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Candidiasis in HIV Positive Female Adults on HAART in Ogun State, Nigeria: Prevalence, Risk Factors and Antifungal Susceptibility Study

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Abstract

Background: *Candidiasis is the most common opportunistic fungal infection reported in human immunodeficiency virus (HIV) positive patients worldwide.*

Aim: *This study was designed to investigate the prevalence of Candida colonization in the mouth and vagina of HIV seropositive adult females on highly active antiretroviral therapy (HAART) in Ogun State, Nigeria, as well as to determine the antifungal susceptibility pattern of the Candida isolates.*

Methods: *A total of one hundred and twenty (120) consenting HIV positive female patients on HAART were recruited for the study. Oral and vagina swabs were collected in duplicates from the participants and streaked on Sabouraud's Dextrose Agar (SDA) plates. Identification of Candida species was performed by conventional methods, while the antifungal susceptibility testing of the yeast isolates was performed using the disc diffusion method with commercially produced antifungal discs. Data were analyzed using Statistical Package for Social Scientist version 18.0 (SPSS-18.0).*

Results: *Out of the 120 participants examined, 60 (50%) of them were colonized by Candida yeasts. 10.8% were positive for only oral candidiasis, 21.7% were positive for only vaginal candidiasis, whereas 17.5% were positive for both oral and vaginal candidiasis. Percentage co-occurrence of oral and vaginal candidiasis was found to be significantly higher ($P<0.05$) among those within 42-49 years (6.7%) and those with primary education (7.5%). Candida albicans (CA) was the dominating specie (54.3%), while the non-albicans Candida (NAC) species accounted for 45.7%. The isolates were most sensitive to Itraconazole and Griseofluvin and less sensitive to Ketoconazole, Nystatin and Fluconazole. Identified risk factors associated with occurrence of mucosal candidiasis in this study include: lack of HAART adherence, lack of anti-candida prophylaxis, poor knowledge of candidiasis, history of oral/vaginal infection, sharing of sanitary facilities with others, nature of anal cleaning, recent change in sexual partners and use of contraceptive amongst others.*

Conclusion: *The outcome of this study underscored the importance of routine checks for candidiasis among HIV patients, use of anti-candida prophylactic, and as well as adequate oral and vaginal care in HIV infection. Early detection of mucosal candidiasis and prompt treatment will help prevent subsequent complications such as candidemia among HIV patients.*

Keywords: *HIV, HAART, Female, Oral, Vaginal, Candidia isolates, Susceptibility Pattern, Risk factors*

1. Introduction

Human immunodeficiency virus (HIV) remains one of the largest pandemics in the world. Globally, an estimated 37.9 million people are living with HIV, 21.7 million people are accessing antiretroviral therapy, 1.8 million people became newly infected and 940,000 people have died from HIV-related illness in 2017 [1-3]. Nigeria has the second largest HIV epidemic in the world and one of the highest new infection rates in Sub-Saharan Africa [3]. Currently, about 1.9 million Nigerians (1.4%, ages 15-49 years) are living with HIV and about 33% are unaware of their HIV status.

There are 130,000 new HIV infection cases in Nigeria, 53,000 AIDs-related deaths, 55% adults and 35% children are on antiretroviral therapy (ART), while 80% HIV positive patients on

ART are virally suppressed. Akwa Ibom has the highest prevalence rate of 5.6%, while Jigawa and Katsina have the lowest prevalence rate (0.3%). Ogun State in particular has a prevalence of 1.2% [4].

One of the most common HIV-associated opportunistic infections is candidiasis (also known as thrush or *moniliasis*). It is caused by Candida species mainly *C. albicans* [5-7]. The most serious outbreaks of candidiasis occur when CD4 counts are very low (below 200). During the course of HIV infection, the rate of Candida infection has been found to be inversely related to the CD4 counts of the patient which in turn depends on the use of Anti-retroviral treatment [8].

Mucosal candidiasis occurs in three forms in persons with HIV infection: oropharyngeal, esophagus and vulvovaginal disease [9]. Oropharyngeal candidiasis (OPC) is among the initial manifestations of HIV infection. The clinical presentation include white or red patches in the mouth, tongue, cracking and soreness at the corners of the mouth, altered taste, mouth pain or burning sensation. Oral lesions might first be seen by General Clinician or Dentist who may prompt the patient to seek HIV testing and possibly benefit from early intervention [10]. Severe OPC can interfere with the administration of medications and adequate nutritional intake, and may spread to the esophagus. Esophageal candidiasis is associated with upper chest pain, sore throat and painful swallowing. While vaginal candidiasis on the other hand, causes itching, burning sensation, redness and soreness in the genital area, with a thick white-yellow cheesy discharge [11].

Early diagnosis of candidiasis is very crucial to reducing the mortality and morbidity rates of infections caused by *Candida* species especially among HIV infected Patients. It can also prevent life threatening complications such as systemic candidiasis, invasive candidiasis or candidemia which may result in death [12, 13].

The evaluations of oral and vaginal candidiasis among HIV infected adult females on HAART will help to determine the main specie of *Candida* causing the infection. This will aid specificity of antifungal therapy and reduce the risk of multidrug resistant candidiasis, because the different species of Candida that causes candidiasis in HIV patients if not identified and properly treated with the appropriate drug could lead to resistance of the drug and make treatment very difficult. It is also very important to identify the predisposing factors for oral and vaginal candidiasis in HIV-infected females, as well as the sensitivity pattern of the Candida species to the available antifungal agents. However, the frequency of occurrence of both oral and vaginal candidiasis in HIV infected adult female patients on HAART attending HIV-clinic of Babcock University Teaching Hospital (BUTH), Ilishan-Remo, Ogun State is not known. Scarcity of information in this regard necessitates this study.

2. METHODS

2.1. Study Design

This is a descriptive prospective study.

2.2. Study Area

This study was carried out among HIV infected adult female patients on HAART attending HIV clinic, Babcock University Teaching Hospital (BUTH), Ilishan-Remo, Ogun State. BUTH is a 300 bed space capacity private hospital and the only tertiary hospital in the community. While Ilishan-Remo community is one of the geo-political wards in Ikenne Local Government Area of Ogun State, situated in the tropical area of South-western part of Nigeria, coordinates 7o29'00"N, 2o55'00"E.

2.3. Duration of Study

This study was carried out between the months of April and June, 2019

2.4. Study Population

This cross-sectional institutional based study was carried out among HIV positive adult female patients on HAART attending HIV-clinic at Babcock University teaching hospital, Ilishan-Remo, Ogun state.

2.5. Sample Size Calculation

The sample size (N) for this study was estimated using the formula described by Charan and Biswas [14]: N=Z2PQ/d2

Where,

N = required sample size

Z = Standard normal variance at 5% ($p<0.05$) error or 95% confidence interval is 1.96

P = Portion of the population of adult female HIV positive patients on HAART with candidiasis from previous study

Q = Portion of the population of adult female HIV positive patients on HAART without candidiasis (1-P) and

D = Absolute error margin is 0.05

For the calculation, a 95% confidence interval, a P value of 0.076, i.e, a prevalence rate of 7.6% candidiasis among African HIV adult females from a previous study by Mushi et al. [15], and margin of error (d) set at 0.05 will be used to determine the minimum sample size required. To minimize errors arising from the likelihood of non-compliance, 10% of the sample size will be added giving a final sample size of 120.

