HSI Health Sciences Investigations Journal

share

Send us an email: info@hsijournal.org

https://www.hsijournal.org

ISSN Online 2704-4890 ISSN Print 2720-7609

Original Research Article

Online first publication

HSI Journal (2020) Volume 1(Issue 1):43-49. https://doi.org/10.46829/hsijournal.2020.6.1.1.43-49

Distribution and susceptibility profile of *Candida* isolates from HIV patients with oropharyngeal candidiasis

Henry A Quansah[1] and Japheth A Opintan [1*]

[1]Department of Medical Microbiology, University of Ghana Medical School, College of Health Sciences, University of Ghana, Korle-Bu, Accra, Ghana

Received December 2019; Revised January 2020; Accepted February 2020

Abstract

Background: Opportunistic infections are the leading cause of morbidity and mortality among immuno-compromised patients. Oropharyngeal candidiasis (OPC) dominates opportunistic fungal infections associated with HIV/AIDS.

Objective: We determined the distribution and prevalence of antifungal resistance in *Candida* isolates recovered from patients infected with HIV and presenting with OPC.

Methods: HIV-infected patients with provisional diagnosis of OPC were consecutively enrolled between May 2017 and June 2018. After patient data collection, oral swabs and blood specimens were collected for culture and CD4 T-lymphocyte estimation, respectively. Presumptive *Candida* isolates were speciated and their antifungal susceptibilities to fluconazole, flucytosine and amphotericin B, including minimum inhibitory concentration was determined using the E-test.

Results: Of 286 patients enrolled, 67.8% (194) cultured positive for *Candida* spp. The mean age of culture positive patients was 40.7 ± 15.2 with more female enrollment (63.4%,123/194). The CD4 counts of culture positive patients were low (211.1 ± 235.6 cells/μL) and 68.6% (133) of them were on anti-retroviral therapy (ART) with 10.3% (20/194) having previous exposure to fluconazole. Seven different *Candida* species, with the following distributions were isolated: *C. albicans* (69.1%, 134), *C. tropicalis* (10.3%, 20), *C. glabrata* (6.7%, 13), *C. parapsilosis* (5.7%, 11), *C. krusei* (4.1%, 8), *C. dubliniensis* (2.6%, 5), and *C. lusitaniae* (1.5%, 3). Of all *C. albicans* isolates tested, 29.1%, 1.5% and 2.3% were resistant to fluconazole, amphotericin B and flucytosine, respectively. Non-*C. albicans* isolates showed 45%, 3.3% and 8.3% resistance to fluconazole, amphotericin B and flucytosine, respectively.

Conclusion: *C. albicans* accounted for majority of oropharyngeal candidiasis (OPC), with non-*C. albicans* showing significantly higher resistance to fluconazole. Positive culture was independent of gender, previous exposure to antifungal drugs, ART status and duration. Without any contraindication, flucytosine and Amphotericin B may be considered for OPC not responding to fluconazole therapy.

Keywords: *Candida* species, *HIV, oropharyngeal candidiasis, susceptibility profile*

Open Access

INTRODUCTION

Opportunistic infections (OIs) are the leading cause of morbidity and mortality among immuno-compromised patients [1,2]. By far, oropharyngeal candidiasis (OPC) dominates opportunistic fungal infections associated with HIV/AIDS. An estimated 90% or more of HIV/AIDS-patients develop OPC, with 60% having at least an episode of infection in a year and 50% - 60% recurrent infections during the course of their illness [3,4]. In Ghana, OPC has been reported as the third commonest clinical oral infection among HIV/AIDS patients [5]. Although not considered life-threatening, OPC can gradually develop into severe complications such as local discomfort, malnutrition, wasting and early death [6]. Invasive infections can also develop following the spread of oral infection into the bloodstream causing significant morbidity and mortality [7, 8]. *Candida albicans* in many studies have been reported as the major cause of OPC in HIV-patients [9-13]. A shift in distribution has however been observed over time, with some non-*C. albicans* species implicated as opportunistic pathogens [14,15]. The clinical significance of isolating these non-*C. albicans* species is that some have been found to possess intrinsic or acquired antifungal resistance, a situation that presents significant problems with patient management [16]. These epidemiological changes in the distribution of *Candida* species underscore the need for constant monitoring to determine the burden of antifungal resistance and to recommend possible prevention and control measures. This study was therefore conducted to determine the distribution and susceptibilities of *Candida* associated oral pharyngeal infections in HIV/AIDS patients and to provide knowledge that could further impact treatment guidelines.

* *Corresponding author*
Email: jaopintan@ug.edu.gh

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.

