

The management of vulvovaginal candidiasis: the results of survey in Lviv, Ukraine

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Vulvovaginal candidiasis (VVC) is a serious clinical and social issue. The questionnaire-based study was performed to assess the management of VVC in Lviv, Ukraine. Totally 408 women were enrolled in the survey. The lifetime prevalence of VVC was high (72.6 %). 35.8 % of women had VVC during the last year with the predominance of 1 episode (72.6 %). The most common symptoms were vaginal itching and cottage cheese-like vaginal discharge, affecting 89.7 % and 71.7 % of women with VVC, respectively. Stress (57.2 %) was the main self-reported factor associated with the VVC, followed by antibiotic therapy (49.7 %). Only 51.0 % of women with VVC sought a doctor's help, 35.2 % of women reported about self-treatment. The management of VVC included usage of medicines and nonmedicinal interventions. Oral antifungals and vaginal medicines prevailed (86.2 % and 80.7 % of woman with VVC used them, respectively). The management of VVC was associated with inappropriate interventions, such as the treatment of an asymptomatic sexual partner (22.8 %), vaginal douching (11.0 %), taking oral antifungals with only local effectiveness for gastrointestinal fungal infections (natamycin and nystatin, 15.2 % vs 14.8 % respectively), using of vaginal drugs with none antifungal activity (5.1 %), and incorrect duration of the treatment (29.1 %). Rural residence ($p=0.000$) and the absence of higher education ($p=0.001$) significantly contribute to the inappropriate management of VVC. The management of VVC is often associated with self-treatment and different inappropriate interventions. Educational programs are required to improve the management of VVC. Pharmacists may significantly contribute to raising patients' awareness and improving the management of VVC, especially in rural areas.

Key words: vulvovaginal candidiasis; management; questionnaire-based study; self-treatment; inappropriate interventions.

Léčba vulvovaginální kandidózy: výsledky průzkumu ve Lvově na Ukrajině

Vulvovaginální kandidóza (VVC) představuje závažný klinický a společenský problém. Dotazníková studie byla provedena za účelem posouzení léčby VVC ve Lvově na Ukrajině. Do průzkumu bylo zařazeno celkem 408 žen. Celoživotní prevalence VVC byla vysoká (72,6 %). Během posledního roku prodělalo VVC 35,8 % žen s převahou 1 epizody (72,6 %). Nejčastějšími příznaky byly vaginální svědění a tvarohovitý vaginální výtok, které postihovaly 89,7 %, resp. 71,7 % žen s VVC. Stres (57,2 %) byl hlavním faktorem spojeným s VVC podle vlastního vyjádření, následovaný léčbou antibiotiky (49,7 %). Pouze 51,0 % žen s VVC vyhledalo pomoc lékaře, o samoléčbě informovalo 35,2 % žen. Léčba VVC zahrnovala užívání léků a nemedicínských intervencí. Převažovala perorální antimykotika a vaginální léky (užívalo je 86,2 %, resp. 80,7 % žen s VVC). Léčba VVC byla spojena s nevhodnými zásahy, jako je léčba asymptomatického sexuálního partnera (22,8 %), vaginální výplach (11,0 %), užívání perorálních antimykotik s pouze lokální účinností při gastrointestinálních plísňových infekcích (natamycin a nystatin, 15,2 % vs 14,8 %), užívání vaginálních léků bez antimykotické aktivity (5,1 %) a nesprávná délka léčby (29,1 %). K nesprávné léčbě VVC významně přispívá bydliště na venkově ($p=0,000$) a absence vyššího vzdělání ($p=0,001$). Léčba VVC je často spojena se samoléčbou a různými nevhodnými zákroky. Ke zlepšení managementu VVC je třeba vzdělávacích programů. Lékárníci mohou významně přispět ke zvýšení informovanosti pacientů a zlepšení léčby VVC, zejména ve venkovských oblastech.

Klíčová slova: vulvovaginální kandidóza; léčba; dotazníková studie; samoléčba; nevhodné intervence.

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Vulvovaginal candidiasis (VVC) represents one of the most common vaginal infections, affecting up to 75 % of women during their lifetime (1). Annually, about 138 million women suffer from recurrent VVC worldwide, and this number is expected to increase to 158 million by 2030 (2). At the same time, the precise estimation of acute VVC prevalence is considered to be unfeasible because self-diagnosis and self-treatment are very common (2, 3).