2.6. Sample Size

A total of 120 consenting HIV positive adult female patients on HAART, attending HIV Clinic, Babcock University Teaching Hospital (BUTH), Ilishan-Remo, Ogun State, Nigeria were recruited for the study.

2.7. Eligibility of Subjects

2.7.1. Inclusion Criteria

Consenting adult females on HAART, with HIV status confirmed using, Determine HIV-1/2, Statpak HIV-1/2 and UniGold HIV-1/2 kits attending the HIV-clinic at Babcock University Teaching Hospital (BUTH), Ilishan-Remo, Ogun State, who were not on antifungal therapy in the preceding two (2) weeks were randomly selected for the study.

2.7.2. Exclusion criteria

The following individuals were excluded from the study: HIV positive females less than 18 years, HIV positive adult females not on HAART, those with history of antifungal therapy in the preceding two weeks, as well as HIV positive adult males (with or without HAART).

2.8. Ethical Approval

Ethical approval was obtained from the Babcock University Health Research Ethics Committee (BUHREC) before the commencement of the study with ethical registration number: BUHREC209/19.

2.9. Consent

Informed consent was obtained from each participant. The purpose and nature of the study, as well as the method of sample collection will be explained to them properly. Afterwards, participants will be requested to voluntarily complete the consent form in their own handwriting and endorsed by their signatures as proof of willingness to provide samples for the test. They will be assured of the confidentiality.

2.10. Data Collection

Prior to specimen collection, demographic and clinical information were obtained from participants through administration of prepared questionnaire and personal interviews. Each questionnaire will have a unique participant identification number (PIDN). The first part of the questionnaire will contain the biodata of the patients e.g. name, sex, age, educational status, religion and marital status. Second part will include history of candidiasis (bad breadth, white tongue, dryness of the mouth, difficulty swallowing, abnormality of taste, vaginal discharge, vaginal itching, painful intercourse etc), risk factors (if any), personal hygiene and health care-seeking behavior. The study population will be stratified by age, marital status and ART. Response to structured questionnaire will be used to collect data on epidemiology and demographic trends of Oral and Vaginal Candidiasis in HIV infection. For the purpose of privacy, all information obtained from the participants will be treated confidentially.

2.11. Specimen Collection, Transportation and Storage

Self-collected early morning oral swabs and high vaginal swabs (HVS) were requested from each study participants. They were provided with sterile swab sticks to collect samples in duplicates, as well as instruction on how to collect samples aseptically. The specimens were collected from each participant and labeled accordingly with their Identification Number on the specimen container. All samples were transported to the laboratory as soon as possible without delay and processed on the same day of collection. Where delay was envisaged, they were kept in the refrigerator at 2-8oC.

2.12. Laboratory Analyses

2.12.1. Direct microscopy

One of the duplicates of the swab sticks (Vaginal and mouth swabs) of each patient were agitated in 1ml of normal saline. A drop of suspension of each sample was transferred to different grease-free glass slide and covered with a cover slip gently to exclude air bubbles and viewed microscopically under 10x and 40x objectives. A drop of the suspension was placed on clean grease-free slide and a drop of potassium hydroxide (KOH) added. The preparation was mixed and covered with a cover

slip and examined for Candida species using 10x and 40x objectives.

2.12.2. Culture

The second duplicates of oral and vaginal swabs of each patient were streaked on Sabouraud dextrose agar (SDA) with chloramphenicol incorporated to inhibit bacterial growth. The culture plates were incubated at 370C and examined for growth after 24 hours.

2.12.3. Identification of isolates

The fungal isolates from the oral and vaginal swabs were identified based on their macroscopic appearances which include elevation, surface, colour, edge and opacity. Microscopic analysis was carried out using the Wet mount, Permanent direct mount, Gram staining technique and the Germ tube test as described by Ochei and Kolhatkar [16].

Wet Mount

A small portion of the yeast colony with a small drop of sterile distilled water was transferred on a clean glass slide and a clean glass cover was placed over it. It was observed immediately under the microscope.

Permanent Direct Mount

A smear was prepared from the fungal culture and heat fixed by passing through a Bunsen flame 2-3 times. A small drop of lactophenol cotton blue (LPCB) was placed on the fixed smear and covered with a glass cover. The edges of the glass cover were sealed with DPX and examined microscopically for budding small oval yeast cells.

Gram Staining

A colony of the isolate was emulsified in normal saline and a smear will be made, allowed to air dry and heat fixed by passing it through Bunsen burner flame thrice. The smear was stained with crystal violet for one minute and washed off with water. The smear was stained with Lugol's iodine for one minute washed off with water. The smear was then decolourized with acetone briefly under running water and stained with neutral red for one minute and the stain washed off with water. The back of the slide was cleaned with cotton wool, allowed to air dry, and examined microscopically with immersion oil using the oil immersion objective lens. Presence of Gram positive yeast-like cells was indicative of Candida spp.

Germ Tube Test

About 0.5ml of human serum or bovine albumin was measured into a small test tube. A sterile wire loop was used to inoculate the serum with a yeast colony from the culture plate. The tube was placed in a water bath or incubator at 35-370C for 2-3 hours. A Pasteur pipette was used to transfer a drop of the serum yeast culture to a glass slide, and covered with a cover slip. The preparation was examined using x10 and x40 objectives with the condenser iris diaphragm closed sufficiently to give good contrast. The preparation was observed for Sprouting yeast cells (i.e., tube-like outgrowth from the cells known as germ tubes). Positive germ tube test was reported as Candida albicans (CA), while negative germ tube test was reported as Non-albicans Candida species (NAC).

2.12.4. Antifungal Susceptibility Testing of Candida Isolates

The antifungal sensitivity pattern of the Candida isolates was determined using the modified Kirby-Bauer disc diffusion technique described by Bauer et al. [17] and Cheesbrough [18]. Using the Interpretative Chart, the zones sizes of each antibiotic was interpreted and the isolate reported as 'Resistant', 'Intermediate susceptible', or 'Susceptible'.

2.13.Data analysis

Data obtained from the test procedures, as well as from the questionnaire were entered into Microsoft Excel. Statistical analysis was carried out using SPSS-18.0 (Statistical Package for Social Scientist version 18.0) statistical program.

Chi-square and Tukey-kramer Multiple Comparisons Test was used to test for significant differences between prevalence rate of oral and vaginal candidiasis among HIV infected adult females. Data was also subjected to Spearman correlation analysis using Graphpad In-stat Software Package to determine the relationship between occurrence of candidiasis and associated risk factors. Significant risk factors for candidiasis were determined with simple logistic regression analysis. Statistical outputs were presented using tables and charts.

3. Results and Discussion

The demographic characteristics of the study participants including age range, religion, tribe,

educational status and marital status is presented in Table 1. Majority of the participants are within the age range of 34-41 years (36.7%), while the least were between 18-25 years (3.3%). 75.8% of the participant are married, 15.8 % are single, 3.3% are divorced, 3.3% are widowed and 1.7% are separated. The overall prevalence of candidiasis among the study participants is presented using a pie chart (Figure 1).

The outcome of the study shows that half of the study participants had candidiasis. Out of the 120 participants screened, 60 of them (50%) tested positive for candidiasis and the other 60 (50%) tested negative. The prevalence of oral and vaginal mono/co-candidiasis among the study participants is presented using a pie chart (Figure 2). 13 (10.8%) out of the 120 participants examined had only oral candidiasis, 26 (21.7%) had only vaginal candidiasis, while 21 (17.5%) of them had both oral and vaginal candidiasis.

