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Original Article

The association between vulvovaginal candidiasis and hormonal contraceptive use in the outpatient clinic of Dr Soetomo Hospital, Surabaya in 2017-2020: A retrospective study

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Abstract

Background Vulvovaginal candidiasis (VVC) is one of the most common sexually transmitted infection (STI). With the increasing use of hormonal contraceptives, it is becoming increasingly important to investigate the role of hormonal contraceptives on the occurrence of VVC. This study aims to explore the association between hormonal contraceptive use and VVC.

Methods This retrospective unmatched case-control study enrolled patients from the STI outpatient clinic of the the Dr. Soetomo Regional General Hospital Surabaya in 2017-2020.

Results A total of 308 patients presented to the clinic, 132 (42.9%) of whom had VVC, and 84 (27.3%) of them used hormonal contraceptives. Hormonal contraceptive use may increase the odds of developing VVC by 3.4-folds (95% CI: 1.97-5.89; p<0.001), independent of STI history and immunodeficiency disorders. In addition, oral contraceptive pills may increase the odds by 2.3-folds (95% CI: 1.25-4.34; p=0.008), while other hormonal contraceptives such as injectable or implants may increase the odds by 8.7-folds (95% CI: 3.13-24.28; p<0.001). Patients using hormonal contraceptives had a probability of suffering from VVC of 58.8%, while in patients using OCPs and other hormonal contraceptives it was 49.5% and 78.6%, respectively.

Conclusion This study proves that hormonal contraceptives are a risk factor to the occurrence of VVC.

Key words
Hormonal contraceptives; Sexually transmitted infection; Vulvovaginal candidiasis.

Introduction

Vulvovaginal candidiasis (VVC) is a very common infection of the vulva and vagina, with 70-75% of women affected by VVC at least once during their lifetime. Globally, approximately 138 million women suffer from VVC each year, with a prevalence of 3871 per 100,000 women. This epidemiological data in Indonesia is still limited. A study of 4000 patients in Manado in 2013 found 0.7% of cases of VVC from the female population who came to the Dermatology and Venereology Department, with the most cases being aged 15-24 years (41.4%) and 25-44 years (41.4%).[1]

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Apart from its large prevalence, VVC is an important disease in women because it is often neglected. One of the signs and symptoms of VVC is vaginal discharge and itching, both of which are often experienced by women during the menstrual cycle, so they are often ignored. In addition, VVC can also be asymptomatic and chronic. If it is not diagnosed and not treated properly, VVC can become chronic, recurrent, and develop into complications such as pelvic inflammatory disease. Because of the frequent cases of VVC and the availability of over-the-counter antifungal drugs, patient often do not consult a doctor and take the medicines themselves. This can lead to increase of drug resistance in population groups.[1,2]

Contraception is a big part of the family planning program organized by the government to reduce the rate of early pregnancy and the rate of population growth. Contraception is easy to obtain and available in primary care, free of cost, in Indonesia. There are various kinds of contraceptives available, such as contraceptive pills, condoms, injections, implants, or intrauterine contraceptive devices (IUDs) etc. According to the Data and Information Center of the Indonesian Ministry of Health (InfoDATIN), in 2013 there were more than 8.5 million new contraceptive users, with the highest proportion being hormone injections (48.5%), followed by pills (26.6%), implants (9.2%), IUD (7.7%), condom (6.1%), female operating method (1.5%), and male operating method (0.25%).[3]

Hormonal contraceptives such as pills, implants, or hormonal IUDs have several side effects, one of which is increasing the risk of Sexually Transmitted Infections (STIs). Two studies in Iraq found that the use of hormonal contraception can increase the risk of VVC infection by around three times, especially oral contraceptive pills.[4,5] Some authors assume that cervical ectopia caused by hormonal oral contraceptives makes the cervical area more vulnerable to trauma, thus increasing the risk of Sexually Transmitted Infections or Human Immunodeficiency Virus (HIV).[6] Given the high VVC rate and the possibility that many cases of VVC will not be brought to health facilities, prevention of VVC risk factors needs to be well understood. The use of hormonal contraceptives is increasing and may correlate with the occurrence of VVC.

This study was created to find out the specific relationship between the two and find out if hormonal contraception is a significant risk factor for VVC. The purpose of this study was to prove that there is a relationship between an increase in the incidence of VVC in women who use hormonal contraception at Department of STI Outpatient Unit in RSUD Dr Soetomo for the 2017-2020 period.