43

Quansah and Opintan 2020. https://doi.org/10.46829/hsijournal.2020.6.1.1.43-49

MATERIAL AND METHODS

Study participants

Confirmed HIV-patients with presumptive diagnosis of OPC across all ages and gender irrespective of their antiretroviral therapy (ART) status were recruited from selected ART centers in the Central Region of Ghana from May, 2017 to June, 2018 for this study.

Sampling

Oral swabs were aseptically taken from patients who consented to the study and transported on ice pack to our laboratory. Patient data, including demographics, year of HIV diagnosis, history of previous fungal infections, history of previous antifungal use, history of ART and duration of ART prior to sampling were collected. Blood samples were also collected in ethylenediaminetetraacetic acid tubes for CD4 T-lymphocyte estimation using the BD FACS count machine (Beckton Dickinson, UK). The oral swabs were aseptically cut into 10 mL Sabouraud brain heart infusion broth and incubated at 35 ± 2°C for 18 to 24 h. The broth was subcultured onto Sabouraud dextrose Agar (SDA) plates supplemented with broad spectrum antibiotics and incubated for 24-48 h to obtain pure yeast isolates. *Candida* species were isolated based on their colonial morphology on the SDA together with distinguishing characteristics microscopic and Gram-stain features. Pure fresh cultures were sub-cultured onto a differential *Candida* agar plate (HICROME, India) obtained from HIMEDIA laboratories (PVT, India), and incubated aerobically at 35°C for 48 h. Species were identified based on the colour and morphology of the colonies on the differential agar plate. Definitive identification was also done using HiCandida identification kit from HIMEDIA laboratories (PVT, India).

Antifungal susceptibility testing

Yeast isolates were evaluated against three antifungals (fluconazole, 0.016-256 µg/mL; amphotericin B, 0.002-32 µg /mL; and flucytosine, 0002-32 µg/mL) using the E-test (AB, Biodisk, Sweden) susceptibility testing method as described in the Clinical and Laboratory Standard Institute (CLSI) M44-A2 document [17]. Prior to antifungal susceptibility testing, all isolates in suspension were sub-cultured unto SDA plates to ensure their purity, viability and to obtain fresh isolates. About five distinct colonies obtained from 24 h incubation at 35°C was suspended in physiological saline (0.85% NaCl) vortexed for 15 sec and adjusted to 0.5 McFarland standard (corresponds to $1x10^6$ to $5x10^6$ colony forming units/mL) by adding sufficient sterile saline or more colonies. The dried surface of a sterile Mueller Hinton agar with 2% glucose and 0.5 µg/mL methylene blue dye agar plate were inoculated with the saline-yeast mixture and antifungal E-test® strips applied. The plates were incubated at 35°C for 24 h. Each plate was examined after 24 h of incubation and read only when sufficient growth was observed. Results were interpreted based on CLSI interpretive criteria (M 60, 2017) [17].

Quality control strains were set-up in similar way for every batch of isolates that was tested using strains of American Type Culture Collection (ATCC) 90028, ATCC 22019 and ATCC 6258.

Statistical analysis

Data obtained from the study were entered into Microsoft Excel 2016 and imported into IBM SPSS Software version 25 for statistical analysis. Categorical variables were summarized as frequencies and percentages, and continuous variables as means and standard deviations. Pearson Chi Square test was used to determine associations between *C. albicans*-associated OPC and categorical variables using odds ratio (OR) and 95% confidence intervals (CI). Point biserial correlation was used to determine the relationship between *C. albicans*-associated OPC and continuous variables at an alpha level of 0.05. Variables that showed significant associations in bivariate comparisons were included in logistic regression analysis to determine possible factors that may predict for *C. albicans*-associated OPC. All $p < 0.05$ were considered significant.

RESULTS

Demographic characteristics

Overall, 197 of 286 (67.8%) patients we sampled between May 2017 and June 2018 were culture positive. The mean age of these culture positive patients was 40.7 ± 15.2 yr. with majority of them being females (63.4%, 123/194). The CD4 counts of the culture positive patients were low (211.1 ± 235.6 cells/µL) and 68.6% (133/194) of them were on ART with 10.3% (20) having previous exposure to fluconazole.

Candida species identified and their distribution

Seven different *Candida* species with the following distributions were identified from the 194 culture positive patients: *C. albicans* (69.1%, 134), *C. tropicalis* (10.3%, 20), *C. glabrata* (7%, 13), *C. parapsilosis* (5.7%, 11), *C. krusei* (4.1%, 8), *C. dubliniensis* (2.6%, 5) and *C. lusitaniae* (1.5%, 3).

