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RESEARCH ARTICLE

VULVOVAGINAL CANDIDIASIS: PREVALENCE, SPECIES DISTRIBUTION AND RISK FACTORS AMONG NON-PREGNANT WOMEN, IN SANA'A, YEMEN

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Abstract

Background and objectives: Vulvovaginal candidiasis is known to be a global issue of concern due to its association with economic costs, sexually transmitted diseases, and the escalation of genital tract infections. This study aimed to determine the prevalence, species distribution and risk factors associated with *Candida* species causing vulvovaginal candidiasis.
Subjects and Methods: Non-pregnant women attending routine antenatal visits at Al-Olaifi-Family Center in Sana'a were enrolled in a cross-sectional study conducted from June 2018 to March 2019. Laboratory work was carried out at the National Center of Public Laboratories (NCPHL). Vaginal swabs were sampled from participants after oral consent was obtained. The swabs were inoculated in Sabouraud glucose agar supplemented with chloramphenicol and incubated at 37°C for 24 to 48 h under aerobic conditions in order to perform a fungal culture. Data on demographic, clinical, and risk factors were collected in a pre-designed questionnaire.
Results: A total of 190 non-pregnant women were included. The prevalence of VVC was 22.1%. *Candida albicans* accounted for 16.3% and non-*Candida albicans* accounted for 5.8% of the isolates, mainly *C. glabrata* (3.2%), *C. rugosa* (1.05%), *C. lipolytica* (1.05%), and *C. dubliniensis* (0.53%). When VVC risk factors were considered, there were significant risk factors with age group 30-34 years (33.3%, odds ratio=2.1) and age group ≥35 years (62.5%, odds ratio=10.3), residence in a rural area (39.5%, OR=3.3), negative emotions (30.2%, OR=2.3), underwear replacement over 1 day (29.3%, OR=4.2), impure cotton underwear (29.4%, OR=4.9).
Conclusions: Guidelines for the management of VVC syndrome in Yemen should be revised to include a protocol specifically for women over 30 years of age. VVC undoubtedly poses a significant threat to women's reproductive health. It is necessary to take appropriate measures to avoid risk factors and to help reduce the prevalence of VVC among women of childbearing age.
Keywords: *Candida*, Vulvovaginal candidiasis, epidemiology, risk factors, Sana'a, Yemen.

INTRODUCTION

Candidiasis is a fungal infection caused by any species of *Candida*. It affects the mouth and vagina, while the penis is less common and very rare, Candida infection may become invasive, spreading to other parts of the body[1-7]. Vulvovaginal candidiasis (VVC) is the second most widespread type of vaginal infection among women of childbearing age, involve mainly the vulva and vagina. It is expected that about 70-75% of women of childbearing age will experience at least one episode of VVC during their lifetime and that 40-50% will experience recurrence[8]. Approximately 80-90% of VVC is produced by *Candida albicans* excluding that only a minor of cases (10-20%) are caused as a result of non-*C. albicans*, commonly *Candida glabrata*[9]. Part

of the normal vaginal microflora is *Candida albicans*. It is known to have become a powerful opportunistic fungal pathogen and is the main causative agent of VVC in case the body lacks protective immunity and has a rebellion of purification insurgence to clearance [10]. Furthermore, the anus is anatomically adjacent to the vagina, which tenders much appropriateness for the migration of intestinal organisms, including *Candida*, into the vagina. VVC causes untold inconvenience to many patients, poses a serious problem for clinicians, and produces significant direct and indirect economic costs associated with medications and healthcare visits. Infection of the vagina or vulva may be associated with symptoms and signs such as pain, severe itching, pruritus inflammation, irritation, foul odor, dysuria and burning during urination[8]. It has been found in the Arab countries that the epidemic of VVC infection varies in different countries[11-13]. Thus, local studies are important to obtain relevant epidemiological data and sensitivity characteristics of *Candida* to antifungal drugs in order to aid the management and treatment of patients with *Candida* infection. Vaginitis in Yemen is one of the most common conditions to seek medical care. In Sana'a city, vaginal infections were prevalent in Yemen among 37.6% of women of reproductive age, 50% among pregnant women and where VVC was significantly associated with younger age female and intrauterine contraceptive use[4, 5,14]. Also in Hadhramaut 372 (39.2%) of 950 pregnant women had abnormal vaginal discharge and were positive for bacterial vaginosis [15]. Currently, the high rate of VVC infection was 70.45% recorded among pregnant women in Hajjah governorate[16]. According to the current epidemiological studies, the prevalence and incidence of genital tract infections differ between countries and ethnicities[4,5,17,18]. Even in similar populations, the epidemiological features of low reproductive tract infection differ[19]. It is therefore important to analyze the risk factors for VVC among women of reproductive age in Sana'a city and then provide a reference for clinical prevention and treatment of VVC.