Methods

This research is a case-control study using an unmatched hospital-based design based on data from the medical records of female patients who were treated at the Sexually Transmitted Infection Outpatient Unit at Dr Soetomo Hospital Surabaya from the period January 2017 to December 2020. This research was approved by the ethical commission number 1256/ LOE/301.4.2/III/2023. The case population in this study was all female patients who were diagnosed with VVC and had been treated at the STI Outpatient Unit of Dermatology and Venereology Department, Dr Soetomo Hospital Surabaya in the period January 2017 - December 2020.

The inclusion criteria was new adult female patients of reproductive age (18-49 years) who were treated at the STI Outpatient Unit of the Department of Dermatology and Venereology, and were recorded in the department of medical record. The exclusion criteria of this study were patients who were pregnant or their pregnancy

status was unknown, patients who were postmenopausal, and patients with missing or incomplete data.

Sampling was carried out sequentially through secondary data from medical records of new female patients at the STI Outpatient Unit of Dermatology and Venereology Department, RSUD Dr Soetomo Surabaya who came from January 2017 to December 2020. This study will compared the two groups, so the total sample required from both groups is 162 samples.

Distribution and frequency analysis of data was performed using SPSS. A test was carried out for the difference in the average VVC incidence rate between users of hormonal contraception and non-users. There are many other risk factors that vary between samples, these differences can be controlled with additional statistical analysis, in the form of stratification, followed by multivariate analysis and interaction analysis. This was done to ensure whether the relationship between the two variables was pure relationship without the contribution of confounding factors.

Result

Based on Electronic Medical Record (EMR) tracing and medical record status at STI Outpatient Unit of Dermatology and Venereology Department, Dr Soetomo Hospital Surabaya in 2017-2020, there were 308 female patients with 132 (42.9%) of them suffering from Vulvovaginal Candidiasis (VVC) **(Table 1)**. Around 176 patients were without VVC, 66 of them had non-specific genital infections (37.5%), followed by condyloma acuminata (37 patients, 21.0%), bacterial vaginosis (16 patients, 9.1%), syphilis (11 patients, 6.3%), Bartholin's cyst/abscess and no abnormality was found in 9 patients (5.1%), fluor albus non-specific (8 patients, 4.5%), herpes simplex (7 patients, 4.0%), gonorrhea (4 patients, 2.3%), anorectal abscess, urinary tract infection, trichomoniasis, and non-specific ulcer (2 patients, 1.1% each), and acute vaginitis (1 patient, 0.6%). The incidence of vulvovaginal candidiasis increased drastically in 2019 (54.4%) and 2020 (50.0%), compared to 2017 (41.8%) and 2018 (26.7%).

Among the 308 female patients, there were 13 patients (4.2%) who had immunosuppression. All patients with immunosuppression came in 2019 and 2020 (9; 8.7% and 4; 8.3% patients respectively), while out of 158 patients who came in 2017 and 2018, none of the patients had immunosuppressive conditions **(Table 2)**. Analysis of the relationship between the state of immunosuppression and the incidence of vulvovaginal candidiasis showed that there were 13 patients (4.2%) who had immunosuppression. Twelve (92.3%) of them had vulvovaginal candidiasis, while only one patient (7.7%) who was immunosuppressed did not have vulvovaginal candidiasis. This is inversely proportional to patients without immunosuppression where there were 120 (40.7%) patients suffering from vulvovaginal candidiasis, and as many as 175 (59.3%) did not

Table 1 Distribution of vulvovaginal candidiasis cases in the Sexually Transmitted Infections Outpatient Unit of Dermatology and Venereology Department, RSUD Dr Soetomo Surabaya in 2017-2020.

			Year				*Total*
			2017	*2018*	*2019*	*2020*	
Incidence vulvovaginal candidiasis (VVC)	No	Total	39	66	47	24	176
		%	58.2%	73.3%	45.6%	50.0%	57.1%
	Yes	Total	28	24	56	24	132
		%	41.8%	26.7%	54.4%	50.0%	42.9%
Total		Total	67	90	103	48	308
		%	100%	100%	100%	100%	100%

Table 2 Distribution of the immunosuppressed condition of patients in the sexually transmitted infections outpatient unit of dermatology and venereology department, RSUD Dr Soetomo Surabaya in 2017-2020.

