

## Original Article

# Vulvovaginal Candidiasis in Reproductive Age Women in Enugu Nigeria, Clinical versus Laboratory-assisted Diagnosis

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ABSTRACT

**Background:** Clinical diagnosis of acute vulvovaginal candidiasis (VVC) depends on evidence of clinical symptoms, but symptomatic treatment widely practiced in low-resource area may lead to overdiagnosis and treatment. **Objective:** The objective of the study is to determine the prevalence of VVC among women attending gynecological clinic in University of Nigeria Teaching Hospital (UNTH) Enugu and the accuracy of clinical-based diagnosis versus laboratory test supported diagnosis and patients' characteristics that affect accuracy. **Materials and Methods:** This study surveyed patients seen in a gynecologic clinic for VVC using a semi-structured, pretested, and interviewer-administered questionnaire. Vaginal examination was done on each patient and findings documented. A pair of swabs was taken from the vagina and cervical os and cultured for *Candida* species using Sabouraud Dextrose Agar. Data were analyzed using statistical software, SPSS version 15 (SPSS Inc., Chicago IL, USA).  $P \leq 0.05$  were considered to be statistically significant. **Results:** The mean age of 209 women surveyed was 35.9 (standard deviation [SD]  $\pm 9.0$ ) years. Their mean parity was 2 (SD  $\pm 3$ ). The prevalence of VVC was 17.7% based on symptoms and laboratory test. Clinically based diagnosis had a sensitivity of 70.3% and specificity of 83.7%. Forty-one (19.6%) of the study population had good knowledge of VVC. More than 44% of the women had self-reported and treated VVC within the year. Young women of 24 years or less (54.5%) and those who had reported other episodes of VVC within the past year (41.1%) were most commonly associated with inaccurate clinical diagnosis. **Conclusion:** Clinically based diagnosis of VVC has an unacceptably high false-positive rate which may encourage continued presumptive treatment with its attendant risks. Clinical evaluation and laboratory culture of vulvovaginal specimen should be the standard diagnostic method.

**KEYWORDS:** *Candidiasis, clinical laboratory diagnosis, vulvovaginal*

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## INTRODUCTION

Vulvovaginal candidiasis (VVC), the generic term for vaginitis resulting from infection by *Candida* species, is reported in 75% of adult women at least once in a lifetime. About 85%–95% of VVC is due to infection by normal body flora *Candida albicans*.<sup>[1]</sup> The rest are due to *Candida glabrata*, *Candida tropicalis*, and *Candida krusei* infections.<sup>[1,2]</sup> *Non-C albicans* infection is particularly prevalent in recurrent VVC.<sup>[2]</sup> Acute VVC has been associated with high estrogen state such as pregnancy and

the luteal phase of the menstrual cycle as well as high estrogen-containing oral contraceptive pills.<sup>[3]</sup> Other associated factors including recent use of broad-spectrum antibiotics, immunosuppressive states, diabetes mellitus, and mechanical factors such as wearing tight nylon under-wears are thought to be facilitative.<sup>[4-8]</sup>

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Clinical diagnosis of acute VVC depends on evidence of clinical symptoms particularly vulval itching, abnormal curd or pap-like vaginal discharge, burning sensation in the vulva, dysuria, and dyspareunia. The quantity and characteristics of the vaginal discharge and inflammatory changes seen during vaginal examination are important signs. Asymptomatic colonization of the vagina by *Candida* is reported in about 10%–15% of women.<sup>[9]</sup> Clinical symptoms are thought to be related to consistently high level of vaginal colonization by *Candida* resulting in reduced tolerance of the vagina to colonization. No definitive conclusions are however known about protective immunity in acute VVC.<sup>[10]</sup> Some investigators challenge the suggestion that high levels of vaginal colonization inevitably equate with symptomatic episodes.<sup>[11,12]</sup> This necessitates the presence of symptoms as well as evidence of fungi in the diagnosis of VVC.