Oropharyngeal candidiasis and associated factors

The demographic characteristics of the study participants were statistically not different in gender, previous exposure to antifungal drugs, duration of ART and CD4 count despite being selected from different sites. However, *C. albicans*-associated OPC was significantly higher among HIV-infected patients on ART compared to ART-naive patients ($p = 0.018$). Details of the associations are presented in Table 1.

Antifungal susceptibility

Overall resistance by *C. albicans* isolates tested against fluconazole was 29.1% (39/134). Comparatively, the non-*C. albicans* isolates were significantly more resistant to fluconazole than the *C. albicans* isolates [non-*C. albicans* = 45% (27/60) vs *C. albicans* = 29.1% (39/134); $p = 0.033$)]. Overall, 1.5% (2/134) of *C. albicans* isolates tested against amphotericin B were resistant. Non-*C. albicans* had more reduced susceptibility to amphotericin B (1.5% vs 3.3%; $p = 0.27$). Overall resistance in isolates of *C. albicans* tested against flucytosine was 2.7% (3/134). The highest resistance was shown by isolates of *C. krusei* (37.5%, 3/8). None of the *C. glabrata*, *C. parapsilosis*, *C. tropicalis* and *C. dubliniensis* isolates tested against flucytosine was resistant. Tables 2 and 3 show the antifungal profile of *Candida* species and their minimum inhibitory concentrations tested against fluconazole, amphotericin B and flucytosine.

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.

Quansah and Opintan 2020. https://doi.org/10.46829/hsijournal.2020.6.1.1.43-49

Antifungal resistance and associated factors

Fluconazole resistance was significantly higher in participants previously exposed to fluconazole compared to fluconazole-naive patients (p = 0.001). No significant association was however found between antifungal use and resistance to Amphotericin B (p = 1.000) or flucytosine (p = 0.925) (Table 4). Fluconazole resistance was significantly higher among ART-naïve patients compared to patients on ART (p = 0.001) (Table 5). Significantly (p = 0.004) high fluconazole resistance was observed among patients with lower CD4 count (≤ 200 cells/μL) compared to patients with higher CD4 counts (>500 cells/μL) (Table 6).

DISCUSSION

Several research findings point to a growing problem of antifungal resistance among *Candida* species especially the non-*C. albicans*. Additionally, there seem to be an epidemiological shift in *Candida* infections, from *C. albicans* to non-*C. albicans* species [18,19]. Not only has this shift been found to differ geographically but also among health settings and even cohorts of patients within a country [13]. This underscores the need for constant monitoring of etiologic agents of *Candida* infections and emergence of antifungal resistance. *C. albicans* accounted for majority of OPC in our study participants. This is consistent with findings obtained from similar studies in Ghana and

Table 1: Logistic regression model with respect to *Candida* infection in HIV patients

Parameter	*C. albicans* (n= 134) OR (95% CI)	Non-*C. albicans* (n= 60) OR (95% CI)	*p* value
Gender			
Males	1.01 (0.54-1.90)	0.99 (0.53-1.87)	0.98
Antifungal histamines			
Yes	1.05 (0.38 -2.88)	0.95 (0.35-2.61)	0.92
ART			
Yes	2.16 (1.14-4.10)	0.46 (0.24-0.88)	0.02
Duration on HAART			
< 3 months	1.03 (0.40-2.66)	0.97 (0.38-2.49)	0.99
3-6 months	0.58 (0.19-1.82)	1.72 (0.55-5.36)	0.35
CD4 Count			
≤ 200	0.85 (0.28-2.58)	1.18 (0.39-3.61)	0.77
201-499	0.92 (0.27-3.07)	1.09 (0.33-3.65)	0.89

* ART, antiretroviral therapy; HAART, highly active antiretroviral therapy; OR, odds ratio; CI, confidence interval