			Year				*Total*
			2017	*2018*	*2019*	*2020*	
Immunosuppresion condition	Absence	Total	67	90	94	44	295
		%	100%	100%	91.3%	91.7%	95.8%
	Present	Total	0	0	9	4	13
		%	0.0%	0.0%	8.7%	8.3%	4.2%
Total		Total	67	90	103	48	308
		%	100%	100%	100%	100%	100%

suffer from vulvovaginal candidiasis. This finding can be translated into an estimated 17.5-fold increased risk of CVV events in immunosuppressed patients compared to non-immunosuppressed patients (OR 17.50; 95% CI: 2.25-136.37). In bivariate analysis using the Chi-square test, a p-value of <0.001 was obtained, thus proving that the condition of immunosuppression significantly affects the incidence of vulvovaginal candidiasis.

When investigated further, of the 13 patients with immunosuppression, six of them (46.2%) had a history of using immunosuppressive, immunomodulatory, and/or steroid drugs (three used methotrexate (50.0%), two used oral steroids (33.3%), and one was taking azathioprine and oral steroids (16.7%), followed by four patients (30.8%) who had an immunosuppressed disease (i.e., systemic lupus erythematosus), and three who had diabetes (23.1%).

The analysis between hormonal contraception and the incidence of vulvovaginal candidiasis was also carried out by considering the type of hormonal contraception used by the patient. In general, the highest proportion of patients using hormonal contraception with vulvovaginal candidiasis were patients using implantable contraceptives (7 patients, 100%), followed by patients using injectable birth control (18 patients, 78.3%), and birth control pills (29 patients, 53.7%). In bivariate analysis using the Chi-square test, it was found that there were two cells (25.0%) that had an expected count of less than five, so the Chi-square test could not be used in this analysis. Because the contingency table has a Kx2 structure, cell merging is done by combining injectable hormonal contraception and implant hormonal contraception so that bivariate analysis can be carried out.

After cell merging, bivariate analysis was performed using the Spearman test which showed a significant correlation between the type of hormonal contraception used and the incidence of VVC ($p<0.001$), although the strength of the correlation was statistically weak ($\rho=0.285$). However, this indicates that the type of hormonal contraception dos have affects on the incidence of vulvovaginal candidiasis.

Further analysis was performed using bivariate logistic regression analysis to compare the effect of each type of hormonal contraception on the incidence of vulvovaginal candidiasis. In the bivariate logistic regression analysis, it was found that patients who use birth control pills or other hormonal contraceptive methods such as injection or implant birth control have a higher likelihood of suffering from vulvovaginal candidiasis than patients who do not use contraception. Patients who used birth control pills were 2.2 times more likely to suffer from vulvovaginal candidiasis than patients who did not use contraception (OR 2.17 [95% CI: 1.19-3.96], p=0.012), while patients who used other hormonal contraception methods such as injectable birth control or implanted birth

Table 3 Analysis of the relationship between types of hormonal contraception and the incidence of vulvovaginal candidiasis in the Sexually Transmitted Infections Outpatient Unit of Dermatology and Venereology Department, RSUD Dr Soetomo Surabaya in 2017-2020.

			VVC incidence		Total	P value
			Present	Absence		
Types of hormonal contraception	Absence	Total	78	146	224	0.285 (<0.001)[a]
		% from types of hormonal contraception	34.8%	65.2%	100%	
		% from CVV incidence	59.1%	83.0%	72.7%	
	Pils	Total	29	25	54	
		% from types of hormonal contraception	53.7%	46.3%	100%	
		% from CVV incidence	22.0%	14.2%	17.5%	
	Others	Total	25	5	30	
		% from types of hormonal contraception	83.3%	16.7%	100%	
		% from CVV incidence	18.9%	2.8%	9.7%	
Total		Total	132	176	308	
		% from types of hormonal contraception	42.9%	57.1%	100%	
		% from CVV incidence	100%	100%	100%	

[a] The value of p is obtained from the Spearman test. Others include injectable birth control (23 patients, 76.7%) and implant contraceptives (7 patients, 23.3%). KB, family planning.

control had a 9.4 times greater chance (OR 9.36 [95% CI: 3.45-25.41], p<0.001; **Table 4**).