SUBJECTS AND METHODS

Non-pregnant women attending routine antenatal visits in Al-Olify–family Center in Sana'a city were enrolled in a cross-sectional study was conducted from June 2018 to March 2019 which is the time given by the NCPHL to complete the study. Inclusion criteria for subject selection were healthy individuals with no systemic disease. In addition, non-pregnant women who currently taking antifungal, steroids, antibiotics, or immunosuppressive drugs in the past 6 months were excluded. The sample included 190 non-pregnant mothers who met the inclusion criteria and agreed to participate in the study. All non-pregnant females at reproductive age was examined clinically by a specialist and vaginal swabs were taken. The vaginal swabs were sent to the National Center of Public Laboratories (NCPHL) where the laboratory works were carried out. Vaginal swabs samples were taken from participants after obtaining oral consent. The swabs were inoculated into Sabouraud's glucose agar supplemented with chloramphenicol and incubated at 37°C for 24 to 48 hours under aerobic conditions in order to perform a fungal culture. The identification of the *Candida* species was done by culture on HiCrome *Candida* Differential Agar at 35°C for 48 h for the production of species-specific colors. Data of demographic, clinical and risk factors were collected in a pre-designed questionnaire.

Ethical approval

The written consent in all cases were obtained. Approval was obtained from the participants prior to collection of samples. Ethical approval was obtained from the Medical Research and Ethics Committee of the Faculty of Medicine and Health Sciences, Sana'a University with reference number (95) on 11/05/2018.

Statistical analysis

The data was statistically analyzed using EPI-Info version 6. The difference in the distribution of Candida types among groups was based on a comparison of repeat distributions by chi-square test. The odds ratio associated with VVC risk factors was performed by 2x2 tables to obtain an OR, 95% CI, Chi squared and p value by uncorrected static tests where the value of $p<0.05$ was considered significant.

RESULTS

A total of 190 non-pregnant women were included. The prevalence of VVC was 22.1%. *Candida albicans* accounted for 16.3% and *non-Candida albicans* accounted for 5.8% of the isolates, mainly *C. glabrata* (3.2%), *C. rugosa* (1.05%), *C. lipolytica* (1.05%), and *C. dubliniensis* (0.53%). When VVC risk factors were considered, there were significant risk factors with age group 30-34 years (33.3%, odds ratio=2.1) and age group, 35 years (62.5%, odds ratio=10.3), residence in a rural area (39.5%), OR=3.3), negative emotions (30.2%, OR=2.3), underwear replacement over 1 day (29.3%, OR=4.2), impure cotton underwear (29.4%, OR=4.9), while Condom use and vulvar cleaning before or after sexual life were found to be highly significant protective factors against VVC (p=0.008, 0.03, respectively). Detailed results of the study are presented in Table 1 to Table 5.

DISCUSSION

VVC is a health problem that affects millions of women and is caused by the overgrowth of yeasts in the vaginal mucosa[20]. It causes many vaginal signs and symptoms, including cottage cheese-like discharge associated with vaginal and vulvar itching, pain, burning sensation, erythema, and edema. External dysuria and dyspareunia may also occur[21]. The rate of infection in the present study (22.1%) was somewhat similar to the reported range[22] and was higher than the rates described by Ahmed *et al.*, in India among pregnant and non-pregnant women[23] and Olowe *et al.*, in Nigeria among pregnant women[24], but a lower rate was described by ERylander *et al.*, among sexually active young women and correlation with oral-genital sex[25].

Table 1: The distribution of non pregnant women according to their age group.

