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Research Article

Distribution and Antifungal Resistance Profile of *Candida* spp. Isolated from Patients Living with HIV at the Yaoundé Central Hospital

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Abstract

Background and Purpose: Candidiasis are the most frequent fungal infection, especially in immunocompromised people such as patients living with the human immunodeficiency virus (PLHIV). Data on the fungal prevalence and antifungal resistance rate particularly in PLHIV in Cameroon are scarce. This study aimed to determine the distribution and the antifungal resistance profile of *Candida* spp. isolated from clinical samples of PLHIV visiting the laboratory service of the Yaoundé Central Hospital. Materials and Methods: A cross-sectional study was carried out on the PLHIV visiting the Central Hospital of Yaoundé laboratory service. Samples were collected according to the signs and symptoms recorded by the patient and inoculated onto Sabouraud + Chloramphenicol agar medium for 24 hours incubation at 35 ℃ ± 2 ℃. Typical *Candida* colonies were subjected to a germ tube test to identify *Candida albicans* and the other species were identified biochemically using API Candida (BioMérieux). The antifungal susceptibility testing was carried out by the disk diffusion method and seven antifungal discs (Bioanalyse) were tested. Results: Overall, 106 unique samples were obtained from participants. The positivity rate of *Candida* spp. was 37.7%. *Candida* isolates were mostly recovered from sputum (n=15/40) followed by the oral swabs (n=10/40) and the vaginal swabs (n=08/40). Out of the 40 isolates, *Candida albicans* was the predominant species 57.5% followed by *Candida krusei* 15%, *Candida glabrata* and *Candida guilliermondii* 10% each and *Candida famata* 7.5%. The antifungal drug resistance profile of *Candida* spp. revealed the highest resistance rates to Amphotericin B (95.0%), Fluconazole (57.5%) and Nystatin (42.5%). Conversely, Clotrimazole, Miconazole and Econazole were the most effective against *Candida* spp. Conclusion: The high frequency of *Candida* spp. isolation, resistant to several commonly used antifungals among PLHIV in a hospital setting is a direct call for stakeholders, policymakers and clinicians about antifungal therapy awareness in this vulnerable population.

Keywords

PLHIV, Candida, Antifungal Drug Resistance

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1. Introduction

Fungal infections are one of the major causes of human diseases and an increasing public health concern worldwide, particularly in low-resource settings [1, 2]. The incidence of mycoses is thought to have tripled over the last 15 years, especially *Candida* infections [3, 4]. *Candida* spp. are commensals of the gastrointestinal tract, vaginal and skin flora and opportunistic in immunocompromised subjects especially those living with human immunodeficiency virus (HIV) [5]. Therefore, candidiasis represents the most frequent invasive fungal infection and several *Candida* species were classified as priority fungal pathogens by the World Health Organization (WHO) [2, 6]. *Candida albicans* in particular is the most frequent specie implicated in various diseases from mild superficial infections to life-threatening invasive infections [7]. Thus these infections need particular attention and much resources to be well investigated in view to estimate their exact burden to permit stakeholders, policymakers and healthcare professionals to manage these infections [2].

Human immunodeficiency virus infections and acquired immunodeficiency syndrome (AIDS) are the leading causes of morbidity and death in Cameroon despite the decreasing prevalence from 4.9% in 2002 to 2.9% in 2021 and remain therefore one of the most important immuno-suppressive infections [8-10]. Furthermore, HIV infections and other risk factors such as diabetes, pregnancy, the usage of catheters, and oral contraceptives have been documented to be significantly associated with the occurrence of candidiasis [11, 12]. In addition to these risk factors, fungal pathogens are becoming increasingly resistant to antifungal treatment while the therapeutic choices are yet limited [2].

Data are scarce on the rate of antifungal drug resistance worldwide, especially in low and middle-income countries including Cameroon. In this context, we proposed to conduct a study to determine the distribution and resistance profile of *Candida* spp. isolated from various samples of patients living with HIV visiting the Yaoundé Central Hospital (YCH), in view of generating evidence-based knowledge to improve the management of fungal infections in this vulnerable population set.