Analysis of the relationship between types of hormonal contraception and the incidence of vulvovaginal candidiasis was also continued with multivariate analysis considering that statistically significant results were obtained in bivariate analysis. Using the same criteria for selecting confounding variables to be included in the multivariate analysis model, namely p<0.200 in bivariate analysis, then history of Sexually Transmitted Infections (p<0.001), history of taking antibiotics (p=0.021), and conditions of immunosuppression (p<0.001) were selected as a confounding variable in the multivariate analysis model.

In multivariate analysis with logistic regression, it was found that patients who used birth control pills had a 2.3 times greater chance of suffering from vulvovaginal candidiasis than patients who did not use hormonal contraception (aOR 2.33 [95% CI: 1.25-4.34], p=0.008), while patients using other hormonal contraceptive methods had an 8.7-fold greater chance (aOR 8.71 [95% CI: 3.13-24.28], p<0.001). All of these risk estimates are independent of a history of previous sexually transmitted infections and immunosuppression. Based on the regression, a regression equation was obtained for patients using birth control pills as follows:

y=-0.866+0.844 (use of birth control pills)+1.715 (history of sexually transmitted infections)+ 2.771 (immunosuppressed conditions).

Table 4 Bivariate logistic regression analysis assessing the relationship between types of hormonal contraception and the incidence of vulvovaginal candidiasis in the Sexually Transmitted Infections Outpatient Unit of Dermatology and Venereology Department, RSUD Dr Soetomo Surabaya in 2017-2020.

Types of hormonal contraception	*Odds Ratio (OR)*	*IK 95%*	*p-value*
Absence	ref		
Pils	2,17	1,19-3,96	0,012
The others	9,36	3,45-25,41	<0,001

[a] Others include injectable birth control (23 patients, 76.7%) and implant contraceptives (7 patients, 23.3%).

Table 5 Multivariate analysis assessing the relationship betweenthe usage of hormonal contraception and vulvovaginal candidiasis Sexually Transmitted Infections Outpatient Unit of Dermatology and Venereology Department, RSUD Dr Soetomo Surabaya between 2017-2020.

Variabel	*Coefficient*	[a]*OR*	*IK 95%*	*p-value*
Types of hormonal contraception				
Absence		ref		
Pils	0.844	2.33	1.25-4.34	0.008
The others[a]	2.165	8.71	3.13-24.28	<0.001
History of sexual transmitted infection	1.715	5.56	2.10-14.73	0.001
Immunosuppression condition	2.771	15.98	1.97-129.59	0.009
Constant	-0.866			

[a]Others include injection contraceptives (23 patients, 76.7%) and implantable contraceptives (7 patients, 23.3%).
[a]OR, controlled odds ratio; 95% CI, 95% confidence interval.

The probability of VVC events for patients using other hormonal contraceptive methods such as injectable birth control or implanted birth control was described by the following equation:

y=-0.866+ 2.165 (use of other hormonal contraception)+ 1,715 (history of sexually transmitted infections)+ 2,771 (immunosuppressed conditions)

where the usage of birth control pills, other hormonal contraception, history of STIs, and immunosuppression conditions are each worth 1 if yes and 0 if no.

Based on this equation, patients using birth control pills have a 49.5% chance of suffering from VVC and patients who use other hormonal contraceptive methods have a 78.6% chance. In the population with a history of sexually transmitted infections, the probability of developing VVC was 84.5% in patients using birth control pills and 95.3% in patients using other hormonal contraceptive methods. Meanwhile, in the immunosuppressed population, the probability of occurrence of VVC was 94.0% in patients using birth control pills and 98.3% in patients using other hormonal contraceptive methods. Finally, in patients using hormonal contraception who have a history of Sexually Transmitted Infections and immunosuppressed conditions, the probability of developing VVC was 98.9% in patients using birth control pills and 99.7% in patients using other hormonal contraceptive methods **(Table 5)**.