Conventionally, the management of acute VVC has remained empirical as it is usually regarded as nonlife-threatening.<sup>[1]</sup> Several women practice self-diagnosis and treatment across the counter, while others merely endure the infection.<sup>[13]</sup> Symptomatic treatment widely practiced in low-resource area probably leads to inappropriate diagnosis and inadequate treatment.<sup>[14]</sup> This cross-sectional study surveyed outpatients in a gynecologic clinic for VVC with the aim of ascertaining its prevalence and the relationship between clinical diagnosis in the same patients and laboratory supported clinical diagnosis. Patients' characteristics particularly educational attainments, knowledge about candidiasis, frequent of self-reported episodes were studied to determine their influence on the accuracy of clinical diagnosis.

## MATERIALS AND METHODS

### Study area and population

This is a prospective, cross-sectional, and observational study among gynecological outpatients at the UNTH Ituku/Ozalla.

The gynecological clinic of the UNTH, Ituku/Ozalla offers general gynecologic and specialist care to patients referred from the hospital's general outpatients department and other referral centers within Enugu and neighboring states.

### Sampling technique

Patients attending the clinic with hospital card numbers ending in an odd number were counseled about the study, consenting women who met the selection criteria were recruited, and recruitment was consecutive until the desired number was completed.

### Inclusions criteria

Women of reproductive age (15–49 years).

They must have had at least one sexual partner in their lifetime.

### Exclusion criteria

Exclusion criteria were as follows:

- Women on hormonal contraceptives
- Women not within reproductive age
- Those known to be positive for HIV antibodies 1 and 2
- Known diabetic mellitus patients
- Women on steroid or antifungal therapy within the previous 2 weeks or broad-spectrum antibiotics in the past month.

### Consent

Informed consent was obtained from each patient. They were informed of their right to withdraw from the study at any stage without any adverse consequence to their care. Ethical clearance was obtained from the Health Research Committee of the UNTH, Ituku/Ozalla.

### Sample size determination

Sample size was determined using the formula  $n = Z^2pq/d^2$  (where  $Z$  = confidence level,  $P$  = prevalence,  $q = 1 - p$ ,  $d$  = the tolerated error) and the prevalence of 15.0 for VVC<sup>[11]</sup> minimum required sample size was 196 women.

### Sampling tools and data collection

A semi-structured, pretested, and interviewer-administered questionnaire was used to get information from each consenting woman by a trained attendant. The questionnaire consisted of sections on patient's socioeconomic, medical, contraceptive, and sexual history and current history of vaginal discharge. Patient's knowledge of *Candida* vaginitis was assessed by direct questions on symptoms and method of transmission then scored as good knowledge 60% or more, moderate knowledge 40%–50%, and poor knowledge <40%. The frequencies of their self-reported episodes of infection were recorded. The interviews were designed to last for 20–25 min and the only self-identifying information included was the hospital card number and the research number to enable follow-up. One of the investigators conducted gynecologic examination on each of the respondents. Nonmoist bivalve speculum was inserted into the vagina, and the cervix and upper vaginal walls were inspected. A pair of swabs was taken from the posterior vaginal vault and cervical os, using cotton-tipped applicators, and immediately sent to the laboratory. The collected samples were aseptically plated on Sabouraud Dextrose Agar (SDA Merck, Germany) and incubated at 35°C

for 48 h. Conventional identification for fungi was made using microscopic morphological features of *Candida*, pseudohyphae, and blastoconidia in the direct smear and positive cultures to confirm *Candida* colonization and infections (VVC).

Patients were deemed to have the clinical disease in the presence of any three of these five listed symptoms: (1) vulva itching, (2) curd or pap-like vaginal discharge, (3) burning sensation in the vulva, (4) dyspareunia, and (5) dysuria. These must be associated with positive findings on genital examination suggestive of VVC, i.e. vaginal erythema, the color, odor, amount, and density of vaginal discharge as well as plaque-like the appearance of the discharge on the wall of the vagina.

### Data processing and analysis

Data entry and analysis utilized the SPSS version 15 software program (SPSS Inc., Chicago IL, USA). Descriptive analysis was done using frequencies and percentages and Chi-square test for comparison of dichotomous variables for statistical association.  $P \leq 0.05$  was considered to be statistically significant.

