ORIGINAL RESEARCH

Increased vulvovaginal candidiasis incidence risk in various gestational ages at a private midwifery practice in Surabaya, Indonesia

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ABSTRACT

Objectives: This study aimed to analyze whether there was an increase in the incidence risk of vulvovaginal candidiasis at various gestational ages.
Materials and Methods: A study examined vaginal smears of pregnant women at a private midwifery practice Farida Hadjri, Surabaya, Indonesia. A total sample of 96 patients was taken by the consecutive sampling method, consisting of 32 patients each from the 1st, 2nd, and 3rd trimester of pregnancy.y The smear was examined using Gram stain at *Balai Besar Laboratorium Kesehatan Daerah Jawa Timur* to detect the presence of fungi elements. Data were analyzed using Chi-square test with 95% confidence interval to investigate whether there was an increased risk of vulvovaginal candidiasis and gestational age.
Results: There was an increased risk of vulvovaginal candidiasis and increased gestational age ($p < 0.05$). This result was related to the hormonal status of pregnant women. An increase in estrogen level during pregnancy leads to an increase in glycogen production by vaginal epithelial cells, which cause the vaginal environment to become more susceptible to fungal growth.
Conclusion: There was increased vulvovaginal candidiasis incidence risk along with gestational age. Pregnancy is one of the predisposing factors for candida infection.

Keywords: Vulvovaginal candidiasis; pregnancy; gestational age; maternal health

ABSTRAK

Tujuan: Penelitian ini bertujuan untuk menganalisis adanya peningkatan resiko kejadian vulvovaginal candidiasis pada berbagai usia kehamilan
Bahan dan Metode: Penelitian dilakukan dengan pemeriksaan apus vagina ibu hamil pada Bidan Praktek Swasta Farida Hadjri, Surabaya, Indonesia. Sampel diperoleh dengan teknik konsekutif sampling dengan jumlah total sampel 96 pasien yang terdiri atas masing-masing 32 pasien untuk kehamilan trimester 1,2 dan 3. Spesimen diperiksa dengan pewarnaan Gram di Balai Besar Laboratorium Kesehatan Daerah Jawa Timur untuk mendeteksi adanya elemen jamur. Analisis data menggunakan tes Chi-square dengan tingkat kesahihan 95% untuk membuktikan adanya peningkatan risiko kejadian kandidiasis vulvovaginal seiring dengan bertambahnya usia kehamilan.
Hasil: Didapatkan peningkatan risiko kandidiasis vulvovaginal seiring dengan bertambahnya usia kehamilan ($p < 0,05$). Hasil ini terkait dengan status hormonal ibu hamil. Peningkatan kadar estrogen selama kehamilan menginduksi peningkatan produksi glikogen oleh sel epitel vagina yang menyebabkan lingkungan vagina menjadi lebih rentan terhadap pertumbuhan jamur.
Simpulan: Terjadi peningkatan resiko kejadian kandidiasis vulvovaginal seiring dengan bertambahnya usia kehamilan. Kehamilan merupakan salah satu faktor predisposisi terjadinya infeksi kandida.

Kata kunci: kandidiasis vulvovaginal; kehamilan; usia kehamilan; kesehatan ibu

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INTRODUCTION

Vulvovaginal candidiasis is the second most common infection found in pregnancy after bacterial vaginosis. *Candida spp*. infection commonly found in pregnant women of reproductive age. Pregnancy is the first risk factors that support vulvovaginal candidiasis due to hormonal changes during pregnancy.[1] The study on pregnant women in Ghana, explained that pregnancy is a predisposing factor for vulvovaginal candidiasis.[2] New York prevalence study suggested that candida species colonize the vagina of at least 20% of all women and increase to 30% in pregnancy, most are asymptomatic. Pregnant women are more likely to experience it than non-pregnant women.[3]

Based on a research report by the Health Research and Development Agency (Ministry of Health of the Republic of Indonesia) in 2016, a study of the prevalence of reproductive tract infections in pregnant women in 3 major cities in Indonesia, namely Pekanbaru, Bandung, and Tangerang district, candidiasis vulvovaginal ranked third (13-45.6%) after trichomoniasis and bacterial vaginosis of all pregnant women sampled.[4]