2. Materials and Methods

This was a cross-sectional study conducted over four months, from March 07 to July 08 2022. The study involved all patients living with HIV who came on consultation and/or follow-up at the YCH. After obtaining consent from the PLHIV, a questionnaire was used to record socio-demographic; and clinical data, including digestive disorders (abdominal pain, diarrhoea, vomiting), micturition pain, vaginal itching, malodorous leucorrhoea, coughing, oral thrush, throat pain and medical history. A unique sample (stool, urine, sputum, tongue swab or vaginal swab) was taken from each participant according to the clinical signs and symptoms recorded. The samples were inoculated directly onto Sabouraud + Chloramphenicol agar medium and incubated at 35 ℃ ± 2 ℃ for 24 hours. Typical Candida colonies were subjected to the germ tube test to differentiate *C. albicans* from other species. The API Candida (BioMérieux, Paris, France) and API WEB software were used to identify the various other species. A panel of seven clinically relevant discs of antifungal agents (Bioanalyse®) were tested: Nystatin (100µg), Econazole (10µg), Miconazole (10µg), Fluconazole (25µg), Clotrimazole (10µg), Amphotericin B (20µg) and Ketoconazole (10µg). Data analysis was performed using SPSS V.26 and Excel 2019.

3. Results

3.1. Socio-Demographic Characteristics of Participants

Overall, 150 participants were contacted and 106 different samples were collected from 66 males and 40 females. Out of 106 samples cultured, 40 (37.7%) were positive for *Candida* spp. and mostly isolated in females PLHIV 23/40 (57.5%). PLVIH aged up to 50 years old (36.8%) were the most represented age group but those in 20-30 years old (58.8%) group were the most infected. Of the 40 positive patients, 44.4% were single people and 41.7% were married as described in Table 1.

Table 1. *Distribution of socio-demographic characteristics of PLHIV.*

Variables	Modality	Frequency (106)	Positive culture n (%)
Age (years)	20 -30	17	10 (58.8)
	31 – 40	27	12 (44.4)
	41 -50	23	08 (34.7)
	50+	39	11 (28.2)
Gender	Male	66	18 (27.3)

Variables	Modality	Frequency (106)	Positive culture n (%)
	Female	40	23 (57.5)
	Single	18	08 (44.4)
Matrimonial status	Married	72	30 (41.7)
	Widow	16	03 (18.8)
	Illiterate	17	06 (35.3)
	Primary	33	12 (36.4)
Educational level	Secondary	35	09 (25.7)
	University	21	14 (66.7)

3.2. Distribution of Candida spp. Isolates

Candida spp. were mostly isolated in the sputum (n=15/40) followed by the oral swab samples (n=10/40) and the vaginal swabs (n=08/40). From the sputum samples, *Candida albicans* (n=08/15) and *Candida krusei* (n= 06/15) were the predominant species. *Candida albicans* strains were isolated from each sample type and were the only ones found in the urine and stool samples. All the *Candida krusei* isolates were only isolated from sputum samples. The distribution according to the sample type is described in Table 2.

Table 2. *Distribution of Candida species according to the sample.*

Candida spp.	Samples (%)				
	Sputum	Oral swab	Vaginal swabs	Stool	Urines
Candida albicans (23)	08 (34.8)	03 (13.0)	05 (21.7)	04 (17.4)	03 (13.0)
Candida famata (03)	00	01 (33.3)	02 (66.7)	00	00
Candida glabrata (04)	00	03 (75.0)	01 (25.0)	00	00
Candida guilliermondii (04)	01 (25.0)	03 (75.0)	00	00	00
Candida krusei (06)	06 (100.0)	00 (0.0)	00 (0.0)	00 (0.0)	00
Total (n=40)	15	10	08	04	03

Out of 40 *Candida* spp. isolated in this study, *Candida albicans* (57.0%) was the most frequent species, followed by *Candida krusei* (15.0%), *Candida glabrata* and *Candida guilliermondii* (n=04/40 each) and *Candida famata* (n=03/40) as illustrated in Figure 1.