Age groups	Non pregnant women n=190	
	No.	%
< 20 years	12	6.3
20-24 years	58	30.5
25-29 years	46	24.2
30-34 years	42	22.1
≥ 35	32	16.8
Mean age	27.1 years	
S. D	5.7 years	
Mode	30 years	
Median	26 years	
Max	40 years	
Min	16 years	
Total	190	

The dissimilarities in rates can be justified by identifying variations in sociodemographic characteristics and immune status of patients[26], and treatment of patients with broad antibiotics, immunosuppressive drugs[27] and hormonal effects[28] as some of the factors for the differences in prevalence and/or recurrent vulvovaginal candidiasis between studies. The prevalence of VVC was 22.1%. *C. albicans* accounted for 16.3% and *non-Candida albicans* accounted for 5.8% of the isolates, mainly *C. glabrata* (3.2%), *C. Rugosa* (1.05%), *C. lipolytica* (1.05%), and *C. dubliniensis* (0.53%) (Table 2). This result with respect to VVC-causing species, is similar to that reported by other researchers where *Candida albicans* is the prodrome and increased prevalence of non-*Candida albicans* species, especially *C. glabrata*, *C. krusei* and *C. parapsilosis*[29].

Table 2: The frequency of different species of Candida isolated from non-pregnant women.

Micro-organism species	Non-Pregnant women	
	No.	%
Candida spp	42	22.1
Candida albicans	31	16.3
Non-*candida albicans* spp	11	5.8
C. globrata	6	3.2
C. dubliniensis	1	0.53
C. rugosa	2	1.05
C. lipolytica	2	1.05

Some researchers have also found that the incidence of infection with *Candida albicans* is reduced and that of other *Candida* species including *C. glabrata*. *C. tropical*, *C. parapsilosis*, *C. kefyr*, *C. africana*, *C. dubliniensis*, *C. Famata*, *C. Guilliermondii* and *C. lusitaniae* mainly associated with vulvovaginitis of immunocompromised patients or in pregnant women[30]. This study showed that women in the age group 30-34 years and >35 years have a double and 10-fold risk of developing VVC, respectively, compared to younger age groups (Table 2, and Table 3).

Table 3: The prevalence rate and risk of developing candidiasis among different age groups of non-pregnant women.

Age group in years	Positive n=42		OR	CI	X^2	PV
	No	%				
< 20 years (n=12)	0.0	0.0	0	undefined	3.6	0.056
20-24years (n=58)	4	8.6	0.18	0.06-0.5	11.2	0.0008
25-29 years (n=46)	14	30.4	1.8	0.8-3.8	2.4	0.11
30-34 years (n=42)	14	33.3	2.1	1.0-4.5	3.9	0.04
> 35 years (n=32)	20	62.5	10.3	4.4-24	36.4	0.000
Total (n=190)	42	22.1				

However, age at first sexual intercourse <20 years increased the risk of VVC by two times (OR=2). The current study differs from that reported by Zeng *et al.*, in which younger women were at double the risk of developing VVC compared to the elderly[21]. The results of the current study are also in line with the facts described that chance was the cause of increased *Candida* vaginitis in women of childbearing age and not in menopause[30]. The reason why VVC is more common in the third and fourth decade of life may lie in the fact that they are easy to suffer from negative factors such as risky sexual behaviors[31]. In addition to some physiological and histological changes caused by reproductive hormones that occur in women during this stage of life (third and fourth decade), which increase the susceptibility to *Candida* infection. In this study, area of rural residence showed a significant effect on the incidence of VVC (OR=3.3, CI=1.5-7, p=0.0001) (Table 4). However, a previous study indicated that episodes of VVC symptoms were not significantly associated with residency[21,32]. The difference can be explained by the fact that there was difference between rural and urban areas with greater awareness of self-care and better medical conditions in current times. At the same time, people from different educational backgrounds cannot get the same avenues to get the vast information related to healthcare through the internet[21,33,34]. In the current study, educational background showed no effect on the incidence of VVC (p=0.29) (Table 4). However, a previous study indicated that higher education can protect against infection[33]. In the current study, use of pads during non-menstruation, trend of wiping after toilet, and frequency of wearing tights clothes did not show any effect on the incidence of VVC. However, previous studies indicated that episodes of VVC symptoms were significantly associated with these factors[21,32]. The overall crude prevalence of diabetes among women of reproductive age in Yemen is 6.3%[35] and this rate is consistent with this study where 14 females had DM2 (6%), resulting in a VVC (OR=3.7, CI=1.1-13.2, p= 0.02) (Table 5).