Both acute and recurrent VVC include a wide range of the same symptoms. Usually, women complain about vaginal symptoms such as itching, burning, redness, pain, and different types of discharge (4). All these issues have a negative influence on physical and mental health, which defines VVC medical and social problems as well (2, 4).

Not only is VVC associated with significant morbidity and the reduction of life well-being, but also with an economic burden (5, 6). Medical care costs and the economic impact of lost productivity in some countries might reach over \$1.8 billion per year (7).

A lot of studies are dedicated to VVC. However, they are mainly focused on the analysis of the species distribution of *Candida* (8), the susceptibility of fungi to antimycotics (9), risk factors of VVC in some groups of patients (8), new perspective medicines (10), etc. Even though VVC is well-described in scientific literature, there is limited data about the management of VVC, especially in Ukraine, which defined the goal and the stages of this study.

Materials and methods

Study design and data collection

This online questionnaire-based study was performed in one of Lviv medical centres over a period of September 2022 to December 2023. The research received ethical approval from the Human Research Ethics Committee of Danylo Halytsky Lviv National Medical University in December 2019 (Protocol №10). The participants of the survey were women who sought consultation with a gynaecologist. The minimum recommended sample size was 385 participants (5 % margin of error), which was calculated using Raosoft Sample size calculator (<http://www.raosoft.com/>) for 1294,8 thousand women population size in Lviv and Lviv Region in 2023 (http://www.lv.ukrstat.gov.ua/ukr/help/gender/description_2_1.htm). Totally 408 women agreed to fill in the anonymous online version of questionnaire on the volunteer basis.

The survey instrument included 29 questions regarding 1) demographic and clinical characteristics of the participants, 2) frequency, symptoms, possible causes and factors of VVC, 3) management of VVC. The questionnaire was peer reviewed by 10 external experts (gynaecologists and pharmacists) and tested in pilot survey on 20 randomly selected women. After peer reviewing and pilot testing, the survey instrument was revised and 3 questions were excluded. The final version of questionnaire included 26 questions.

Statistical analysis

The characteristics of the enrolled participants were summarized using descriptive statistics. Continuous variables were presented as

medians. Categorical variables were described using frequencies and percentages. A value of $p < 0.05$ was considered to be statistically significant.

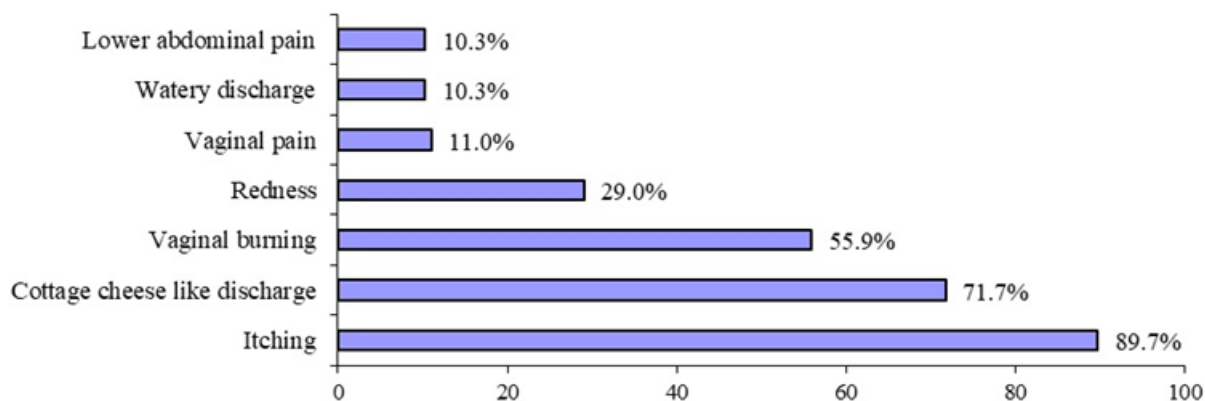
Univariable analysis with simple logistic regression was used to find out the association between 1) different social-demographical factors and 2) inappropriate interventions for the management of VVC. An intervention was considered inappropriate if it was either not mentioned in at least one of the guidelines (11, 12, 13) or explicitly listed in any of them (11, 12, 13) as not recommended due to a lack of evidence. Inappropriate interventions included: 1) the treatment of an asymptomatic sexual partner, 2) vaginal douching, 3) taking oral