Discussion

The results of this study indicate that the use of hormonal contraception has an effect on the incidence of VVC, where female patients who used hormonal contraception for at least one month before visiting the STI Outpatient Unit were 3.4 times more likely to suffer from VVC than patients who did not use hormonal contraception. Furthermore, patients who use hormonal contraception have a 58.8% chance of suffering from VVC. In this study, it was found that 64.3% of patients who used hormonal contraception suffered from VVC, compared to only 34.8% of patients who did not use hormonal contraception. These results are similar to previous findings from Semarang (66.7% of patients with hormonal contraception suffer from VVC)[7] and slightly lower than previous studies from Bali (80.0%).[8] The difference in findings on the proportion of VVC events in patients using hormonal contraception can be explained by differences in sociodemographic factors and differences in patient behavior such as hygiene habits in the genital area, sexual and non-sexual behavior, sexual orientation, and the type of hormonal contraception used, and other factors. These include age, body mass index, history of

sexually transmitted infections, history of taking antibiotics, and conditions of immunosuppression, which will be discussed in depth in subsequent chapters.

The findings in this study confirm the findings by Salih *et al*. which states that the use of contraception affects the occurrence of VVC. Salih *et al*. studied 270 women where 202 (74.8%) of them used hormonal contraception. It was found that the proportion of VVC in patients using hormonal contraceptives compared to patients who were not using hormonal contraceptives differed drastically (with contraception: 122 patients [60.4%]; vs. without contraception: 23 patients [33.8%]; $p<0.001$). This finding applies to almost all Candida species, including Candida albicans (88.5% vs. 11.5%), Candida tropicalis, Candida ciferii, and Candida famata (75.0% vs. 25.0% each), Candida glabrata (73.3% vs. 26.7%), Candida krusei and Candida lusitaniae (66.7% vs. 33.3% respectively).[4] The same thing was also observed by Jasim S.T. who stated that the proportion of VVC events was higher in contraception users than in patients who did not use contraception (88 patients [65.3%] vs. 23 patients [39.7%]; $p<0.001$).[5]

The relationship between the use of hormonal contraception and the incidence of VVC cannot be separated from the role of the hormones contained in the contraceptive method in changing the normal flora of the vulvovagina. Several mechanisms have been found that can explain the relationship between hormonal contraception and VVC events. Firstly, estrogen has been shown to be able to induce glycogen maturation and deposition in vaginal epithelial cells thereby increasing glycogen levels in the vulvovagina.[4,8] The glycogen will then be catabolized by the α-amylase enzyme into maltose, maltotriose, and α-dextrin, which will then be metabolized by Lactobacillus sp. to lactic acid. Lactobacillus sp. is one of the most common normal flora in the vagina.[9] Increased levels of lactic acid due to metabolism by Lactobacillus sp. can lower the pH of the vagina to become more acidic (around 3.5-4.5) thereby creating an optimal environment for the growth of fungi, including Candida.[10]

Secondly, an in vitro study by Barousse *et al*. proved that vaginal epithelial cells have the potential to inhibit Candida fungal colonization. The function of these vaginal epithelial cells becomes optimal during the ovulation phase when estrogen levels are at their lowest. This sparked the hypothesis that estrogen can reduce the number of vaginal epithelial cells thereby reducing protection against Candida colonization. This is also supported by the fact that the production of estrogen decreases during the ovulation phase due to the role of the hormone progesterone in providing negative feedback control to the pituitary gland, thereby inhibiting the production of follicle stimulating hormone (FSH).[11]

Thirdly, estrogen has also been shown to support the process of Candida colonization by inducing changes in Candida morphology and increasing the virulence of the fungus. Estrogen can activate the stress response via the production of heat shock protein (HSP), in which the HSP will then trigger changes in the morphology of the fungus from yeast to hyphae through the mitogen-activated protein (MAP) kinase pathway. In addition, this effect can also be achieved through the estrogen receptor on Candida which has a strong binding affinity with the 17-β-estradiol particle found in estrogen. This binding will then trigger transcription of the phosphatidylinositol transfer protein (PDR16) thereby increasing the activity of phospholipid D, which also plays an important role in changing the morphology of the fungus into hyphae. Estrogen can also increase the ability of

Candida to adhere to vaginal epithelial cells, as well as inhibit the function of T-helper 1 (Th1) cells in the body's defense mechanism against Candida colonization. These two things play an important role in increasing the immune invasion of fungal colonies, thus increasing the virulence of Candida fungi in VVC.[8]