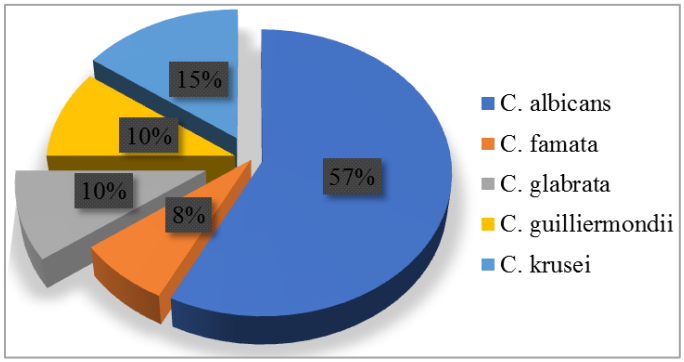

Figure 1. *Distribution of Candida species among PLHIV.*

3.3. Antifungal Resistance Profile

The overall resistance rate of *Candida* spp. to antifungal agents in PLHIV is summarised in Table 3. Almost all isolates were resistant to Amphotericin B (95.0%), followed by Fluconazole (57.5%), Nystatin (42.5%) and Ketoconazole (40.0%). In contrast, resistance to Clotrimazole (25.0%), Econazole (27.5%) and Miconazole (27.5%) was low. *Candida albicans* isolates were highly resistant to Amphotericin B (95.7%), Fluconazole (47.8%) and Nystatin (42.5%) while Miconazole was especially effective against *Candida albicans* (13.0%) and *Candida famata* (00%). The resistance rate was at least 50% against all the tested antifungal discs except Clotrimazole (16.7%) in *Candida krusei*.

Table 3. *Antifungal resistance profile of Candida spp. isolates.*

Isolates (n)	Resistance rate n (%)						
	ECO	CLT	FLU	MCZ	KTC	AMB	NY
Total (40)	11 (27.5)	10 (25.0)	23 (57.5)	11 (27.5)	16 (40.0)	38 (95.0)	17 (42.5)
Candida albicans (23)	06 (26.1)	06 (26.1)	11 (47.8)	03 (13.0)	07 (30.4)	22 (95.7)	10 (42.5)
Candida famata (03)	00	01 (33.3)	01 (33.3)	00	01 (33.3)	03 (100)	01 (33.3)
Candida glabrata (04)	01 (25.0)	02 (50.0)	02 (50.0)	01 (25.0)	02 (50.0)	03 (75.0)	01 (25.0)
Candida guilliermondii (04)	01 (25)	00	03 (75.0)	03 (75.0)	02 (50.0)	04 (100)	02 (50.0)
Candida krusei (06)	03 (50.0)	01 (16.7)	06 (100)	04 (66.7)	03 (50.0)	06 (100)	03 (50.0)

ECO: Econazole, CLT: clotrimazole, FLU: Fluconazole, MCZ: Miconazole, KTC: Ketoconazole, AMB: Amphotericin B, NY: Nystatin