Tab. 1. Demographic and clinical features of the sample (n = 408)

Main characteristics	n (%)
Age, years	
min-max	19–65
median	28.5
Age (range), years	
21–29	218 (53.4)
30–39	94 (23.0)
40–49	61 (15.0)
More 50	35 (8.6)
Residence	
urban	308 (75.5)
rural	100 (24.5)
Education	
university	375 (91.9)
school	33 (8.1)
Occupation	
work	275 (67.4)
study	114 (27.9)
other (maternity leave, retired, etc.)	19 (4.7)
Having children	
none	223 (54.7)
yes	185 (45.3)
Sexual encounters	
yes	381 (93.4)
none	27 (6.6)
Chronic diseases	
yes	106 (26.0)
none	302 (74.0)
Permanent using of medicines	
yes	302 (74.0)
none	285 (69.9)
Lifetime history of VVC:	
yes	311 (76.2)
none	97 (23.8)
Number of VVC in the lifetime history²	
more than 10 episodes	21 (6.8)
5–10 episodes	19 (6.1)
1–5 episodes	157 (50.5)
1 episode	98 (31.5)
don't remember	16 (5.1)
VVC during the last year	
yes	145 (35.5)
none	263 (64.5)
Number of VVC episodes past year	
1 episode	105 (72.4)
2 episodes	23 (15.9)
3 episodes	5 (3.4)
≥4 episodes	7 (4.8)
don't remember	5 (3.4)

¹SD standard deviation.

²The total number 311.

Fig. 1. Self-reported symptoms of VVC

antifungals with only local effectiveness for gastrointestinal fungal infections, 4) using of vaginal drugs with none antifungal activity. Additionally, neglect of the recommendations regarding treatment regimens (incorrect duration of fluconazole treatment) was also assessed as an inappropriate intervention.

Crude odds ratios and 95 % confidence intervals were calculated. Variables with p-values < 0.25 were entered into multivariate logistic regression. The results were presented as adjusted odds ratios and confidence intervals. Classification table and area under the ROC-curve were used to check the accuracy of the model.

Data were analysed with SPSS statistics.

Results

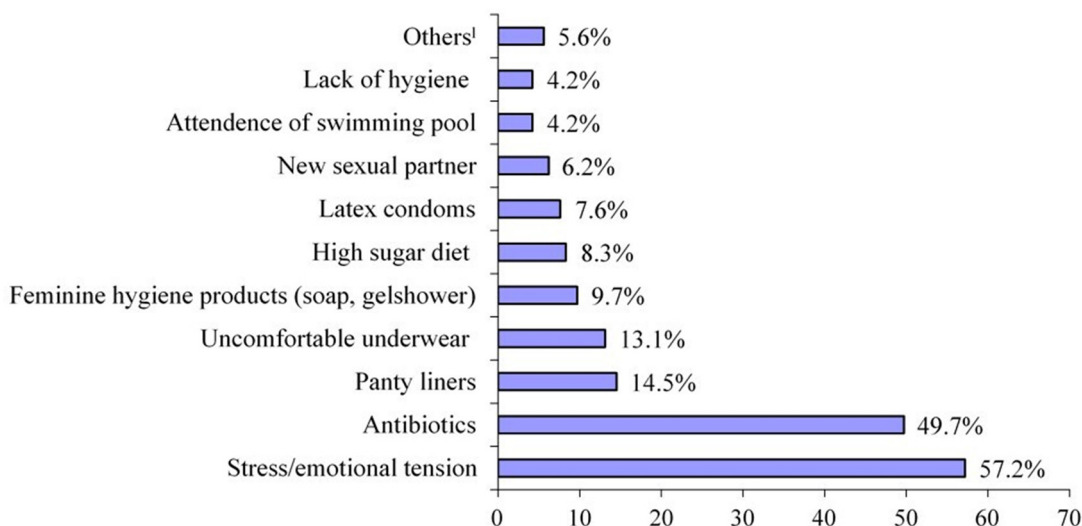
Demographic and clinical characteristics of respondents are summarized in Table 1. Most of participants were of age 21-29 years, lived in urban areas, graduated from the universities, worked, had active sexual life, did not have children and chronic diseases.