## RESULTS

### Participants demography

Two hundred and nine women surveyed were aged 19–49 years with mean age of 35.9 (standard deviation [SD]  $\pm 9.0$ ) years. Their parity ranged from 0 to 9 with mean of 2 (SD  $\pm 3$ ). Table 1 shows the characteristics of the women studied. Most (68.4%) were married, and forty-nine women (23.4%) had no formal education or only primary education, seventy (33.5%) received secondary school education while the rest had Diploma or University degrees. Participants were predominantly civil servants and artisan/petty traders, comprising 32.5% and 29.7%, respectively. Ninety-two (44%) women were nulliparous.

### Diagnosis based on clinical evaluation compared to added laboratory culture

Sixty-five of 209 (31.1%) participants had symptoms suggestive of VVC, 54 (25.8%) had clinical-based diagnosis of VVC (based on symptoms and findings on clinical examination), while 155 (74.25%) participants had not. Forty-three (20.6%) had culture-positive laboratory results of which 37 (17.7%) had symptoms and 6 (2.9%) had no symptoms. The prevalence of VVC was 17.7% calculated based on those that had symptoms with culture-positive results; while asymptomatic *candida* colonization was 2.9%. Only 26 (12.4%) of those with clinical-based diagnosis had positive-laboratory culture of *Candida*, hence 11 (false negative) of 37

**Table 1: The demographic characteristics of 209 women surveyed**

Characteristics	Frequency (%)
Age (years)	
24 and below	23 (11)
25-29	39 (18.7)
30-34	35 (16.7)
35-39	32 (15.3)
40 and above	80 (38.6)
Parity	
Nulliparous	92 (44.0)
Multiparous	70 (33.5)
Grand multiparous	47 (22.5)
Marital status	
Married	143 (68.4)
Single	61 (29.2)
Divorced/widowed	5 (2.4)
Education attainment	
Primary/no formal	49 (23.4)
Secondary	70 (33.5)
Tertiary	90 (43.1)
Occupation	
Students	24 (11.5)
Farmers/homemakers	55 (26.3)
Artisans/petty traders	62 (29.7)
Civil servants	68 (32.5)

**Table 2: Sensitivity and specificity of clinical diagnosis of vulvovaginal candidiasis compared to laboratory culture**

Test result	Disease confirmed	Disease unconfirmed	Total	Predictive value (%)
Positive	26	28	54	48.1
Negative	11	144	155	92.9
Total	37	172	209	

Sensitivity=70.3%; Specificity=83.7%

culture-positive cases with symptoms were missed by clinical-based diagnosis. While 28 (false positive) of the 54 clinical-based diagnosis of VVC were not confirmed by laboratory culture.

### Sensitivity, specificity, and positive/negative predictive value of clinical diagnosis

Table 2 shows sensitivity, specificity, positive and negative predictive value of clinical-based diagnosis of VVC alone compared to clinical diagnosis and laboratory culture. This gave a sensitivity of 70.3% and positive predictive value of 48.1% and specificity of 83.7% with negative predictive value of 92.9% for clinically diagnosis of VVC in women studied.

### Participant's knowledge and sources of information

The knowledge and practice of the women with regards to VVC is shown in Table 3. Forty-one (19.6%) of

**Table 3: Knowledge and practices toward vulvovaginal candidiasis**

Knowledge and practices	Frequency (%)
Level of knowledge (n=209)	
Good	41 (19.6)
Moderate	89 (42.6)
Poor	79 (37.8)
Sources of information (n=94)	
Patent medicine shop	2 (2.1)
Formal education	8 (8.5)
Print and electronic media	24 (25.5)
Friends and relations	28 (29.8)
Health workers and doctors	32 (34.0)
Frequency of occurrence of VVC (at least one in one year) (n=209)	
<1 year	56 (26.8)
1-2 years	19 (9.1)
3 years and above	22 (10.5)
No previous report	112 (53.6)
Methods of diagnosis (n=149)	
Relation and friends	4 (2.7)
Pharmacists	13 (8.7)
Disregarded the symptoms	13 (8.7)
Laboratory	29 (19.5)
Self	43 (28.9)
Doctors clinically	47 (31.5)