In this study, there were no patients with recurrent VVC-defined as patients who had four or more VVC within a year. This is a different finding from a previous study by Arfiputri *et al*. who found that recurrent VVC was found in as many as 44.1% of women who went to Department of Sexually Transmitted Infections Outpatient Unit of Dermatology and Venereology Department, RSUD Dr Soetomo Surabaya in 2011-2013.[11] Several studies have also proven that the use of hormonal contraception in the form of oral birth control pills, especially those containing high levels of estrogen, can increase the risk of patients suffering from recurrent VCC.[12] This can be explained by the finding that Candida sp. may colonize chronically and persistently due to incomplete clearance. In addition, previous studies have also proven that, in women with VVC who have recovered (negative vaginal swab culture) with antifungal drugs, as many as 20-25% of them become positively colonized with Candida sp. again within 30 days after the last day of treatment.[11] However, some other literature also found that long-term use of oral birth control pills (>6 months) or use of birth control pills containing low doses of estrogen did not increase the incidence of recurrent.[10,12] This shows that the incidence of recurrent VVC is strongly influenced by various other factors such as genetics, habits, and normative; one of them includes the behavior of people who often consume antifungal drugs freely.[12] There were no patients presenting with recurrent VVC in the immunosuppressed condition of patients with vulvovaginal candidiasis.

In this study, 13 patients (4.2%) were immunosuppressed, and 12 (92.3%) of them had VVC. The condition of immunosuppression can increase the likelihood of patients suffering from VVC by 16.7 times (p=0.008). This finding is in line with several previous studies which stated that immunosuppressive conditions, including HIV infection, use of immunosuppressive drugs, or immunosuppressive diseases such as diabetes or other immunosuppressive diseases can increase the risk of VVC.[14-16]

Diabetes Mellitus is a disease that can cause a state of immunosuppression, especially in patients with uncontrolled blood sugar. Uncontrolled hyperglycemia can cause immune system dysfunction such as decreased cytokine production, impaired leukocyte recruitment, dysfunction of local and systemic immune defense mechanisms, dysfunction of neutrophils, macrophages, monocytes, and NK cells, as well as inhibition of antibody effectors and the complement system. All of these things will reduce immune function and put the patient at risk of suffering from infectious diseases, including VVC. Specifically, female patients with diabetes are thought to have higher levels of glucose in vaginal secretions, which can be used by Candida as a growth medium. In addition, glucose contained in vaginal secretions can also be metabolized into lactic acid which can lower the vulvovaginal pH thereby creating an optimal environment for Candida adhesion and growth. Increased glucose levels in vaginal secretions can also increase the activity of hydrolytic enzymes such as phospholipids and secreted aspartyl proteinase (SAP) thereby increasing the pathogenicity of Candida.[17]

Immunosuppressive diseases such as systemic lupus erythematosus (SLE) can also increase the risk of patients suffering from VVC. Systemic lupus erythematosus can cause immunosuppression directly or indirectly.

Directly, SLE involves genetic factors such as mannose-binding lectin deficiency which can cause immunodeficiency. Indirectly, patients suffering from SLE consume large amounts of corticosteroids over a long period of time that can cause immunosuppression.[18] Steroids can cause an increase in blood sugar levels which can change the normal flora of the vagina and create an optimal environment for Candida to grow.[12]

There is a relationship between the use of hormonal contraception and increase in the likelihood of patients suffering from vulvovaginal candidiasis, by 3.4 times (95% CI: 1.97-5.89; p<0.001), independent of previous STI history and immunosuppression.

Conclusions and recommendations

This study proves that hormonal contraceptives are a risk factor to the occurrence of VVC. Prior STI history and immunosuppressive conditions are the variables most associated with VVC events in women in RSUD Dr Soetomo 2017-2020.

Further research can be carried out by considering risk factors for sexually transmitted infections that have not been considered in this study, such as other sociodemographic factors, history of previous use of hormonal contraception, sexual behavior and orientation, and other sexual habits such as vulvovaginal hygiene, clothing habits, and lifestyle.

The high incidence of vulvovaginal candidiasis in patients using hormonal contraception proves that a more comprehensive modification of education and informed consent is needed so that patients can understand the risk of side effects from the use of hormonal contraception. In addition, patients using hormonal contraception are also advised to increase the frequency of routine check-ups, maintain the cleanliness of genital areas, and not engage in risky behavior or other things such as douching or wearing underwear and/or tight pants, to prevent vulvovaginal candidiasis.

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