Table1. *Socio-demographic Characteristics of the study participants*

Socio-demographic Characteristics	Category	Frequency (N)	Percentage (%)
Age Range	18-25yrs	4	3.3
	26-33yrs	12	10.0
	34-41yrs	44	36.7
	42-49yrs	31	25.8
	Above 50yrs	29	24.2
	Total	120	100.0
Educational Status	None	8	6.7
	Primary	18	15.0
	Secondary	66	55.0
	Tertiary	28	23.3
	Total	120	100.0
Marital status	Single	19	15.8
	Married	91	75.8
	Divorced	4	3.3
	Separated	2	1.7
	Widow	4	3.3
	Total	120	100.0

The frequency of occurrence of oral candidiasis in relation to the socio-demographic characteristics of the study participants is presented in Table 2.

Based on age distribution of oral candidiasis, the highest occurrence was recorded among participants within the age 34-41 years (4.2%), followed by 50 years and above (3.2%), while none (0%) was recorded for 26-33 years.

Based on their marital status, 9.1% of those positive for oral candidiasis were married, while 1.7% were singles.

On the basis of their educational status, the highest occurrence was recorded among those with tertiary education (4.2%), but none was recorded among those without any formal education (0%).

There is no significant difference ($P>0.05$) in the prevalence of oral candidiasis among the study participants with respect to all the demographic factors considered.

Table 3 shows the frequency of vaginal candidiasis in relation to the socio-demographic characteristics among the study participants. The highest occurrence of vaginal candidiasis was found among those within 42-49 years (11.8%), followed by those within 34-41 years (8.3%). A total number of 26 (21.7%) out of the 120 participants examined, had vaginal candidiasis.

The prevalence of vaginal candidiasis was found to be significantly ($P<0.05$) higher among participants within the age range of 42-49 years and those with secondary education.

Furthermore, the frequency of co-occurrence of oral and vaginal candidiasis in relation to the socio-demographic characteristics among the study participants is presented in Table 4.

Out of the 120 study participant examined, 21 (17.5%) had both oral and vaginal candidiasis. Percentage co-occurrence of oral and vaginal candidiasis was found to be significantly higher ($P<0.05$) among those within 42-49 years

(6.7%) and those with primary education (7.5%).

The distribution of Candida species among the study participants is presented in Table 5. Out of the 60 Candida isolates recovered, 34 (56.7%) were Candida albicans (CA); whereas 26 (43.3%) were non-albicans Candida (NAC). The occurrence of Candida albicans and Non albicans Candida was found to be highest among those that are married (36.8% and 40.0%, respectively), and those with secondary education (31.7% and 18.3%, respectively).

Table2. *The frequency of occurrence of oral candidiasis in relation to the socio-demographic characteristics of the study participants*

Socio-demographic Characteristic	Category	Number of participants examined N (%)	Number positive for only oral candidiasis N (%)	Number negative for only oral candidiasis N (%)	*P-value*	Pearson Chi-Square (χ^2)
Age Range	18-25yrs	4 (3.3)	2(1.7)	2(1.7)	0.420	8.702
	26-33yrs	12(10)	0(0)	12(10)	0.164	
	34-41yrs	44(36.7)	5(4.2)	39(32.5)	0.998	
	42-49yrs	31(25.8)	2(1.7)	29(24.2)	0.911	
	≥ 50yrs	29(24.2)	4(3.2)	25(20.8)	0.430	
	Total	120 (100)	13 (10.8)	107 (89.2)		
Educational Status	None	8(6.7)	0(0)	8(6.7)	0.098	6.375
	Primary	18(15)	4(3.3)	14(11.6)	0.999	
	Secondary	66(55)	4(3.3)	62(51.7)	0.934	
	Tertiary	28(23.3)	5(4.2)	23(19.2)	0.076	
	Total	120 (100)	13 (10.8)	107 (89.2)		
Marital status	Single	19(15.9)	2(1.7)	17(14.2)	0.871	1.365
	Married	91(75.8)	11(9.1)	80(66.7)	0.850	
	Divorced	4(3.3)	0(0)	4(3.3)	1.000	
	Separated	2(1.7)	0(0)	2(1.7)	1.000	
	Widow	4(3.3)	0(0)	4(3.3)	1.000	
	Total	120 (100)	13 (10.8)	107 (89.2)		

NB: P–value >0.05 is considered statistically not significant.

Table3. *The frequency of occurrence of vaginal candidiasis in relation to the socio-demographic characteristics among the study participants*

Socio-demographic Characteristic	Category	Number of participants examined N (%)	Number positive for only vaginal candidiasis N (%)	Number negative for only vaginal candidiasis N (%)	*P-Value*	Pearson Chi-Square (χ^2)
Age Range	18-25yrs	4(3.3)	0(0)	4(3.3)	0.377	18.146
	26-33yrs	12(10)	1(0.8)	11(9.2)	0.999	
	34-41yrs	44(36.7)	10(8.3)	34(28.3)	0.551	
	42-49yrs	31(25.8)	14(11.8)	17(14.2)	0.046*	
	≥50yrs	29(24.2)	1(0.8)	28(23.3)	0.996	
	Total	120 (100)	26 (21.7)	94 (78.3)		
Educational Status	None	8(6.7)	0(0)	8(6.7)	0.999	10.093
	Primary	18(15)	0(0)	18(15)	0.999	
	Secondary	66(55)	20(16.7)	46(38.3)	0.049*	
	Tertiary	28(23.3)	6(5)	22(18.3)	0.081	
	Total	120 (100)	26 (21.7)	94 (78.3)		
Marital status	Single	19(15.9)	4(3.3)	15(12.5)	0.882	3.108
	Married	91(75.8)	22(18.4)	69(57.5)	0.540	
	Divorced	4(3.3)	0(0)	4(3.3)	0.999	
	Separated	2(1.7)	0(0)	2(1.7)	0.999	
	Widow	4(3.3)	0(0)	4(3.3)	1.000	
	Total	120 (100)	26 (21.7)	94 (78.3)		

NB: P–value <0.05 is considered statistically significant.

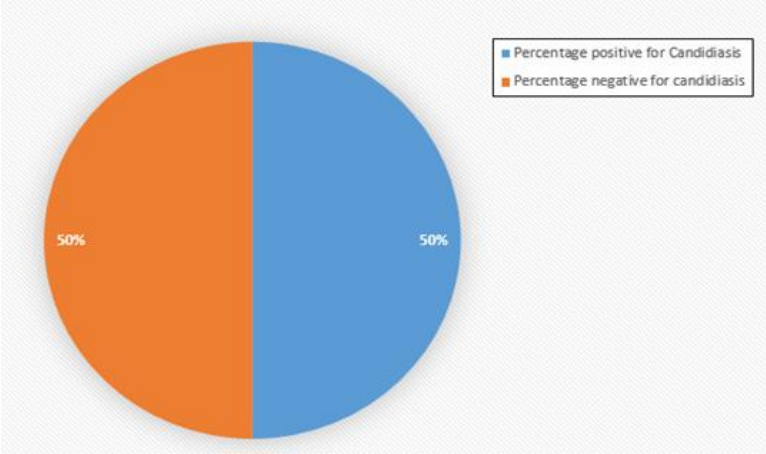


Figure1. *A pie chart showing overall prevalence of Candidiasis among the study participants*