VVC=Vulvovaginal candidiasis

**Table 4: Patient attributes influencing inaccurate clinical diagnosis of vulvovaginal candidiasis**

Characteristics	Inaccurate diagnosis (%)	P
Age		
24 years or less (n=22)	12 (54.5)	0.007
25-29 (n=39)	15 (38.5)	
30-34 (n=34)	6 (17.6)	
35-36 (n=31)	7 (22.6)	
40 and above (n=80)	16 (20)	
Parity		
Nulliparous (n=91)	29 (31.9)	0.12
Multiparous (n=67)	20 (29.9)	
Grand multiparous (n=45)	1 (15.6)	
Educational level		
No formal/primary (n=46)	10 (21.8)	0.40
Secondary (n=70)	23 (32.9)	
Tertiary (n=87)	23 (26.4)	
Knowledge of VVC		
Good (n=40)	10 (25.0)	0.83
Moderate (n=86)	23 (26.7)	
Poor (n=77)	23 (29.9)	
Frequency of reporting		
Annually or less (n=56)	23 (41.1)	0.005
1-2 yearly (n=19)	7 (36.8)	
3 or more yearly (n=22)	8 (36.4)	
Nonpreviously (n=112)	18 (16.0)	

VVC=Vulvovaginal candidiasis

them had good knowledge, and the rest had moderate knowledge (42.6%) and poor knowledge (37.8%). Their most common source of information about VVC was from health-care providers (15.3%), friends and relations (13.45%), and print and electronic media (11.5%). Most of the women (44.5%) had self-reported and treated VVC within the year. Their most common means of diagnosis was by doctors clinically (31.5%), self (28.8%), and laboratory (19.5). Thirteen (7.4%) of the women who had ever been symptomatic claimed that they usually ignored the symptoms.

### Respondents characteristics associated with inaccurate diagnosis

Table 4 shows maternal factors associated with inaccurate clinical diagnosis, maternal age, and self-reporting frequency of VVC was significantly associated with inaccurate clinical diagnosis ( $P \leq 0.05$ ). Young women of 24 years or less 12/22 (54.5%) and those who had reported other episodes of VVC within the past year 23/56 (41.1%) were most commonly associated with inaccurate clinical diagnosis.

## DISCUSSION

*Candida* is usually a commensal fungus residing on the skin, mucosa of the vagina, and gastrointestinal tract in about 30%–50% of healthy adults<sup>[15]</sup> VVC is estimated to be the second-most common cause of vaginitis after bacterial vaginosis depending on the population studied.<sup>[1,16]</sup> The incidence increases with the initiation of sexual activity though there has been no direct evidence to prove that it is sexually transmitted.<sup>[17,18,19]</sup> In this study, only sexually active women were sampled to enable ease of comparison and allow effective vaginal examination. The prevalence of VVC based on the laboratory culture confirmation was 17.7%. This was comparably higher than 14% reported by a study among nonpregnant women in a tertiary health facility in Abuja Nigeria.<sup>[20]</sup> A study among female sexual workers in Nellore, India found a slightly higher prevalence of 18.9%.<sup>[21]</sup> Our study was more restrictive than that in India and women at very high risk of VVC were excluded from the study. Furthermore, the study resided in a tertiary center and excluded women who may have received care in primary health-care centers which are mostly involved in treating uncomplicated VVC.