Table 4: Univariate analysis of socioeconomic factors and daily living habits among non-pregnant women of reproductive age.

Character	Candida species positive (n=42)		OR	CI	X^2	PV
	No.	%				
Residence						
Rural area (n=43)	17	39.5	3.3	1.5-7	10.5	0.0001
Urban (n=147)	25	17	0.29	0.14-0.7	10.5	0.0001
Educational background						
Secondary or below (n=152)	36	23.7	1.6	0.6-4.2	1.1	0.29
College or above (n=38	6	15.8	0.6	0.2-1.5	1.1	0.29
Daily emotional state						
Negative emotions (nervousness, anxiety, etc.) (n=86)	26	30.2	2.3	1.1-4.8	6	0.001
Comfort (n=104)	16	15.4	0.47	0.2-0.8	6	0.001
Usage of pad during non-menstruation						
No (n=121)	23	27.3	0.6	0.3-1.2	1.8	0.17
Yes (n=69)	19	27.5	1.6	0.8-3.2	1.8	0.17
Wiping direction after the toilet						
Forward wiping (n=83)	17	20.5	0.8	0.4-1.6	0.22	0.6
Backward wiping (n=107)	25	23.4	1.1	0.6-2.3	0.22	0.6
Frequency of underwear replacement						
Over one day(n=123)	36	29.3	4.2	1.6-10.6	10.3	0.0001
Less than one day n=67)	6	8.9	0.2	0.09-0.59	10.3	0.0001
Frequency of wearing tights						
Occasionally or never (n=111)	24	21.6	0.9	0.4-1.8	0.36	0.84
Frequently (n=79)	18	22.8	1.1	0.5-2.1	0.36	0.84
Underwear material						
Others (n=126)	37	29.4	4.9	1.8-13	11.4	0.0002
Pure cotton (n=64)	5	7.8	0.2	0.07-0.5	11.4	0.0002

This finding is similar to studies[34,36,37] that showed that diabetes mellitus, especially uncontrolled diabetes mellitus, led to VVC. This study explored that frequent vaginal douching can increase susceptibility to VVC with risk factors equal to 7 times (p<0.0001) (Table 5). This is in line with the results of previous studies[21,32,33]. The reason may lie in the fact that intravaginal practices can cause damage to the tissues of the vagina and rectum and also disrupt the vaginal flora. Furthermore, the use of a vaginal douche may upset the balance of the delicate ecosystem of the vagina, lead to a regression of the vaginal balance, encourage the growth of yeasts, and also cause VVC. By contrast, one study confirmed that the association between intravaginal practices and VVC was not specific[38].

This study identified one-day underwear substitution as a risk factor for VVC (OR=4.2, CI=1.6-10.6, p=0.000 1) (Table 4), as there was an association between under-wear material and VVC where impure cotton underwear clothing 4.9 times compared to pure cotton underwear (p=0.0002) (Table 4) This result is similar to a recent study that found that risk factors for VVC include synthetic underwear[21,39] and another study showed this type of underwear (cotton/synthetic) was statistically associated with frequent VVC[40] and this may be attributed to the fact that wearing synthetic underwear appears to enhance friction and maceration, thereby increasing local acidity and thus fungal infection. The study discovered that condoms were a protective agent helping to prevent VVC (OR=0.2, p=0.008) (Table 5). It is unfortunate that this study classified ligation, intrauterine device (IUD), oral contraceptives (OCP), etc. into one category. It was therefore difficult to determine the effect of a particular species on the incidence of VVC (Table 5). Likewise, Du *et al.*,[33] Zheng *et al.*,[21] also found no relationship between OCP and VVC. However, a study reported that there is a link between IUD use and VVC[41]. Therefore, the role of the IUD in the development of VCC remains unclear, and needs further investigation. At the same time, this study showed that the frequency of vulvar cleaning did not affect the incidence of VVC significantly (OR=1.7, p=0.13), while vulvar cleaning before or after sexual life was a beneficial factor for VVC prophylaxis (OR=0.4, p=0.03) (Table 5). There have been a limited number of studies exploring the relationship between the two before[21]. Also pad use while not menstruating may increase the risk of VVC, but in this study, pad use while not menstruating was not a risk factor for VVC (Table 5). Often, sexual life can reduce the risk of suffering from VVC. An observational study reported that sexual contact more often was only associated with asymptomatic colonization[42]. The result did not find a clear association between prior history of vaginitis and suffering from VVC (OR=1.5, p=0.24) (Table 5). This finding was different from some previous epidemiological studies that believed that there was an association between episodes of VVC symptoms and a history of lower genital tract infection[32,43,44].