4. Discussion

Mycoses are a major public health problem, particularly in immunocompromised patients. *Candida* are principally commensals of various human mucous but they can easily be infectious in PLVIH because of their weakened immune defences [2, 5]. Antimicrobial resistance worsens the therapeutic management of these infections and increases the rate of death. Thus, this study sought to determine the distribution and the antifungal drug resistance profile of *Candida* spp. isolated from PLHIV at the Yaoundé Central Hospital. Overall, we found a prevalence of 37.7% of *Candida* spp. in PLVIH. This is low compared to 67.8% and 42.8% reported by Njunda et *al*. (2012) in Douala and by Ambe et *al*. (2020) in Kumba respectively from the clinical samples of PLHIV/AIDS in Cameroon [13, 14]. Also, Khedri et *al*. (2018) found a higher prevalence (59.3%) of oropharyngeal candidiasis in Iranian HIV/AIDS patients and Ordonez et *al.* (2017) reported a prevalence ranging from 56.3% to 75.5% of *Candida* spp. from oral samples in many cities of Mexico [15, 16]. The differences in study population size, sample types, and previous exposure to antimicrobials could explain this observed disparity. Moreover, the quality of hygiene and an unsafe lifestyle play a key role in the occurrence of these infections in this population set [14]. Participants aged more than 50 years old (36.8%) were the most represented age group but those in the 20-30 years old (58.8%) group were the most infected. Candidiasis commonly occurs in participants around this age group and has been documented by many studies in low and middle-income countries in particular [13, 14, 17]. This may be explained by the fact that people at this age due to their different activities enter into contact with various environments that are not always hygienic and safe.

Out of 40 *Candida* spp. isolated, *C. albicans* was the most prevalent specie (57.0%) and was mostly isolated from sputum/oral swabs, stool, and vagina wabs and was rare in urine samples. Similar results were recorded where *Candida albicans* was the most implicated in candidiasis by several authors in Cameroon and other countries as well [13-16, 18-21]. Indeed, *Candida albicans* is a commensal specie of the gastrointestinal tract, vagina and skin flora contrarily to the urinary tract and opportunistic in immunocompromised people, especially PLHIV [5].

The antifungal susceptibility testing revealed a high antifungal drug resistance rate of *Candida* spp. to Amphotericin B (95%), Fluconazole (57.5%), Nystatin (42.5%) and Ketoconazole (40.0%). A comparable resistance profile was reported by Gonsu et *al.* (2014) where *Candida* spp. isolated from oral swabs and stool samples of PLHIV were highly resistant to Nystatin, Fluconazole and Amphotericin B while Miconazole was the most effective [21]. The high resistance rate to Fluconazole compared to other azoles in this current study could be attributed to the frequent use of this drug in the prevention and treatment of Candida infections among PLHIV. Moreover, Fluconazole as well as Amphotericin B

are readily accessible even over the counter in Cameroon thus, may contribute to the overuse and misuse of these drugs and consequently to antifungal drug resistance.

The current study highlighted the importance of antifungal drug resistance management in PLHIV. However, this study has several limits. Firstly, the small sample size precludes a robust conclusion and generalisability of results. Secondly, the non-investigation of risk factors for *Candida* infections among these PLHIV hinders the implementation of context-specific infection prevention and prevention measures. Notwithstanding, this study fills an important data gap regarding the epidemiology and antifungal drug resistance of diverse *Candida* species causing infections in PLHIV. Future studies are needed to unravel the genetic determinants of this observed resistance and to explore virulence traits among *Candida* spp. causing infections in PLHIV.

5. Conclusion

This study aimed to determine the distribution and resistance profile of *Candida* spp. isolated from clinical samples in PLHIV at HCY. Our results revealed a high frequency of *Candida* spp. in PLHIV. Several *Candida* spp. were isolated in particular *Candida albicans*, which was the most frequent and found in all types of samples including sputum, oral swab, stool, vaginal swab and urine. *Candida* spp. isolates were highly resistant to commonly used antifungal agents including; Amphotericin B, Fluconazole and Nystatin. These results warrant the rational use of antifungal therapies in both community and hospital settings coupled with improved infection prevention and control measures in this vulnerable population set.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome

HIV: Human Immunodeficiency Virus

PLHIV: Patients Living with the Human Immunodeficiency Virus

YCH: Yaoundé Central Hospital

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Author Contributions

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All authors read and approve the final version of the manuscript.

Ethical Consideration

The institutional ethics committee for research on human health [Ref:3186 CEI-UDo/06/2022/M] and the Yaoundé Central Hospital research authorizations [2022/166/AR/MINSANTE/SG/DHCY/UAF] were granted for this study.

Conflicts of Interest

The authors declared no conflicts of interest.

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