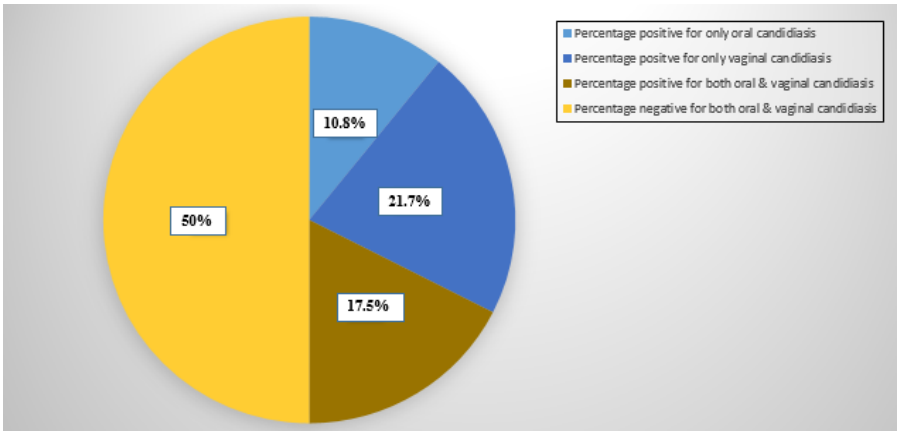


Figure2. *A pie chart showing prevalence of oral and vaginal mono/co-candidiasis among the study participants*

Table4. *The frequency of co-occurrence of oral and vaginal candidiasis in relation to the socio- demographic characteristics among the study participants*

Socio-demographic Characteristic	Category	Number of participants examined N (%)	Number positive for both oral & vaginal candidiasis N (%)	Number negative for both oral & vaginal candidiasis N (%)	*P-Value*	Pearson Chi-Square (χ^2)
Age Range	18-25yrs	4(3.3)	0(0)	4(3.3)	0.999	2.689
	26-33yrs	12(10)	2(1.7)	10(8.3)	0.725	
	34-41yrs	44(36.7)	7(5.8)	37(30.9)	0.134	
	42-49yrs	31(25.8)	8(6.7)	23(19.2)	0.038*	
	Above 50yrs	29(24.2)	4(3.3)	25(20.8)	0.824	
	Total	120 (100)	21 (17.5)	99 (82.5)		
Educational Status	None	8(6.7)	2(1.7)	6(5)	0.143	16.913
	Primary	18(15)	9(7.5)	9(7.5)	0.049*	
	Secondary	66(55)	6(5)	60(50)	0.082	
	Tertiary	28(23.3)	4(3.3)	24(20)	0.107	
	Total	120 (100)	21 (17.5)	99 (82.5)		
Marital status	Single	19(15.8)	4(3.3)	15(12.5)	0.318	14.021
	Married	91(75.9)	13(10.8)	78(65)	0.133	
	Divorced	4(3.3)	2(1.7)	2(1.7)	0.724	
	Separated	2(1.7)	2(1.7)	0(0)	0.091	
	Widow	4(3.3)	0(0)	4(3.3)	0.999	
	Total	120 (100)	21 (17.5)	99 (82.5)		

NB: P–value <0.05 is considered statistically significant.

While Candida albicans was more common among those that are 34-41 years (28.3%), Non-albicans Candida was more common among 42-49 years (20.0%). There was however, no significant difference (P>0.05) in the distribution of the Candida species based on all the socio-demographic factors of the study participants considered.

The risk factors associated with the occurrence of oral and vaginal candidiasis among the study participants is presented in Table 6. All the study participants were on HAART and 117 (97.5%) of the respondent use their medication always, while 3 (2.5%) use their medications often. Out of the 97.5% that use their HAART medications often, 13 (10.8%) have only oral candidiasis, 26 (21.7%) have only vaginal candidiasis, while 21 (17.5%) have both oral and vaginal candidiasis. Out of the 100 (83.3%) respondents with no knowledge of Candida as the causative agent of oral and vaginal thrush, 11 (9.1%) had only oral candidiasis, 21 (17.5%) had only vaginal candidiasis, while 17 (14.2%) had both oral and vaginal candidiasis.

Furthermore, 20 respondents indicated that they have history of oral infection, out of which *4 (3.3%)* were positive for oral candidiasis, whereas 11 (9.1%) had both oral and vaginal candidiasis. 33 (27.5%) of the respondents indicated that they have history of vaginal infection. 9 (7.5%) of them tested positive for only vaginal candidiasis, whereas 2 (1.7%) tested positive for both oral and vaginal candidiasis

Table5. *Distribution of Candida species among the study participants*

Socio-demographic Characteristic	Category	Type of Candida species		Total Number of isolates	*P-Value*	Pearson Chi-Square (χ^2)
		Candida albicans	**Non *albicans Candida***			
Age Range	18-25yrs	0(0)	2(3.3)	2(3.3)	0.886	13.497
	26-33yrs	3(5)	0(0)	3(5)	0.999	
	34-41yrs	17(28.3)	5(8.3)	22(36.7)	0.999	
	42-49yrs	12(20)	12(20)	24(40)	0.998	
	Above 50yrs	2(3.3)	7(11.7)	9(15)	0.999	
	Total	34(56.7)	26(43.3)	60(100)		
Educational Status	None	0(0)	2(3.3)	2(3.3)	0.981	8.656
	Primary	10(16.7)	3(5)	13(21.7)	1.000	
	Secondary	19(31.7)	11(18.3)	30(50)	0.729	
	Tertiary	5(8.3)	10(16.6)	15(25)	.954	
	Total	34(56.7)	26(43.3)	60(100)		
Marital status	Single	8(13.3)	2(3.3)	10(16.6)	1.000	6.740
	Married	22(36.8)	24(40)	46(76.8)	0.999	
	Divorced	2(3.3)	0(0)	2(3.3)	1.000	
	Separated	2(3.3)	0(0)	2(3.3)	1.000	
	Total	34(56.7)	26(43.3)	60(100)		

NB: P–value >0.05 is considered statistically not significant.

In addition, 10 (8.3%) respondents indicated that they share their sanitary facilities with others, 4 (3.3%) out of the 10 were found to be positive for only vaginal candidiasis. 15 (12.5%) out of the 44 (36.7%) respondents who indicated that they clean from back to front after using the toilet, were positive for vaginal candidiasis. 10 (8.3%) of the 85 respondents who indicated that they have 1-2 sexual partners had only oral candidiasis, 19 (15.8%) had only vaginal candidiasis, whereas 14 (11.7%) had both oral and vaginal candidiasis.

Two (2) of the 9 participants who indicated recent change in sexual partners, had oral candidiasis (1.7%) and vaginal candidiasis (1.7%). 2 (1.7%) out of the 7 participants who indicated they use contraceptives, have oral candidiasis, 3 (2.5%) had vaginal candidiasis, whereas only 2 (1.7%) had both oral and vaginal candidiasis.