More than 76.0 % of study participants reported at least one episode of VVC in their lifetime. 35.8 % of women had VVC during the last year, with the predominance of 1 episode (72.6 %).

It is apparent from Figure 1 that the main symptoms included vaginal itching (89.7 %) followed by cottage cheese-like vaginal discharge (71.7 %), vaginal burning (55.9 %) and redness (29.0 %). Additional clinical features of VVC included vaginal pain (11.0 %), watery discharge (10.3 %) and lower abdominal pain (10.3 %) as well.

According to the survey results, 57.2 % and 49.7 % of women associated their episodes of VVC with stress/emotional tension and antibiotic therapy, respectively. They were followed by using panty liners (14.5 %), uncomfortable underwear made from synthetic fabrics (13.1 %), perfumed feminine hygiene products (9.7 %), high sugar diet and baked goods (8.3 %), using latex condoms (7.6 %), a new sexual partner (6.2 %), swimming pool attendance (4.2 %), the lack of hygiene (4.1 %), warmth and humid weather (2.8 %), and pregnancy (2.1 %). A small number of respondents related their VVC episodes with the oral contraceptives (0.7 %). At the same time, 4.2 % of the respondents did not mention any factor that might have caused their VVC episodes (Fig. 2).

Among those with a history of VVC during the last year, 51.0 % (n = 74) of respondents sought a doctor's help, 13.8 % (n = 20) – pharmacist's advice. 35.2 % (n = 51) of women who experienced VVC reported about self-treatment.

Fig. 2. Self-reported factors associated with VVC episodes

¹Oral contraceptives, pregnancy, warmth and humid weather.

The management of VVC included treatment with medications and alternative/nonmedicinal interventions (Tab. 2).

86.2% of women who had VVC during the last year, took oral antifungal medicines. The most common was fluconazole (55.7%), followed by natamycin (15.2%), nystatin (14.8%), itraconazole (11.0%) and nifuratel (3.3%).

In 49.6% of cases woman used fluconazole once, 29.1% – three times (on the 1st, 4th and 7th days of treatment), 9.4% – twice (on the 1st and the 4th day of treatment), 0.9% – throughout 6 months. In 11.1% of cases woman did not remember the dosage and duration of fluconazole treatment. 7.2% of women who took oral drugs, experienced adverse drug reactions that included headache, stomachache, nausea and diarrhoea.

80.7% of respondents who had at least one episode of VVC during the last year used vaginal medicines (n=176). The most common vaginal drugs were natamycin (22.1%), combinations of nystatin with nifuratel/corticosteroids/antibiotics (16.0%), clotrimazole (15.3%) and ketoconazole (12.5%). Other vaginal drugs included the combination of miconazole with metronidazole (10.8%), nystatin (7.4%), povidone iodine (6.8%), chlorhexidine (5.1%), sertaconazole (2.8%), and econazole (1.1%). 25 of 117 of women who used vaginal medicines (21.4%) had at least 1 adverse reaction. They encompassed the deterioration in itching, burning, rashes in genital area. To relieve these symptoms women took H1-histamine blockers, interrupted the treatment and used vaginal douching.

Other medication interventions included: 1) the treatment of an asymptomatic sexual partner, 2) vaginal douching (with special medicines or herbal infusions/decocts) and 3) the treatment of symptomatic sexual partner, which were reported by 22.8%, 11.0% and 9.7% of women, respectively.

Tab. 2. Management of VVC

Treatment with medications	n, %
Oral medicines	125 (86.2%)
Vaginal medicines	117 (80.7%)
Treatment of an asymptomatic sexual partner ¹	33 (22.8%)
Vaginal douching ²	16 (11.0%)
Treatment of sexual partner with some symptoms	14 (9.7%)
Alternative/nonmedicinal interventions	
Hygiene improvement	27 (18.6%)
Stop using perfumed soap/gel shower/wet wipes	27 (18.6%)
Stop using perfumed panty liners	23 (15.9%)
Avoid sex contacts ³	22 (15.2%)

¹There is no evidence to support this intervention (11–13).

²Does not need to be avoided (11–13).

³Were calculated from the total number of women who had VVC during the last year.