Table 2: Antifungal susceptibility profile of HIV/AIDS patients with OPC

Parameter	Fungi Species	Susceptible n (%)	S-DD. n (%)	Intermediate n (%)	Resistant n (%)	*p* value
Fluconazole						0.001
	C. albicans	89 (66.4)	6 (4.5)	-	39 (29.1)	
	C. krusei	0 (0.0)	0 (0.0)	-	8 (100.0)	
	C. parapsilosis	8 (72.7)	0 (0.0)	-	3 (27.3)	
	C. glabrata	0 (0.0)	4 (30.8)	-	9 (69.2)	
	C. lusitaniae	3 (100.0)	0 (0.0)	-	0 (0.0)	
	C. dubliniensis	5 (100.0)	0 (0.0)	-	0 (0.0)	
	C. tropicalis	12 (60.0)	1 (5.0)	-	7 (35.0)	
Amphotericin B						0.27
	C. albicans	132 (98.5)	-	-	2 (1.5)	
	C. krusei	7 (87.5)	-	-	1 (12.5)	
	C. parapsilosis	11 (100.0)	-	-	0 (0.0)	
	C. glabrata	12 (92.3)	-	-	1 (7.7)	
	C. lusitaniae	3 (100.0)	-	-	0 (0.0)	
	C. dubliniensis	5 (100.0)	-	-	0 (0.0)	
	C. tropicalis	20 (100.0)	-	-	0 (0.0)	
Flucytosine						0.01
	C. albicans	130 (97.0)	-	1 (0.7))	3 (2.3)	
	C. krusei	5 (62.5)	-	0 (0.0)	3 (37.5)	
	C. parapsilosis	11 (100.0)	-	0 (0.0)	0 (0.0)	
	C. glabrata	13 (100.0)	-	0 (0.0)	0 (0.0)	
	C. lusitaniae	3 (100.0)	-	0 (0.0)	0 (0.0)	
	C. dubliniensis	5 (100.0)	-	0 (0.0)	0 (0.0)	
	C. tropicalis	18 (90.0)	-	0 (0.0)	2 (10.0)	

* S-DD, Susceptible dependent dose; p value < 0.05 implies statistically significant.

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.
45

Quansah and Opintan 2020. https://doi.org/10.46829/hsijournal.2020.6.1.1.43-49

Table 3: Minimum Inhibition Concentration of antifungals to *Candida* species

Drug / Fungi	Sensitive		Resistant		*p* value
	MIC Range	Mean MIC (SD)	MIC Range	Mean MIC (SD)	
Fluconazole					0.04
C. albicans	0.016-2.00	0.58 (0.62)	16.00-256.00	173.54 (75.63)	
C. krusei	-	-	64.00-256.00	88.00 (67.88)	
C. parapsilosis	0.016-2.00	0.61 (0.87)	16.00-64.00	37.33 (24.44)	
C. glabrata	-	-	96.00-256.00	149.33 (67.88)	
C. lusitaniae	0.023-1.50	0.84 (0.75)	-	-	
C. dubliniensis	0.016-2.00	1.04 (0.94)	-	-	
C. tropicalis	0.016-1.00	0.40 (0.37)	24.00-256.00	131.43 (117.20)	
Amphotericin B					0.02
C. albicans	0.002-1.00	0.11 (0.19)	1.50-4.00	2.75 (1.77)	
C. krusei	0.004-1.00	0.25 (0.36)	≥6.00	16.00 (0.00)	
C. parapsilosis	0.004-0.75	0.11 (0.22)	-	-	
C. glabrata	0.002-1.00	0.26 (0.40)	≥32.00	32.0 (0.00)	
C. lusitaniae	0.004-0.05	0.02 (0.02)	-	-	
C. dubliniensis	0.004-0.064	0.02 (0.02)	-	-	
C. tropicalis	0.002-0.75	0.12 (0.23)	-	-	
Flucytosine					0.001
C. albicans	0.002-3.00	0.41(0.65)	≥32.00	32.0 (0.00)	
C. krusei	0.016-0.75	0.26 (0.30)	≥32.00	32.0 (0.00)	
C. parapsilosis	0.004-0.75	0.14 (0.23)	-	-	
C. glabrata	0.002-2.00	0.26 (0.54)	-	-	
C. lusitaniae	0.094-0.50	0.26 (0.21)	-	-	
C. dubliniensis	0.008-1.00	0.42 (0.53)	-	-	
C. tropicalis	0.006-2.00	0.51(0.67)	≥32.00	32.0 (0.00)	

*MIC, minimum inhibitory concentration; SD, standard deviation

Table 4: Association between exposure to antifungal drug and resistance

Parameter	Antifungal History n (%)		*p* value
	Yes (n= 20)	No (n= 174)	
Fluconazole			0.001
Sensitive	6 (30.0)	111 (60.3)	
Resistance	14 (70.0)	52 (29.9)	
S-DD	0 (0.0)	11 (6.3)	
Amphotericin			1.00
Sensitive	20 (100.0)	170 (97.7)	
Resistance	0 (0.00)	4 (2.3)	
Flucytosine			0.93
Sensitive	19 (95.0)	166 (95.4)	
Resistance	1 (5.0)	7 (4.0)	
Intermediate	0 (0.0)	1 (0.6)	

*SDD, susceptible dependent dose.