The prevalence of symptomatic and asymptomatic candidiasis among the study participants is presented using a bar chart (Figure 3). 3.3% had symptomatic oral candidiasis, 7.5% had both asymptomatic oral candidiasis and symptomatic vaginal candidiasis. While 14.2% had asymptomatic vaginal candidiasis, 3.3% and 14.2% had symptomatic and asymptomatic co-occurrence of oral and vaginal candidiasis, respectively. The indications for oral candidiasis

in relation to the occurrence of candida species is presented in Figure 4. Candida albicans was recovered from 1.7% case of white tongue, 3.3% case of difficulty in swallowing, 3.3% case of bad breath. On the other hand, Non-albicans Candida were recovered from 3.3% case of oral sores, and 3.3% case of mouth dryness. There were no significant differences (P>0.05) in the

Table6. *Risk factors associated with the occurrence of oral and vaginal candidacies among the study participants*

Characteristics	Responses	Total No. of Participants examined N (%)	No. Positive for only oral candidiasis N (%)	No. Positive for only vaginal candidiasis N (%)	No. Positive for both oral&vaginal candidiasis N (%)	No. Negative for both oral & vaginal candidiasis N (%)	P-Value	OR
Adherence to HAART Medication	Always	117(97.5)	13(10.8)	26(21.7)	21(17.5)	57(47.5)	0.380	.000
	Often	3(2.5)	0(0)	0(0)	0(0)	3(2.5)		
Knowledge of Candida as causative agent of oral and vaginal thrush	Yes	20(16.7)	2(1.7)	5(4.2)	4(3.3)	9(7.5)	0.952	.559
	No	100(83.3)	11(9.1)	21(17.5)	17(14.2)	51(42.5)		
History of oral infection	Yes	20(16.7)	4(3.3)	3(2.5)	2(1.7)	11(9.1)	0.355	4.058
	No	100(83.3)	9(7.5)	23(19.2)	19(15.8)	49(40.9)		
History of vaginal infection	Yes	33(27.5)	7(5.8)	9(7.5)	2(1.7)	15(12.5)	0.032	1.921
	No	87(72.5)	6(5)	17(14.2)	19(15.8)	45(37.5)		
Frequency of brushing	Once daily	83(69.2)	9(7.5)	19(15.8)	11(9.2)	44(36.7)	0.327	24.795
	Twice daily	37(30.8)	4(3.3)	7(5.8)	10(8.3)	16(13.3)		
Sharing toothbrush with others	Yes	2(1.7)	0(0)	0(0)	0(0)	2(1.7)	0.565	.000
	No	118(98.3)	13(10.8)	26(21.7)	21(17.5)	58(48.3)		
Sharing sanitary facilities with others	Yes	10(8.3)	0(0)	4(3.3)	0(0)	6(5)	0.172	.000
	No	110(91.7)	13(10.8)	22(18.4)	21(17.5)	54(45)		
Sharing underwear with others	Yes	3(2.5)	0(0)	1(0.8)	0(0)	2(1.7)	0.744	65.490
	No	117(97.5)	13(10.8)	25(20.9)	21(17.5)	58(48.3)		
Frequency in changing underwear	Everyday	109(90.9)	13(10.8)	20(16.7)	20(16.7)	56(46.6)	0.180	87.231
	Every 2 days	4(3.3)	0(0)	2(1.7)	0(0)	2(1.7)		
	Neither of the two options	7(5.8)	0(0)	4(3.3)	1(0.8)	2(1.7)		
Nature of Cleaning up after using the toilet	Back to front	44(36.7)	5(4.2)	15(12.5)	5(4.2)	19(15.8)	0.069	1.491
	Front to back	76(63.3)	8(6.6)	11(9.2)	16(13.3)	41(34.2)		
Number of sexual partners	None	35(29.2)	3(2.5)	7(5.8)	7(5.8)	18(15)	0.920	.887
	1-2	85(70.8)	10(8.3)	19(15.8)	14(11.7)	42(35)		
Recent change of sexual partner	Yes	9(7.5)	2(1.7)	2(1.7)	0(0)	5(4.2)	0.403	6.903
	No	111(92.5)	11(9.2)	24(20)	21(17.5)	55(45.8)		
Use of contraceptives	Yes	7(5.8)	2(1.7)	3(2.5)	2(1.7)	0(0)	0.047	58.985
	No	113(94.2)	11(9.2)	23(19.2)	19(15.8)	60(50)		

NB: P–value >0.05 is considered statistically not significant.

Occurrence of Candida albicans and Non-albicans candida in relation to the indication for oral candidiasis.

The indications for vaginal candidiasis in relation to the occurrence of Candida species is presented in Figure 5. Candida albicans was recovered in 3.3% case of suprapubic discomfort, 10% case of vaginal itching, and 6.7% case of vaginal discharge. On the other hand, Non-albicans Candida species were isolated in 6.7% case of vaginal itching and in 3.3% case of vaginal discharge.

The antifungal sensitivity pattern of the candida isolates is presented using a bar chat (Figure 6). A total number of 35 (19 Candida albicans and 16 Non-albicans Candida) isolates were selected and tested for their antifungal susceptibility pattern. All the isolates (100%) tested were sensitive to Itraconazole and Griseofulvin.

For Candida albicans; 48.6%, 51.4% and 48.6% of the isolates were sensitive to Nystatin, Ketoconazole and Fluconazole, respectively; whereas 5.7%, 2.9% and 5.7% were resistant to Nystatin, Ketoconazole and Fluconazole, respectively. On the other hand, 40%, 42.8% and 40% of the Non-albicans Candida species were sensitive to Nystatin, Ketoconazole and Fluconazole, respectively; whereas 5.7%, 2.9% and 5.7% were resistant to Nystatin, Ketoconazole and Fluconazole, respectively.

The 50% overall prevalence rate of candidiasis recorded in this study was slightly lower than the 52.5% reported by Esebelahie et al. [19] in a study carried out among HIV patients in Benin City, Southern Nigeria. It was however, higher than the 30.1% reported by Njunda et al. [20] in a work carried out in Cameroon, a neighboring African Country that share boundary with Nigeria, east-ward.

Meanwhile, it was comparable to studies done outside the continent of Africa. For instance, Li et al. [21] and Lin et al. [22] reported 49.5% and 51.4%, respectively, in separate studies carried out in China and Taiwan. It was also found to be similar to the works of Paula et al. [23] and Goulart et al. [24], who reported 50.4% and 51.3%, respectively, in another separate studies, both carried out in Brazil.

With regard to the single occurrence of oral candidiasis, the 10.8% recorded in this study was slightly higher than the 9.68% reported by Lar et al. [25] among HIV seropositive population in Jos, Nigeria. On the other hand it was slightly lower than the 12.5% reported by Okonkwo et al. [26], in a study done in Abakaliki, Nigeria. Meanwhile, it was found to be very similar to the work of Vijeta et al. [27], who reported a prevalence rate of 11% among HIV positive patients in Northern India. Other works done outside the shore of Africa, reported a much higher prevalence rates including those of Schuman et al. [28], Tsang and Samaranayake [29], Campis et al. [30], Gugnani et al. [31] and Pongsiriwet et al. [32] who reported a prevalence of 22%, 54.8%, 61.9%, 65.3% and 70% in USA, Hongkong, Italy, India and Thailand, respectively.

The 21.7% single occurrence of vaginal candidiasis recorded in this study was about four times lower than the 88.8% reported by Umeh and Umeakanne [33] in Benue State, Nigeria. However, a not too high prevalence rate was reported by Njunda et al. [20] and Schuman et al. [28], 36.3% in Cameroon and 37% in Atlanta, Georgia, USA, respectively. The reasons for the above reported variation in prevalence rates include differences in methodology, geographic location, sample size, educational, socio-economic and cultural status, level of personal hygiene and adherence to HAART and prophylaxis for opportunistic infection by the study participants amongst others.

With regard to the co-occurrences of oral and vaginal candidiasis, a prevalence of 17.5% was recorded in this study. We can say that to the best of our knowledge, this is the first work to consider such. Most previous works done on candidiasis among HIV infected patients, consider either single occurrence of oral and vaginal candidiasis, or in combination with candidaemia and/or candidiuria. Co-occurrences of oral and vaginal candidiasis in the same individual suggest concomitant poor oral and vaginal hygiene amidst HAART medication. This calls for an all-round improvement in the level of their personal hygiene.