Moreover, different alternative/nonmedicinal interventions were applied: 1) the improvement of hygiene, 2) stopping using perfumed panty liners, soap and/or gel shower and 3) avoiding sex contacts.

Univariable analysis showed the association between using of inappropriate interventions for the management of VVC and 4 variables, such as residence, occupation, education, and having children. The subsequent multiple logistic regression analysis revealed that only residence (p=0.000) and education (p=0.001) remain statistically significant factors (Tab. 3).

Discussion

As far as we are concerned, this was the first survey-based study in Ukraine examining the management of VVC.

VVC is very common around the world (7, 12). Plenty of studies have been dedicated to this issue so far. Despite this, the precise epidemiological evidence is still lacking. Consequently, the prevalence of VVC varies

Tab. 3. Factors associated with the use of inappropriate interventions for the management of VVC

Exposure Variables	Crude OR ¹ (95% CI ²)	P-value	Adjusted OR ¹ (95% CI ²)	Wald	P-value
Age	1.012 (0.990–1.035)	0.277			
Residence					
rural	1.000		3,145 (1.769–5.591)	15.229	0.000
urban	0.293 (0.167–0.514)	0.000	1.000		
Occupation					
others	1.000				
study	2.298 (0.696–7.584)	0.172			
work	2.547 (0.752–8.627)	0.133			
Education					
school	1.000		1.000	11.392	0.001
university	0.132 (0.045–0.390)	0.000	0.150 (0.050–0.451)		
Having children					
none	1.000				
yes	0.726 (0.459–1.146)	0.169			
Sexual encounters					
none	1.000				
yes	1.013 (0.417–2.458)	0.978			
Chronic diseases					
none	1.000				
yes	1.359 (0.803–2.301)	0.253			
Permanent using of medicines					
none	1.000				
yes	0.984 (0.596–1.624)	0.950			

¹OR – odds ratio; ²CI – confidence interval

significantly by studies, accounting for 5.2% of women at reproductive age in the USA (4), 14.6% in Spain (5), 41.4% in Ethiopia (14), 53.7% in Iraq (15), with an average rate of 39% across different countries (16). In this study, we estimated the incidence of VVC during the lifetime and annually. According to our results, 76.2% of study participants experienced VVC during their lifetime. The annual rate was 35.5%, with the predominance of 3 or fewer episodes per year. Simultaneously, almost 5% of women who had VVC in the past year reported at least four episodes of VVC, which meets a criterion of recurrent VVC (11-13). Similar results have been found in the USA and some European countries (4, 6).

Symptoms of VVC have emotional, physical, and economic burdens on women's lives (17). As different studies report, the most common symptom of VVC is vaginal itching, affecting up to 90% of women with VVC (18). Other symptoms are burning, redness, and vaginal discharge (white or cottage cheese-like) (17, 19). Usually, women complain about multiple symptoms at the same time (11, 12). In the present survey, the similar ranking of symptoms was estimated.

The main self-reported factor that might have caused VVC was stress, followed by antibiotic use, panty liners, and uncomfortable underwear made from synthetic fabrics. Interestingly, all these factors have been mentioned in other studies but with antibiotic use predominance (8, 20). Also, such social-demographical characteristics as age and number of sexual encounters contribute to VVC (4). The extended list of contributing factors includes previous genital tract infection, number of lifetime male sex partners, diabetes, and having children (4, 14, 21).

In this study, only a half of respondents with signs and symptoms of VVC sought a doctor's help. These findings confirm the problem of self-diagnosis and self-treatment of VVC, which could bring about numerous negative outcomes, such as misdiagnosis, incomplete infection resolution, inadequate treatment, etc. (2). Moreover, self-diagnosis and self-treatment of VVC are associated with different complications during the pregnancy. According to the scientific reports, some oral antifungals (for example, fluconazole) might cause spontaneous abortion, craniofacial or heart problems (22). However, our findings showed that about 27.2% of women consider antifungals to be safe during the pregnancy with none risk for a woman and a baby. This situation reveals such problems as the affordances of treatment options, lack of knowledge and plausible underestimation of VVC in the society (3). Thus, different interventions, for example educational programs, are needed to raise awareness about the VVC.