Table 5: Association between ART intake and antifungal resistance

Parameter	ART intake		*p* value
	Yes (n= 133)	No (n= 61)	
Fluconazole			0.001
Sensitive	89 (66.9)	28 (45.6)	
Resistance	34 (25.6)	32 (52.5)	
S-DD	10 (7.5)	1 (1.6)	
Amphotericin B			1.00
Sensitive	130 (97.7)	60 (98.4)	
Resistance	3 (2.3)	1 (1.6)	
Flucytosine			0.31
Sensitive	127 (95.5)	58 (95.1)	
Resistance	6 (4.5)	2 (3.3)	
Intermediate	0 (0.0)	1 (1.6)	

*Antiretroviral therapy; SDD, susceptible dependent dose.

elsewhere [9,10,13]. The spectrum of non-*C. albicans* species and rate of isolation was however observed to differ from those reported in previous studies. We identified seven *Candida* species, compared to twenty and eight reported in Accra and Kumasi, respectively [9,10]. The 67.8 % rate of isolation reported in this current work is also lower compared to 75.3%, and 82.3% obtained in earlier studies [9,20]. Non-*C. albicans* species constituted about 31% of all isolated cases in our study, which was consistent with 30.5% reported in Accra by Kwamin et al. (2013) [9]. In Mexico [21], Tanzania [22], and USA [23], lower rates of 16.5%, 15%, and 22%, respectively, were recorded in studies done few decades ago. In Nigeria and Brazil [13,24], non-*C. albicans* species constituted more than 50% of all isolated *Candida* species.

Increased isolation of non-*C. albicans* species has serious clinical implications and underscores the need for routine identification before treatment, especially, since majority of them have been demonstrated to be less susceptible to commonly administered antifungals [19,21]. Positive culture was found to be independent of gender, previous exposure to antifungal drugs, whether participant was on ART or not and duration of patients on ART. A study by Kwamin et al. (2013) [9] involving two groups of HIV-positive patients, those on highly active ART (HAART) and HAART-naive also reported that the difference in the prevalence of OPC among patients on HAART and HAART-naive was insignificant. *C. albicans*-associated OPC was however found to be higher among patients on ART compared to ART-naive patients. The absence of information on ART regime and level of immune suppression of the patients makes it difficult to explain this trend. However, in Southern Brazil, OPC development was found to be associated with severe immunodeficiency and high viral loads irrespective of ART use. Alcohol consumption and smoking were also found as high-risk

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.

Table 6: Association between CD4 counts level and antifungal resistance

Parameter	CD4 count, n (%)			*p* value
	≤ 200 (n= 112)	20 –499 (n= 48)	≥ 500 (n= 17)	
Fluconazole				0.001
Sensitive	59 (52.7)	32 (66.7)	13 (76.5)	
Resistance	50 (44.6)	10 (20.8)	4 (23.5)	
S-DD	3 (2.7)	6 (12.5)	0 (0.0)	
Amphotericin				0.78
Sensitive	109 (97.3)	47 (97.9)	17 (0.0)	
Resistance	3 (2.7)	1 (2.1)	0 (0.0)	
Flucytosine				0.81
Sensitive	105 (93.8)	46 (95.8)	17 (100.0)	
Resistance	6 (5.4)	2 (4.2)	0 (0.0)	
Intermediate	1 (0.9)	0 (0.0)	0 (0.0)	

factors [25]. Globally, prevalence of azole resistance has been estimated in a range of 9.3 to 56.7% among HIVAIDS patients [26–30]. This varies from samples, patients and countries in terms of incidence and prevalence rates [31].

We observed that about 30% of *C. albicans* isolates were resistance to fluconazole with significantly higher resistance found among patients whose CD4 counts were low (≤ 200 cells/μL). This was consistent with findings of related study where significant correlation was established between CD4 T lymphocytes and fluconazole resistance. In that study, *Candida* isolates from HIV-patients with reduced CD4 cells (< 200 cells/μL) were significantly resistant to fluconazole [18]. Comparatively, we also observed that the Non-*C. albicans* species were significantly more resistant to fluconazole than the *C. albicans* species. This trend could be attributed to inherent resistance exhibited by isolates of *C. krusei* and *C. glabrata* to fluconazole [30].