Considering the types of Candida species isolated in this study, the commonest was Candida albicans (54.3%), while Non-albicans Candida (NAC) accounts for the remaining 45.7%.

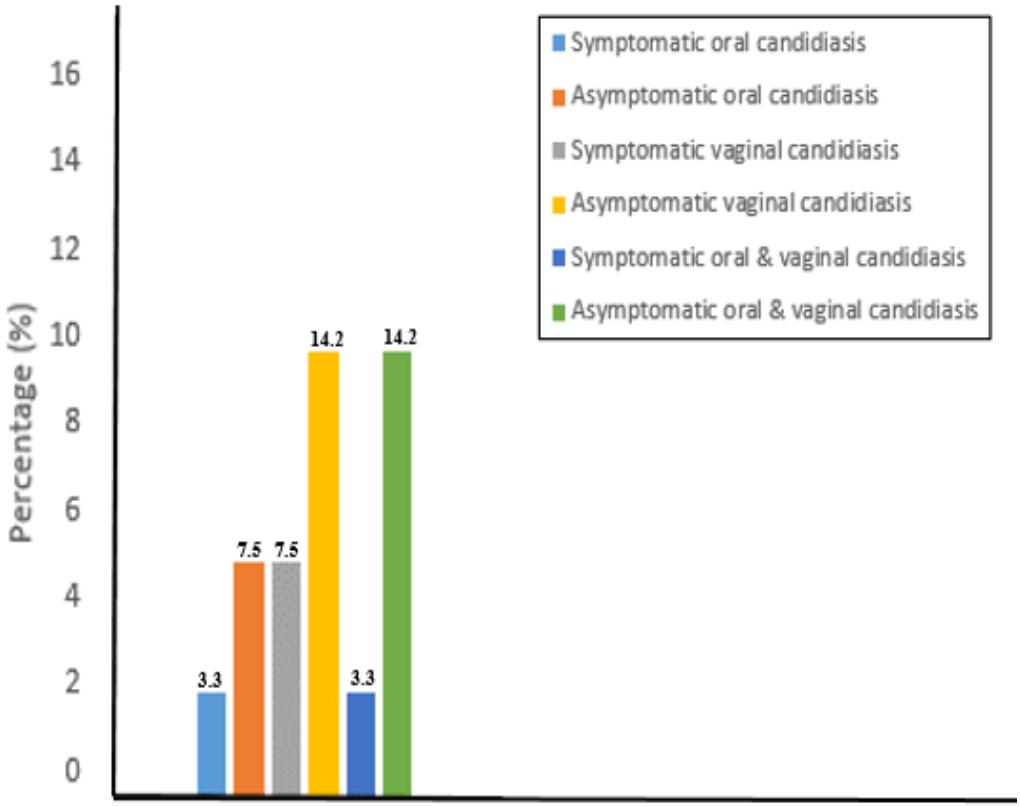


Figure3. *Bar chart showing prevalence of symptomatic and asymptomatic candidiasis among the study participants*

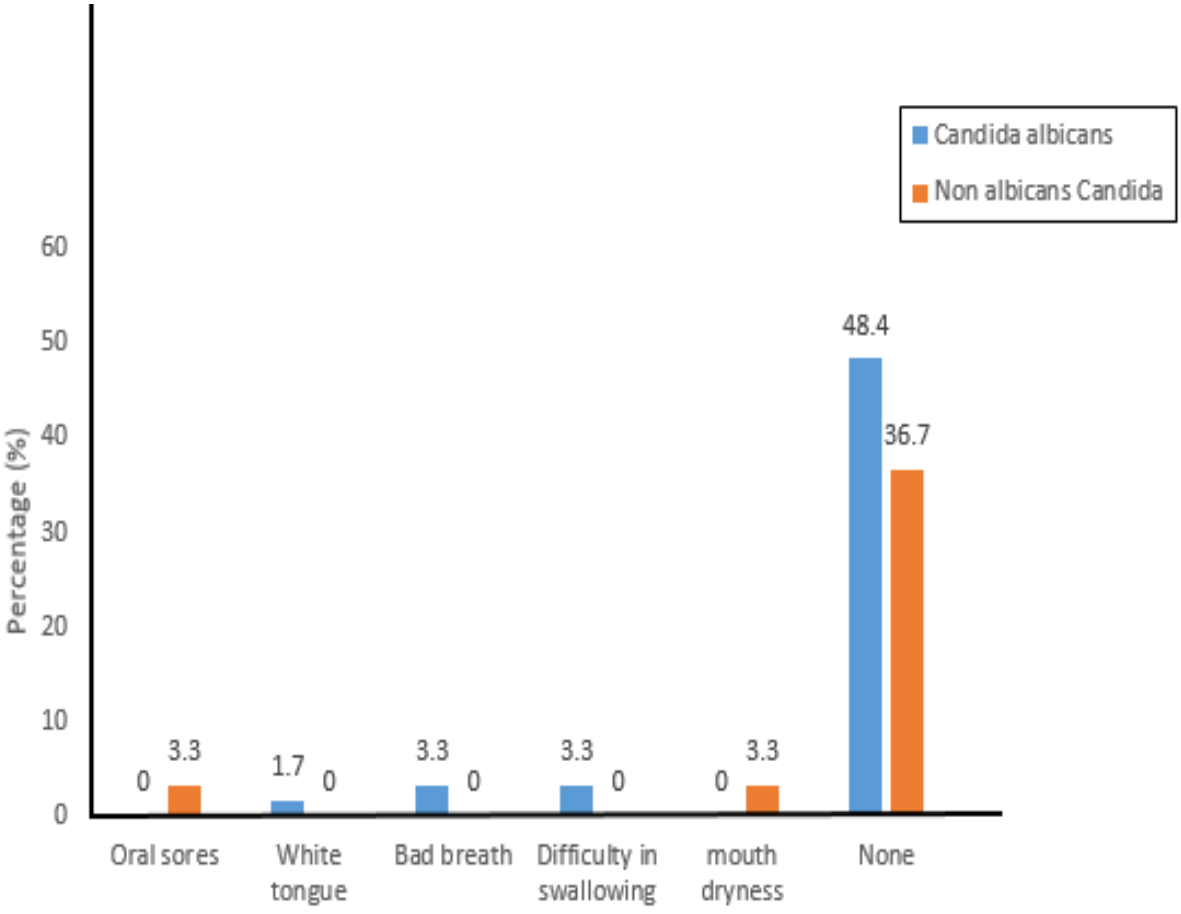


Figure4. *Indications for oral candidiasis in relation to the occurrence of candida species*