According to our results, women used a lot of medications and non-medical interventions for VVC treatment. The most frequently used medicines were oral drugs (86.2%), followed by vaginal medicines (80.7%). Fluconazole and natamycin prevailed among oral and vaginal drugs, respectively. These results partially differ from other studies, where the most common antifungals were oral fluconazole and vaginal clotrimazole (23). Almost half of the women (49.6%) used only 1 dose of fluconazole, which corresponds to the guidelines of acute VVC management (11, 13). 9.4% of women used fluconazole twice - on the 1st and the 4th day of treatment, which is consistent with modern principles of treatment of a severe episode of VVC (11, 13). Almost one third (29.1%) of women took 3 doses of fluconazole - on the 1st, 4th

and 7th days of treatment. This scheme of therapy is indicated for a recurrent course, but requires further maintenance therapy for 6 months (11, 13). However, only 1 patient indicated the use of fluconazole for six months. Thus, in these cases, there was probably either excessive use of antifungal drugs during an acute episode of VVC (3 days instead of 1 or 2) or insufficient duration of therapy for recurrent VVC (only initial therapy for 3 days without further maintenance therapy). Anyway, it could be assessed as inappropriate duration of VVC.

Also, we found that women used oral forms of natamycin and nystatin (15.2% and 14.8% respectively), which provide only local effectiveness for gastrointestinal fungal infections (24). Moreover, chlorhexidine was used as vaginal treatment, which doesn't affect fungi (24, 25). Thus, our results revealed the inappropriateness of VVC treatment that requires the necessity of further investigations.

The treatment of asymptomatic sexual partners (22.8%) and vaginal douching (11.0%) were frequent as well. However, there is no evidence of the effectiveness of the last two interventions in the guidelines (11-13). Moreover, according to some studies, vaginal douching is the factor contributing to the recurrent VVC (26).

Thus, such interventions as: 1) the treatment of an asymptomatic sexual partner, 2) vaginal douching, 3) taking oral antifungals with only local effectiveness for gastrointestinal fungal infections, 4) using of vaginal drugs with none antifungal activity, 5) incorrect duration of fluconazole treatment could be considered as inappropriate interventions for the management of VVC. According to our results, such social-demographical characteristics as rural residence ($p=0.000$) and the absence of higher education ($p=0.001$) significantly contribute to the inappropriate management of VVC.

Numerous studies have demonstrated the positive impact of pharmacists' interventions on patients' pharmacotherapy, particularly in areas with limited healthcare services (27, 28, 29, 30). Today, pharmacists not only dispense medications but also play a crucial role in expanding access to various primary health care services, including the management of VVC (27, 30). Pharmacist-led interventions can be integrated into antifungal stewardship programs and may contribute to increasing of patients' awareness, reducing of inappropriate self-medication, and the prevention of adverse health outcomes (27, 28, 29, 30).

Conclusion

The prevalence of VVC was found to be high. The main symptoms included itching and cottage cheese like discharge. Most of participants associated the VVC with stress/emotional tension and antibiotic use. The management of VVC included numerous medications and alternative/nonmedicinal interventions. The most common inappropriate interventions for the management of VVC were 1) the treatment of an asymptomatic sexual partner, 2) vaginal douching, 3) taking oral antifungals with only local effectiveness for gastrointestinal fungal infections, 4) using vaginal drugs with none antifungal activity, 5) incorrect duration of fluconazole treatment. Living in rural areas and the absence of higher education were defined as the factors that significantly contribute to the inappropriate management of VVC, which requires the implementation of different educational programs to raise

awareness about VVC. Pharmacists, as the most accessible healthcare professionals, including those in rural areas, might significantly contribute to improving of VVC management.

Limitations

Although our findings are considerable, there are some important limitations in this study. The self-reported origin of the data is considered to be the main drawback because of the recalling challenges, personal differences in symptoms' perception and attitude towards them. All these factors may have affected the results and contributed to the precision of the study findings. Another limitation is including to the

sample size only women who sought doctor's advice in the medical centre owing to different gynaecological problems or regular health check-up, which might have had some impact on the respondent's answers.

Additionally, the survey was focused only on the main clinical and sociological features of the participants. Consequently, we did not cover all possible factors plausibly affecting the management of VVC. The thing is that inappropriate management of VVC could decrease the effectiveness of empirical treatment, lead to the drug resistance, provoke the recurrent VVC, etc. Thus, it is no doubtful that further studies are required.

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