but treatment of asymptomatic pregnant women is not effective in reducing these outcomes, and the use of metronidazole has been shown to increase preterm birth rates. This fact has not been explained, but it has been suggested that changes in the flora facilitated by the use of antibiotics or toxic substances produced by the death of the parasite may be responsible for this fact.

According to Giraldo PC, et al. (2014), the treatment of symptomatic pregnant women is reasonable because disruption of the vaginal mucosal barrier increases the risk of transmission of acquired immunodeficiency virus and other STIs. Cure rates increase as

partners are treated, which is an excellent opportunity to screen for other STIs and recommend preventive measures.

VULVOVAGINAL CANDIDIASIS (CVV) AND PREGNANCY

Konadu DG, et al. (2019) understand that CVV is an acute inflammation that affects the vulvar and vaginal mucosa and is caused by the hyperproliferation of Candida species that usually colonize the vagina asymptomatically. *Candida albicans* is the main species that causes CVV. In addition, *Candida glabrata* and *Candida tropicalis* may also be related to the occurrence of this vulvovaginitis.

When symptomatic, CVV presents with signs and symptoms, including white nodules with vaginal discharge, local pain, pruritus, and possibly dyspareunia (Ghaddar N, et al., 2019).

Mulinganya G, et al. (2021) point out that pregnancy favors candidiasis due to hormonal changes, higher local humidity, and immunological changes due to the state of pregnancy. Candidiasis is easily diagnosed by observing hyphae and spores on fresh slides, a pH below 4.5, and a negative amine test. The Gram classification shows that the vaginal flora is type 1, and culture is an indication when there is recurrence of the infection or treatment failure, and should therefore be performed in a specific environment.

The treatment of candidiasis in pregnancy should preferably be carried out with an idazole diagnosis, with no difference in superiority between them. There is an expected 90% cure rate after 7 days of treatment (KONADU DG, et al., 2019).

For Ghaddar N, et al. (2020), neonatal candidiasis is associated with an increased risk of pregnancy complications, such as premature rupture of membranes, preterm labor, chorioamnionitis, and congenital cutaneous candidiasis. In newborns, the disease can occur by vertical transmission from the mother during the perinatal period or by horizontal transmission in the nursery or neonatal intensive care unit (NICU). Studies have shown that between 5% and 30% of colonized preterm infants develop invasive candida infection (ICI) while in the NICU. *Candida albicans* has been shown to play an important role in the colonization of newborns in the first days of life and has also been documented in a group of premature infants

Chatzivasileiou P, Vyzantiadis TA, (2019) state that vulvovaginitis is a worldwide health problem that affects both pregnant and non-pregnant women. For pregnant women, hormonal changes can cause these conditions. If not recognized and treated, it can lead to complications for both the mother and the fetus, as studies show: premature rupture of

membranes, premature birth, low birth weight, miscarriage, infertility, chronic infection, and even death.

It was noted during the study that vulvovaginitis is quite common during pregnancy. To avoid adverse effects on the mother and fetus, an investigation during the prenatal consultations, so that an early diagnosis can occur (HOLANDA AKS, et al., 2020).

CONCLUSION

Vulvovaginitis is a public health problem, especially when present during pregnancy. Knowing the possible consequences of untreated vulvovaginitis during pregnancy, it is important to encourage further studies with maternal-fetal binomial results in the long-term follow-up of pregnant women with vulvovaginitis. Despite the existence of guidelines for the diagnosis and treatment of vulvovaginitis, it is still necessary to strengthen the culture of prevention in pregnant women, warn about the most prevalent diseases, and raise awareness among the population about the signs, symptoms, and risk factors that can serve as warnings.

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