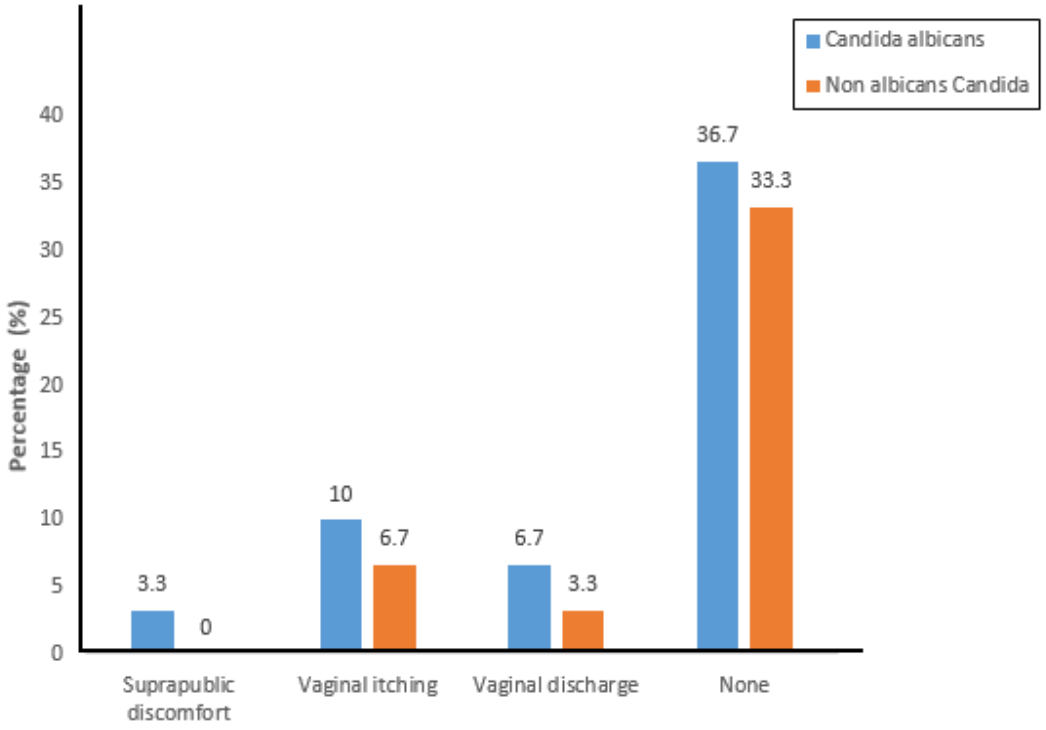
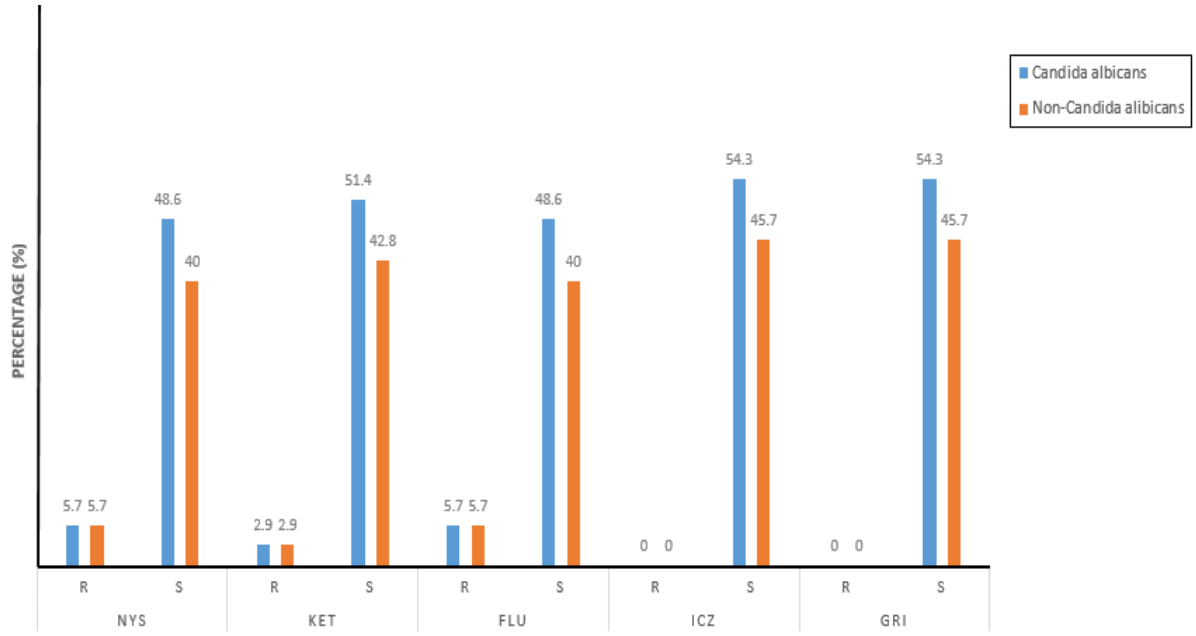


Figure5. *Indications for vaginal candidiasis in relation to the occurrence of candida species*



Keys: *R = Resistant, S = Sensitive, NYS = Nystatin, KET = Ketoconazole, FLU = Fluconazole, ICZ = Itraconazole, GRI = Griseofluvin*

Figure6. *A bar chart showing the antifungal susceptibility pattern of Candida albicans and Non-albicans Candida isolates recovered from the oral and vaginal swabs of the study participants*

This shows the predominance of *Candida albicans* (CA) over Non-*albicans Candida* (NAC) as causative agent of candidiasis. This agrees with other works done in Africa and elsewhere. For instance, Hamza *et al.* [11] reported 84.5% (CA) and 15.5% (NAC) in a work done in Tanzania, Okonkwo *et al.* [26] reported 80% (CA) and 20% (NAC) in Abakaliki, Nigeria, Kwamin *et al.* [34] reported 68.5% (CA) and 31.5% (NAC) in Accra, Ghana. Still, Vijeta *et al.* [27] reported 90.5% (CA) and 9.5% (NAC) in Northern India. Meanwhile, in studies carried out in Brazil, Spalanzani *et al.* [35] reported 66.7% (CA) and 33.3% (NAC),

while Goulart *et al.* [24] reported 80% (CA) and 20% (NAC).

Regarding the indications for oral candidiasis (oral sores, white tongue, difficulty in swallowing, bad breath and mouth dryness) and vaginal candidiasis (suprapubic discomfort, vaginal itching and vaginal discharge) in relation to the occurrence of *candida* species, it appears that these indications were more pronounced among HIV positive patients infected with *Candida albicans* rather than Non-albicans Candida. This suggests that CA may be a more virulent and aggressive opportunistic fungi pathogenic than the NAC, hence the occurrences of more indications for oral and vaginal candidiasis among the study participants infected with CA.

With regard to the prevalence of symptomatic and asymptomatic candidiasis among the study participants, the former was found to be lower than the later in all forms of candidiasis considered. This confirms that there is a high incidence of asymptomatic cases. It has also been demonstrated that persistent asymptomatic carriage of Candida specie is a possible risk factor for subsequent infection [24].

In this study, we define symptomatic candidiasis as the detection of Candida species in the oral/vaginal swab culture of the study participants in the presence of one or more signs and symptoms consistent with oral/vaginal candidiasis. On the other hand, we defined asymptomatic candidiasis as the detection of Candida species in the oral/vaginal swab culture of the study participants in the absence of one or more signs and symptoms consistent with oral/vaginal candidiasis.

Asymptomatic individuals serve as crucial reservoir of infection within the community. Although they exhibit no outward signs and symptoms of the disease, their saliva or vaginal discharge contain the pathogen and are capable of infecting others either through kissing or sexual intercourse. In the light of the above, asymptomatic patients must be identified and treated in order to halt the cycle of infection within the community.