Reproductive health services for antenatal care need to check for reproductive tract infections and sexually transmitted infections in all pregnant women by providing sufficient education about the importance of screening, infection prevention and treatment, especially in the third trimester of pregnancy, to prevent complications for pregnant women and their fetuses.[5]

Vulvovaginal candidiasis in pregnant women may result in labor complications such as premature membrane rupture and low birth weight. Therefore detection of vulvovaginal candidiasis in antenatal care can prevent these complications.[6]

This study aimed to analyze whether there was an increased incidence of vulvovaginal candidiasis in various trimesters at a private midwifery practice Farida Hadjri, Surabaya, Indonesia.

MATERIALS AND METHODS

Samples for this study were taken from pregnant women who did antenatal care at the private midwifery practice Farida Hadjri Surabaya from August until October 2020 (inclusion criteria of this study). There were 540 patients during this period, and the patients who refused to join the study were excluded. The sample size was calculated using Slovin's formula with a 5% error margin, and the result was 96 patients, consisting of 32 patients from each trimester of pregnancy. The samples were obtained by the consecutive sampling method (non-random sampling). This study did not separate between low-risk and high-risk pregnancies. The incidence of vulvovaginal candidiasis was assessed by finding the presence of fungi in vaginal smear stained with gram stain. The smears were examined at *Balai Besar Laboratorium Kesehatan Daerah Jawa Timur*, to assess whether there were yeast cells or pseudo hyphae in the gram-stained slide. The results of the smear examination were analyzed with the Chi-square statistic formula to obtain odd ratio at various gestational age trimesters. This study had been ethically approved by Health Research Ethic Committee, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia, No.159/EC/KEPK/FKUA/2020.

RESULTS AND DISCUSSION

Ninety-six patients were enrolled in this study. Most of the samples were in the age of 20-29 years old (72.92%), and patients with multi pregnancy were more than those with first pregnancy (62.5%). Most of the patients (61.46%) had complaints such as fluor albus and itchy vulva, half of the patients had senior high school education (50%), and most (80.21%) had profession as a housewife (Table 1).

Table 1. Patients' clinical characteristics for this study.

Variables	Total	n (%)
Age		
< 20	6	6.25
20-29	70	72.92
30-40	19	19.79
>40	1	1.04
Total	96	100
Pregnancy status		
First pregnancy	36	37.5
Multi pregnancy	60	62.5
Total	96	100
Complaints experienced		
No complaints	37	38.54
Specific complaints	23	23.96
Other complaints	36	37.50
Total	96	100
Level of education		
Primary school	11	11.46
Junior high school	25	26.04
Senior high school	48	50
Faculty education	12	10.42
Total	96	100
Profession		
Housewife	77	80.21
Private employees	19	19.79
Total	96	100

Vaginal smear examination revealed 25 patients (26.04%) had *Candida spp.* infection, while 71 patients (73.96%) had no candida infection. Positive smears

were found primarily on patients aged 20-29 years (72%), patients with multi-pregnancy (80%), patients with genital complaints such as fluor albus and itchy vulva (72%), senior high school education background (56%) and housewife profession (72%). Candida infections were identified with gram stain as a cluster of fungi in the form of blastospores, hyphae or pseudo-hyphae, or a mixture of the two. Tissue cells such as epithelium, leucocytes, erythrocytes, and other microbes such as bacteria or parasites were also observable in the preparation. Fungi appeared in the form of budding yeast cells and pseudo-hyphae. *Candida albicans* was seen as a monomorphic yeast and yeast-like organism that grows well at temperatures of 25-30 ºC and 35-37 ºC (Figure 1).