Both *C. albicans* and non-*C. albicans* species displayed low resistance against amphotericin B and the difference in resistance between the two was not statistically significant. The relatively low resistance prevalence of *Candida* species to amphotericin B reported in the current study falls within 0% and 3% reported by Barchiesi et al. in 2003 [32] and in 2000 [33], respectively. The results also indicate that amphotericin B is still an effective drug for treating *Candida* species infections. The reason for the low amphotericin B resistance could be because usage of the drug is restricted in the country, and so is not easily obtained over the counter. Prevalence of flucytosine resistance among *C. albicans* and non-*C. albicans* was less than 9%. With the exception of *C. krusei* which showed a high resistance (37.5%), all the other non-*C. albicans* species (*C. glabrata*, *C. parapsilosis*, *C. tropicalis* and *C. dubliniensis*) were susceptible to flucytosine. Flucytosine is rarely administered in isolation; it is combined with other antifungal agents. Besides, resistance to the drug among *Candida* species has been generally low and differ geographically [36]. Resistance of 2.3% among *C. albicans* observed in this study is higher than the 0% and 0.6% reported by Barchiesi et al. (2000) [34] and Cuenca-Estrella et al. (2001) [35] respectively and could be attributed to geographical variations or co-resistance with other antifungal drugs. The current study had limitations. CD4 count, history of previous antifungal use, anti-viral treatment and duration are important, however this information were accurately available in a limited number of patients. We sampled patients with provisional clinical diagnosis of OPC, and may have missed a limited number of patients without symptoms. Additionally, antifungal susceptibility profile of fungal isolates from HIV patients without OPC and therefore not on any antifungal therapy would have enriched the study.

Conclusion

C. albicans was the most commonly isolated *Candida* species in OPC among the HIV-infected participants, with non-*C. albicans* species also showing a rising trend. Non-*C. albicans* species were more resistance to fluconazole, and prior fluconazole therapy and ART were associated with reduced susceptibilities to fluconazole. Without any contraindication, flucytosine and Amphotericin B may be considered for OPC not responding to fluconazole therapy.

DECLARATIONS

Ethical considerations

Ethical approval was sought from the Ethics and Protocol Review Committee (EPRC) of the College of Health Sciences, University of Ghana (CHS –Et/M.4-P2.9/2017-2018). Written informed consent was also obtained from all participants before sampling.

Funding

None

Competing Interests

None

Author contributions

HAQ conceived the study idea. JAO and HAQ contributed to the design and implementation of the research. JAO made significant input to the analysis of the results. JAO and HAQ wrote the manuscript. All authors agreed to the content of the final draft and gave consent to publish

Acknowledgements

We are grateful to the HIV programme coordinators at the various health facilities we sampled from and also laboratory scientist of the Cape Coast Teaching Hospital and the Department of Medical Microbiology, University of Ghana, for their support.

Availability of data

Data is available upon request from the corresponding author

REFERENCES

1. Lawn SD, Butera ST, Folks TM (2001) Contribution of immune activation to the pathogenesis and transmission of human immunodeficiency virus type 1 infection. Clin. Microbiol. Rev. 14:753–777
2. Walensky RP, Paltiel AD, Losina E, Mercincavage LM, Schackman BR, Sax PE, Weinstein MC, Freedberg KA (2006) The Survival Benefits of AIDS Treatment in the United States. J Infect Dis 194:11–19. https://doi.org/ 10.1086/505147
3. Samaranayake LP, Fidel PL, Naglik JR, Sweet SP, Teanpaisan R, Coogan MM, Blignaut E, Wanzala P (2002) Fungal infections associated with HIV infection. Oral Dis. 8:151–160

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.
47

4. Li X, Lei L, Tan D, Jiang L, Zeng X, Dan H, Liao G, Chen Q (2013) Oropharyngeal Candida colonization in human immunodeficiency virus infected patients. APMIS 121:375–402

5. Kwamin, F., Hewlett S., Ndanu T.A., Lartey M., Nartey N.O. 2010. Incidence of orofacial lesions in relation to CD-4 Count in HIV/AIDS Patients at The Fevers Unit – Korle-Bu Teaching Hospital. Ghana Dental J 7: 22-26

6. Diro E, Feleke Y, Guteta S, Fekade D, Neway M (2009) Assessment of risk behaviours and factors associated with oral and peri-oral lesions in adult HIV patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. Ethiop J Heal Dev 22:10. https://doi.org/10.4314/ejhd.v22i2.10069

7. Akpan A, Morgan R (2002) Oral candidiasis. Postgrad Med J 78:455–459. https://doi.org/10.1136/pmj.78.922.455

8. Fanello S, Bouchara JP, Sauteron M, Delbos V, Parot E, Marot-Leblond A, Moalic E, Le Flohicc AM, Brangerd B (2006) Predictive value of oral colonization by Candida yeasts for the onset of a nosocomial infection in elderly hospitalized patients. J Med Microbiol 55:223–228. https://doi.org/10.1099/jmm.0.46155-0

9. Kwamin F, Nartey NO, Codjoe FS, Newman MJ (2013) Distribution of Candida species among HIV-positive patients with oropharyngeal candidiasis in Accra, Ghana. J Infect Dev Ctries 7:41–45. https://doi.org/10.3855/jidc.2442