Furthermore, the mere presence of oral sores for instance, doesn't necessary mean that the individual is suffering from oral candidiasis. The reason is simple; other pathogens other than Candida like some viruses (e.g Herpes Simplex Virus-1), parasites (e.g *Entamoeba gingivalis*, *Trichomonas tenax*) and numerous bacteria including *Streptococcus mutans*, *Staphylococcus aureus* and *Klebsiella pneumoniae*) have been implicated in oral infection. Similarly, the mere presence of vaginal itching for instance, doesn't necessary mean that the individual is suffering from vaginal candidiasis. The same reason as mention above; other pathogens like *Trichomonas vaginalis*, *Neisseria gonorrheae* and *Chlamydia trichomatis* can be responsible. For this single reason, differential diagnosis is critical in order to know the actual causative agent of infection presenting with similar indications. Wrong diagnosis can lead to wrong reporting and treatment. Besides, self-diagnosis through experience or otherwise could lead to wrong diagnosis and medication. Purchase of drugs from the counter without appropriate laboratory test results is large responsible for the development of antimicrobial resistance Clinicians are currently battling with.

With respect to the risk factors associated with occurrence of candidiasis in this current study, lack of HAART adherence, poor knowledge, history of oral/vaginal infection, sharing of sanitary facilities with others, nature of anal cleaning, recent change in sexual partners and use of contraceptives were identified amongst others. The outcome of this study shows that most of the study participants have little or no knowledge of candidiasis. Knowledge and information is a very vital epidemiologic tool in the fight against infectious diseases, hence the need for more public health awareness programs for such category of population.

Due to poor HAART adherence among a few of the study participants, there is need for more adherence counseling, adherence monitoring with evidence, pill counting and strict recording of treatment alongside other clinical parameters upon every follow-up and visitation. This is so important because high rate of adherence (≥95%) is central to HAART effectiveness and immune reconstitution in HIV/AIDS patients [8, 36, 37].

Similarly, lack of prophylaxis against opportunistic infections or adherence to the same, may also predispose HIV/AIDS individuals to having oral and vaginal candidiasis. Preventive medicine using appropriate antimicrobial agents (antibacterial, antifungal, antiparasitic) is now very critical because of the development of opportunistic infections (OIs) even in the presence of HAART

medication. Besides, development of HIV resistance to the available antiretroviral drugs is becoming increasingly worrisome.

History of oral/vaginal infection is other important risk factors. About one quarter of the study participants who tested positive for either oral or vaginal candidiasis or both indicated that they have suffered either oral and/or vaginal infection before. Once an individual has been exposed to Candida pathogens before, re-occurrence of Candidiasis is possible even after treatment and it has been associated with the opportunistic nature of Candida species especially in the presence of immunosuppression as in the case of HIV infection [38].

Vaginal douching practices are also thought to be another important risk factor that predispose to vaginal candidiasis. According to Ness *et al.* [39] and Martino et al. [40], most women do vaginal douching either for symptoms or hygiene, both of which may elevate bacterial vaginosis [41] and vaginal colonization by organisms like Candida species. No doubt this practice alters the vagina ecosystem and when the vaginal flora are disrupted like it does with indiscriminate use of antibiotics, Candida species flourish and cause infection. Women health experts strongly advised that douching with soap, antiseptics/deodorant products and herbal concoction should be discouraged as these items alter the pH of the vaginal environment and are therefore capable of distorting the ecology of the vagina which may eventually lead to bacterial vaginosis and its complications including vaginal candidiasis. Meanwhile, the use of clean water only should be encouraged as clean water has not been documented to have any negative effect on the vagina ecosystem. Besides, health care workers should continue to instruct women on proper personal hygiene and appropriate use of contraceptives [40, 41].

Nature of cleaning up after using the toilet has also been documented to play a very important role in the epidemiology of vaginal candidiasis. The anus is close to the vagina anatomically, this provides much convenience for the migration of organisms like Candida which normally resides in the gut to move into the vagina especially in women with poor toilet hygiene who wipe from back to front after defecation. Recent change in sexual partners, having multiple sexual partners and not cleaning the vulva before or after sexual life amongst others also plays a role in triggering vaginal candidiasis [40, 41].

Regarding the antifungal susceptibility pattern of the candida isolates, the results of this study is comparable to the work of Goulart *et al.* [24] carried out among HIV-positive patients in Brazil. According to them 84%, 99% and 73% of the isolates were sensitive to Fluconazole, Ketoconazole and Itraconazole, respectively; while in this study 88.6% (48.6% CA; 40% NAC), 94.2% (51.4% CA; 42.8%) and 100% (54.3% CA; 45.7 NAC) of the isolates were sensitive to Fluconazole, Ketoconazole and Itraconazole, respectively. Similarly, 1%, 1%, and 4% of the Candida isolates were resistant to Fluconazole, Ketoconazole and Itraconazole, respectively. Meanwhile in this study, 11.4% (5.7% CA; 5.7% NAC), 5.8% (2.9% CA; 2.9 NAC) and 0% of the isolates were resistant to Fluconazole, Ketoconazole and Itraconazole respectively. According to Abrantes *et al.* [42] and Goulart *et al.* [24], resistance to azolic compounds in Candida is often attributed to selection pressures exerted by the antifungal agents in response to exposure of candidiasis patients to repeated, short- or long-term suppressive therapy.

Furthermore; the outcome of our antifungal susceptibility testing is also comparable to that of Spalanzani *et al.* [35] with few exceptions. For instance, two other antifungal drugs (Voriconazole and Amphotericin B) in addition to our Fluconazole and Itraconazole, were tested. Most of the Candida species tested were sensitive to these drugs except, *C. krusei*, a non-albicans Candida specie which was found to be intrinsically resistant to fluconazole. However, in this current study, 5.7% of the CA and NAC isolates were resistant to the said antifungal drug, while none was resistant (0%) to Itraconazole.

Furthermore, the results obtained in this study partly agrees with that of an earlier work carried out by Njunda *et al.* [20], who tested ten (10) different antifungal agents (Ketoconazole, Itraconazole, Fluconazole, Nystatin, as well as Voriconazole, Econazole, Miconazole, Clotrimazole, Flucytosine and Amphotericin B which were not used in this current study) against Candida isolates recovered from the Oropharyngeal and urine specimens of HIV patients in Cameroon. They noted that 85.5% of the Candida isolates were sensitive to

Ketoconazole, while 68.1% were resistant to Nystatin; unlike in this current in which 94.2% (51.4% CA, 42.8% NAC) of the Candida isolates were sensitive to Ketoconazole, while 11.4% (5.7% CA, 5.7% NAC) were resistance to Nystatin.

The most probable reason for this marked disparity could be related to intrinsic resistance by Candida isolates to Nystatin in this study. The national guideline for the management of HIV/AIDS patients actually recommends the use of Nystatin as prophylaxis against Candida and other fungi infections. The prolonged nature in the management of mucosal candidiasis has been documented as the cause of drug resistance amongst users. Furthermore, Nystatin resistance could have also arisen from the abusive usage as prophylaxis and auto-medication, because among the five antifungal agents tested, Nystatin is the most accessible in terms of cost and availability, hence can easily be obtained over the counter without prescription, giving room for excessive drug abuse leading to the development of drug resistance [20, 42].

Antifungal susceptibility testing permits accurate treatment selection and provides significant contributions to the understanding of local and global fungal resistance epidemiology. The possible reason for the slight disparity observed in this study in comparison to those of previous studies [42-44] could be due to the differences in time/duration of study, geographical location and drug usage amongst other reason.

4. CONCLUSION

The outcome of this study underscored the importance of routine checks for candidiasis among HIV patients, use of anti-candida prophylactic, and as well as adequate oral and vaginal care in HIV infection. Early detection of mucosal candidiasis and prompt treatment will help prevent subsequent complications such as candidemia among HIV patients.

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