This study revealed that most patients infected with candida were at the age of 20-29 years old. This result was in accordance with the previous study, which showed that vulvovaginal candidiasis rarely occurred before puberty, increased in women of childbearing age, and decreased after menopause.[7] Studies of candida in women in Saudi Arabia found a similar result that candida infection was most common in the age group of 21 to 30 years, which was of reproductive age, and their hormonal status was still active.[8] Candidiasis was found more often in patients with multi-pregnancy than the first pregnancy. This finding shows that pregnancy is a risk factor for vulvovaginal candidiasis.[9] Most women in this study had vulvovaginal symptoms such as fluor albus and itchy vulva. Pereira et al. found that 62.2% of women with candidiasis were symptomatic while 37.8% were asymptomatic.[10]

Vaginal smear examination revealed that the most candida infections (13 patients or 52%) were experienced by pregnant women in the 3rd trimester of pregnancy. Among those in 2nd trimester of pregnancy, seven patients (28%) were positive for candidiasis, and the lowest candida infection was experienced by pregnant women during the first trimester of pregnancy (five patients or 20%).

Analysis of candida infection risk had shown that infection of candida in the 2nd trimester of pregnancy did not show a significant increase of infection compared with 1st-trimester pregnancy ($p > 0.05$), while those in the third trimester had a significant increase of candida infection risk compared those in the 1st and 2nd trimester of pregnancy ($p < 0.05$). From these results, it can be concluded that the third trimester of pregnancy was associated with a higher incidence of candida spp infection, that is the candidiasis incidence in 3rd trimester of pregnancy increases 3.7 times more than in the 1st and 2nd trimester of pregnancy. The risk of candidiasis in various gestational age was 15.625% in 1st trimester, 21.875% in 2nd trimester and 40.625% in 3rd trimester.

The study's results found that gestational age correlates with an increased risk of candida infection. The probability test for the 2nd trimester of pregnancy was found to be 1.51 times, or there was no significant increase in the frequency of the incidence of vulvovaginal candidiasis compared to the 1st trimester of pregnancy. However, when the probability test was carried out on 3rd trimester pregnant women, it was found that pregnant women at the 3rd trimester of pregnancy had 3.7 times the risk of being infected by *Candida spp*.

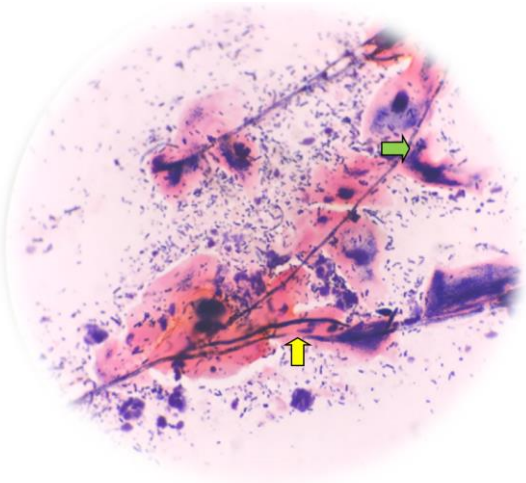

Figure 1. Yeast cell ( ) and pseudohyphae ( ) of *Candida spp.* appearance on microscopic examination with the Gram stain (400 x magnification).

The results of the study on samples whose gestational age was in the 1st trimester found that only a small proportion of five pregnant women (15.7%) had vulvovaginal candidiasis in 32 patients. This was in accordance with a study conducted by Fardiazar, et al who had conducted a study of vulvovaginal candidiasis in pregnant women, comparing recurrence rates of vulvovaginal candidiasis during the first, second, and third trimesters of pregnancy. They found that 90.7% of the patients were in the second and third trimesters of pregnancy. The study showed a significant difference of frequency between symptomatic recurrences that occurred during the three trimesters of pregnancy, with most occurring in the second and third trimesters.[11] During pregnancy, there was an increase in the levels of progesterone and estrogen hormones. Despite of inhibitory effect of progesterone on candida activity in neutrophils, estrogen reduces the ability of vaginal epithelial cells to inhibit candida growth. As many as 75% of women are generally at risk of being infected with this fungus without any symptoms or asymptomatic, which has no negative impact on the pregnancy itself.[12] Samples in the 2nd trimester of gestational age revealed that seven patients (21.88%) suffered from vulvovaginal candidiasis. This result was in accordance with the research by Zisova et al., who conducted a study concluding that increased gestational age, hyperestrogenemia, hormonal imbalance, and suppression of the mother's immune system all contribute to increased susceptibility to infections.[13] A study conducted in southern Nigeria found that pregnancy is a process that involves various hormonal changes in the body. After endometrial oxidation, estrogen and progesterone hormones will continue to increase gradually until the last week of pregnancy. The increase in estrogen levels begins at the 11th week of pregnancy and will continue to increase until the 24th week and still increase until the end of pregnancy.[14] The results of this study on patients in 3rd trimester of pregnancy found 13 patients (40.63%) with vulvovaginal candidiasis. These results were similar to those in the study by Brandao et al. on pregnant women in Brazil. They found that vulvovaginal candidiasis was the second most common cause of vaginitis after bacterial vaginosis.[15]