10. Feglo P (2012) Prevalence and Antifungal Susceptibility Patterns of Yeast Isolates at the Komfo Anokye Teaching Hospital (KATH), Kumasi, Ghana. Br Microbiol Res J 2:10–22. https://doi.org/10.9734/bmrj/2012/861

11. Sánchez-Vargas LO, Ortiz-López NG, Villar M, Moragues MD, Aguirre JM, Cashat-Cruz M, Lopez-Ribot JL, Gaitán-Cepeda LA, Quindós G (2005) Point prevalence, microbiology and antifungal susceptibility patterns of oral Candida isolates colonizing or infecting Mexican HIV/AIDS patients and healthy persons. Rev Iberoam Micol 22:83–92. https://doi.org/10.1016/S1130-1406(05)70014-0

12. Amran F, Aziz MN, Ibrahim HM, Atiqah NH, Parameswari S, Hafiza MR, Ifwat M (2011) In vitro antifungal susceptibilities of Candida isolates from patients with invasive candidiasis in Kuala Lumpur Hospital, Malaysia. J Med Microbiol 60:1312–1316. https://doi.org/10.1099 /jmm.0.027631-0

13. Nweze EI, Ogbonnaya UL (2011) Oral Candida isolates among HIV-infected subjects in Nigeria. J Microbiol Immunol Infect 44:172–177. https://doi.org/10.1016 /j.jmii.2011.01.028

14. Shang ST, Lin JC, Ho SJ, Yang YS, Chang FY, Wang NC (2010) The Emerging Life-threatening Opportunistic Fungal Pathogen Kodamaea ohmeri: Optimal Treatment and Literature Review. J Microbiol Immunol Infect 43:200–206. https://doi.org/10.1016/S1684-1182(10)60032-1

15. Mushi MF, Mtemisika CI, Bader O, Bii C, Mirambo MM, Groß U, Mshana SE (2016) High Oral Carriage of Non-albicans Candida spp. among HIV-infected individuals. Int J Infect Dis 49:185–188. https://doi.org/10.1016/j.ijid.2016. 07.001

16. Mane A, Panchvalli S, Bembalkar S, Risbud A (2010) Species distribution & antifungal susceptibility of oral Candida colonising or infecting HIV infected individuals. Indian J Med Res 131:836–838

17. Clinical and Laboratory Standards Institute (2009) M44-A2: Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts; Approved Guideline—Second Edition. CLSI Doc

18. Lortholary O, Petrikkos G, Akova M, Arendrup MC, Arikan-Akdagli S, Bassetti M, Bille J, Calandra T, Castagnola E, Cornely OA, Cuenca-Estrella M, Donnelly JP, Garbino J, Groll AH, Herbrecht R, Hope WW, Jensen HE, Kullberg BJ, Lass-Flörl C, Meersseman W, Richardson MD, Roilides E, Verweij PE, Viscoli C, Ullmann AJ (2012) ESCMID guideline for the diagnosis and management of Candida diseases 2012: Patients with HIV infection or AIDS. Clin Microbiol Infect 18:68–77. https://doi.org/10.1111/1469-0691.12042

19. Arendrup MC, Dzajic E, Jensen RH, Johansen HK, Kjældgaard P, Knudsen JD, Kristensen L, Leitz C, Lemming LE, Nielsen L, Olesen B, Rosenvinge FS, Røder BL, Schønheyder HC (2013) Epidemiological changes with potential implication for antifungal prescription recommendations for fungaemia: Data from a nationwide fungaemia surveillance programme. Clin Microbiol Infect 19:e343–e353 . https://doi.org/10.1111/1469-0691.12212

20. Mulu A, Kassu A, Anagaw B, Moges B, Gelaw A, Alemayehu M, Belyhun Y, Biadglegne F, Hurissa Z, Moges F, Isogai E (2013) Frequent detection of "azole" resistant Candida species among late presenting AIDS patients in northwest Ethiopia. BMC Infect Dis 13:82. https://doi.org/10.1186/1471-2334-13-82

21. Manzano-Gayosso P, Méndez-Tovar LJ, Hernández-Hernández F, Lopez-Martinez R (2008) Antifungal resistance: an emerging problem in Mexico. Gac Med Mex 144(1): 23–26.