Understanding the mechanism by which vaginal candidiasis change from commensal to pathogenic remains important for both prevention and diagnosis. Host-related factors especially antibiotics use, blood glucose level, and hormonal changes associated with pregnancy were controlled for in this study. The immediate pathological

sequence of infection has been postulated to include mucosal irritation, itching, and erythema. Clinical diagnosis is based on the presence of symptoms, evidence of inflammatory changes, and identification of white or yellowish chunky curd-like or pap-like discharge in the vagina or vulva. Pruritus is a very important complaint in VVC and often the reason for consultation and identification of the disease. Nevertheless, only about 50% of women with genital pruritus suffer from VVC.<sup>[22]</sup> This militates against treatment based on self-diagnosis and the common office practice of clinically based diagnosis and treatment of VVC. Clinically based treatment has persisted due chiefly to patients' preference because of their convenience, belief that VVC is not life-threatening and its empirical treatment harmless.<sup>[1]</sup> Clinically based evaluation in this study which followed more strict criteria than in most gynecological practices showed moderate sensitivity and unacceptably high false-positive rates when relied on exclusively. This no doubt would encourage overtreatment and abuse of antimycotic drugs especially since they are usually available across the counter.

The level of satisfactory knowledge of VVC in the women studied was only 19.6%. Almost the same percentage obtained information about VVC from hospital workers and friends and relations. Most (60.4%) respondents studied were treated empirically, and another 7.4% of them merely disregarded their symptoms.

Vulvovaginal conditions including VVC often reduce quality of life and may produce psychological, social, and sexual repercussions. Loss of intimacy with partners due to discomfort, dyspareunia, and frustration as well as low self-esteem has been reported.<sup>[23]</sup> Clinical diagnosis in this study followed strict criteria, and its sensitivity was 70.3% while the specificity was 83.7%. This had a lower sensitivity but almost a similar specificity as the study by Lowe *et al.* who found sensitivity of 83.8% and specificity of 84.8% clinical diagnosis of *candida* vaginitis compared with DNA probe laboratory diagnosis.<sup>[24]</sup> This study found that clinical-based diagnosis alone is likely to lead to significant over diagnosis and treatment. This would lead to unnecessary financial burden on the patients, increased risk of developing drug-resistant strains and possibly exposing patient unduly to potential drug side effects. Lander *et al.* counseled against the use of symptoms alone in directing treatment for lower genital tract infections.<sup>[14]</sup>

Apart from cultures, confirmation of VVC may also be based on an office evaluation using the Amsel criteria to exclude bacteria vaginosis in which the pH is <4.5, Whiff test is positive, and clue cells are seen on microscopic examination. Comparative diagnostic

methods were not examined in this study based on convenience and the goals of the study. However, laboratory cultures are known to perform better than standard office evaluation techniques including wet mounts with potassium hydroxide.<sup>[25]</sup> Furthermore, the added personnel cost of running a side laboratory within the gynecological clinics must be weighed against the extra cost of cultures in low-resource centers that are not primarily sexually transmitted infection preventive clinics.

An attempt was made in this study to identify any patients' attributes which may be associated with poor precision of clinical diagnosis. Women aged 24 years or less and those who had reported other episodes of VVC within the year were most vulnerable. Clinical diagnosis is strongly influenced by the ability to report symptoms accurately as well as the diagnostic acumen of the practitioner. Women 18–30 years are known to be most vulnerable to genital tracts infection.<sup>[26]</sup> Those who have been recently exposed to VVC may attribute any similar symptoms to it.

Generalization of the prevalence of VVC in this study is limited due to the high selectivity of the population studied and its location. Laboratory tests utilized the hospital facilities and reflect what is usually done in every day clinical practice which adds feasibility and applicability to the study. However, financial considerations limited the investigator's ability to characterize the species of *candida* involved in affected women.

## CONCLUSION

The diagnosis of VVC based on clinical features alone had low positive predictive value in this study especially in young women and those previously reporting a similar attack within the year. The low knowledge of participants about VVC underscores the need to discourage treatment based on self-diagnosis and over the counter dispensation of antimycotic medications for this condition. Clinical evaluation and laboratory culture of vulvovaginal specimen should be the standard diagnostic method to eliminate the risk of misdiagnosis and possibly eliminate the potential long-term consequences of incomplete treatment, balanitis in the males, and vulvodinia in the affected women.

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## Conflicts of interest

There are no conflicts of interest.

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