Table 5: Univariate analysis of previous history, reproductive history, and sexual behaviors among women of reproductive age.

Character	Candida species positive (n=21)		OR	CI	X^2	PV
	No.	%				
History of vaginitis						
Yes (n=43)	12	27.9	1.5	0.6-3.2	1	0.24
No (n=147)	30	20.4	0.6	0.3-1.44	1	0.24
Frequency of intra-vaginal douching						
Occasionally or never (n=79)	5	6.3	0.13	0.05-0.3	19	00000
Frequently (n=111)	37	33.3	7.1	2.6-19	19	0000
Frequency of cleaning the vulva						
More than three days (n=112)	29	25.9	1.7	0.8-3.6	2.2	0.13
Less than two days (n=78)	13	16.7	0.57	0.2-1.1	2.2	0.13
Contraceptive methods						
Condom (n=41)	3	7.3	0.2	0.06-0.7	7	0.008
Others (ligation, IUD, and so on) (n=79)	18	22.8	1.1	0.5-2.1	0.03	0.89
Age at marriage						
≤20 y (n=97)	27	27.8	2	0.9-4	3.7	0.051
>20 y (n=93)	15	16.1	0.4	0.2-1	3.8	0.05
Frequency of sexual life						
More than twice a week n=69)	18	26.1	1.4	0.7-2.2	0.99	0.31
Less than once a week n=121)	24	19.8	0.7	0.3-1.4	0.99	0.31
Cleaning the vulva before or after sexual life						
Yes =133	24	18	0.4	0.2- 0.9	4.2	0.03
No (n= 57)	18	31.6	2.1	1.0-4.2	4.2	0.03
Diabetic mellitus (n=14)	4	28.6	3.7	1.1-13.2	4.7	0.02

IUD: intrauterine device; y: year; OR: odds ratios; CI: confidence interval.

Besides, the study was concerned with the effect of daily emotional state, in the end, positive emotions were a protective factor (OR=0.47, p=0.001), while negative feelings (nervousness, anxiety, etc.) were risk factors (OR=2.3, p=0.001) (Table 4) and increased susceptibility to VVC approximately 2.3-fold. So far, little is known about the relationship between affective factors and VVC prevalence.

CONCLUSIONS

The study has demonstrated a high incidence of VVC among non-pregnant women and this highlights the need for health authorities to develop strategies for diagnosing VVC, including vaginal swabs for candidiasis as a standard method for all women who attend family centers. This study also revealed a steady increase in time with non-*C. albicans* species spreading. Guidelines for the management of VVC syndrome in Yemen should be revised to include a protocol specifically for women over 30 years of age. VVC clearly poses a significant threat to women's reproductive health. Risk factors for VVC are varied, and include ages, health habits, history of the disease, and other aspects. It is necessary to take appropriate measures to avoid risk factors and to help reduce the prevalence of VVC among women of childbearing age.

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AUTHOR'S CONTRIBUTION

This research work is part of a National Center for Public Health Laboratory (NCPHL) project. The authors did clinical and laboratory work. **Al-Hatami SMM:** study design, writing original draft. **Al-Moyed KAA:** literature survey. **Al-Ankoshy AAM:** methodology, formal analysis. **Al-Haddad AM:** data interpretation. **Al-Shamahy HA:** supervision. The final manuscript was read and approved by all authors.

DATA AVAILABILITY

The data and material are available from the corresponding author on reasonable request.

CONFLICT OF INTEREST

None to declare.

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