22. Hamza OJM, Matee MIN, Simon ENM, Kikwilu E, Moshi MJ, Mugusi F, Mikx FHM, Verweij PE, Van Der Ven AJAM (2006) Oral manifestations of HIV infection in children and adults receiving highly active anti-retroviral therapy [HAART] in Dar es Salaam, Tanzania. BMC Oral Health 6:12. https://doi.org/10.1186/1472-6831-6-12

23. Redding SW, Zellars RC, Kirkpatrick WR, McAtee RK, Caceres MA, Fothergill AW, Lopez-Ribot JL, Bailey CW, Rinaldi MG, Patterson TF (1999) Epidemiology of oropharyngeal Candida colonization and infection in patients receiving radiation for head and neck cancer. J Clin Microbiol 37:3896–3900. https://doi.org/10.1128/jcm.37. 12.3896-3900.1999

24. Costa CR, De Lemos JA, Passos XS, De Araújo CR, Cohen AJ, Souza LKHE, Silva MDRR (2006) Species distribution and antifungal susceptibility profile of oral Candida isolates from HIV-infected patients in the antiretroviral therapy era. Mycopathologia 162:45–50. https://doi.org/10.1007/s11046-006-0032-y

25. Petruzzi MNMR, Cherubini K, Salum FG, De Figueiredo MAZ (2013) Risk factors of HIV-related oral lesions in adults. Rev Saude Publica 47:52–59. https://doi.org/10.1590/ S0034-89102013000100008

26. Chakrabarti A (2011) Drug resistance in fungi – an emerging problem. Reg Heal Forum 15:97–103

27. Falagas ME, Roussos N, Vardakas KZ (2010) Relative frequency of albicans and the various non-albicans Candida spp among candidemia isolates from inpatients in various parts of the world: A systematic review. Int J Infect Dis 14:e954–e966 . https://doi.org/10.1016/j.ijid.2010.04.006

28. Rosana Y, Yasmon A, Lestari DC (2015) Overexpression and mutation as a genetic mechanism of fluconazole resistance in candida albicans isolated from human immunodeficiency virus patients in Indonesia. J Med Microbiol 64:1046–1052. https://doi.org/10.1099 /jmm.0.000123

29. Salari S, Khosravi AR, Mousavi SAA, Nikbakht-Brojeni GH (2016) Mechanisms of resistance to fluconazole in Candida albicans clinical isolates from Iranian HIV-infected patients with oropharyngeal candidiasis. J Mycol Med 26:35–41. https://doi.org/10.1016/j.mycmed.2015.10.007

30. Terças ALG, Marques SG, Moffa EB, Alves MB, de Azevedo CMPS, Siqueira WL, Monteiro CA (2017) Antifungal drug susceptibility of Candida species isolated from HIV-positive patients recruited at a public hospital in São Luís, Maranhão, Brazil. Front Microbiol 8:eCollection 2017 . https://doi.org/10.3389/fmicb.2017.00298

31. Toure OA, Ama B-I, Etienne A et al. (2016) Species identification of Candida isolates in various clinical specimens and their antifungal susceptibility patterns in Côte d'Ivoire. Afr. J. Microbiol. Res (2016) 10: 66–72.

32. Barchiesi F, Caggiano G, Maracci M, Arzeni D, Scalise G, Montagna MT (2003) Antifungal susceptibility patterns of yeast isolates causing bloodstream infections. J Antimicrob Chemother 51:431–433. https://doi.org/10.1093/jac/dkg073

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.

33. Anderson JB (2005) Evolution of antifungal-drug resistance: Mechanisms and pathogen fitness. Nat Rev Microbiol 3:547–556 . https://doi.org/10.1038/nrmicro1179

34. Barchiesi F, Arzeni D, Caselli F, Scalise G (2000) Primary resistance to flucytosine among clinical isolates of Candida spp. J Antimicrob Chemother 45:408–409. https://doi.org /10.1093/jac/45.3.408

35. Cuenca-Estrella M, Díaz-Guerra TM, Mellado E, Rodríguez-Tudela JL (2001) Flucytosine Primary Resistance in Candida Species and Cryptococcus neoformans. Eur J Clin Microbiol Infect Dis 20:0276–0279. https://doi.org/10.1007 /s100960100468

36. Gualco L, Debbia EA, Bandettini R, Pescetto L, Cavallero A, Ossi MC, Schito AM, Marchese A (2007) Antifungal resistance in Candida spp. isolated in Italy between 2002 and 2005 from children and adults. Int J Antimicrob Agents 29:179-184.https://doi.org/10.1016/j.ijantimicag .2006.08.04 7

Thank you for publishing with

HSI Health Sciences Investigations Journal

Visit or download articles from our website https://hsijournal.org

Copyright © 2020 University of Ghana College of Health Sciences on behalf of HSI Journal. All rights reserved.
This is an Open Access article distributed under the Creative Commons Attribution License, which permits use of article provided the original work is properly cited.

49