Ghaddar, et al. stated that estrogen is the most dominant reproductive hormone in supporting and maintaining *Candida spp.* infection. In vitro studies have shown that β-estradiol increases the growth of *Candida albicans* and directly stimulates dimorphic transmission from yeast to the hyphal form as well as increasing hyphae length.[16]

Gonzalves, et al. (2016) said that the candida species secrete hydrolytic enzymes that play an important role in tissue penetration, invasion, and damage to the host tissues. The enzymes most frequently involved in the pathogenesis and virulence of candida are aspartyl proteinase, phospholipase, lipase, and hemolysin. Aspartyl proteinase facilitates adhesion to host tissues, and its damage is associated with changes in the host immune response.[9] Several factors are associated with physiological changes, such as decreased cellular immunity, increased hormones, reduced vaginal pH, and increase the higher glycogen content in pregnancy. In fact, candida infection during pregnancy occurs due to high levels of placental estrogen, progesterone, and corticosteroids, which can decrease the vaginal defense mechanism to facilitate yeast growth.[17]

Pregnancy predisposes to primary and recurrent infections, and pregnant women have a two-fold increase in the frequency of vulvovaginal candidiasis compared to non-pregnant women. This is related to high levels of estrogen, glycogen stores, and other substrates.[18] Zhai, et al. found that the incidence of vulvovaginal candidiasis increases 100% during the 3rd trimester of pregnancy. The older the gestational age, the higher the risk of a pregnant woman to be infected with candida. High levels of progesterone have a suppressive effect on the cellular immune system, and, on the other hand, the promoter effect of gene expression affects the cellular synthesis of epithelial receptors that can bind candida.[19] The increase in estrogen facilitates yeast adherence to vaginal epithelial cells. In addition, it encourages hypha formation and elaboration of enzymes such as aspartyl proteinase and wasted phospholipase. The prevalence of vulvovaginal candidiasis increased by 36% in the third trimester of pregnancy.[20] Other factors that can increase the risk of vulvovaginal candidiasis in pregnancy, including diabetes mellitus and, in this study, poor hygiene can also act as confounding factor.[21]

Vulvovaginal candidiasis affects women globally, and therefore a better knowledge of the problem of candidiasis and colonization is needed, especially in pregnant women. Correct diagnosis, clinical symptom tracing, and risk factor screening should always be carried out in all women, both during pregnancy and women of reproductive age, to prevent labor complications such as premature rupture of membrane and low birth weight.[6,22] Vulvovaginal candidiasis is more susceptible to infecting women with high hormone levels, such as pregnant women, despite the fact that it does no harm to the fetus. However, if left untreated, the baby can be infected (oral thrush) during delivery and face serious health problems such as premature delivery.

Babies with oral thrush can cause the mother to be infected in the breastfeeding process, which causes candidiasis of the nipple.[23] Screening of risk factors is needed to prevent complications in both pregnant women and women of reproductive age for a meaningful psychological and sexual life.[24]

CONCLUSION

There is a tendency for increased frequency of vulvovaginal candidiasis infection with increased gestational age. Pregnant women, especially in the 3rd trimester of pregnancy, are more likely to have candida infection. Therefore, they should be examined and treated to control the infections.

DISCLOSURES

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Conflict of Interest

The authors declare there is no conflict of interest.

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Author Contribution

All authors have contributed to all processes in this research, including preparation, data gathering and analysis, drafting, and approval for publication of this manuscript.

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