

# Oral Candidiasis in HIV Patients Subjected to Anti-retro Viral Therapy (ART) in Wad Medani HIV Center, Gezira State, Sudan (2021)

## Abstract

**Back ground:** Oral candidiasis is the most common fungal infection in immune compromised individuals such as AIDS patients. *Candida albicans* alone is responsible of more than 95% of candidiasis. The increase prevalence of oral candidiasis among African HIV infected people has resulted in increased in usage of antifungal agents for both prophylactic and treatment purposes. This was cross- sectional descriptive study based on secondary data from patient's records and laboratory investigations, conducted in Wad Medani HIV Center during the period between March to December 2021.

**Aim:** The aim of the study was to detect oral candidiasis in HIV patients subjected to anti-retro viral therapy.

**Method:** A total of 100 participants were included, oral swab samples were collected and processed immediately by culturing on potatoes dextrose agar (PDA), *Candida* species were identified on the base of morphology, germ tube test and chlamydo-spre formation and the participants were categorized according the WHO classification of viral stages into I, II, III and IV. Demographic data was obtained by questionnaire and analyzed by SPSS program version 21.

**Result :**In the results, Female and male infected with HIV were 55 (55/100)% and 45 (45/100) % respectively , most frequent age group was from 31 to 41 years with frequency of 47% (47/100), while HIV participants with basic education level and illiterate constituted 87% (87/100). *Candida* species was detected in 21% (21/100)of tested samples. All isolated candida showed positive germ tube test and produced beta hemolysis on blood agar while chlamydo-spre were observed among 85.7% (18/21) and recorded as *Candida albicans*. Only 18.75% (3/16) of stages 1 subject showed viral load of more than 40 copies/ml,

while stage II,III and IV showed 0 %, 29.8% (17/57) and 27.3(6/22) % respectively. Oral candidiasis recorded in stages III and IV with percentage 57% (57/100) and 22% (22/100) respectively.

**Conclusion:** There was no significant association between HIV stages and viral load among participants with oral candidiasis (*p. value* 0.431). The study recommendation, early detection of HIV patients to ensure good management and continuous availability of anti-retro viral drugs in AIDS centers.

**Key word:** HIV-1, *Candida albicans* , ART, Sudan , 2022

## **Introduction:**

Acquired immune deficiency syndrome (AIDS) is an important dreadful disease in humans that caused by human immune deficiency virus (HIV). The infection is a chronic disease that can be managed, but not treated and could take 10- 15 years to develop<sup>(1)</sup>. AIDS weakens the immune system and makes the affected individuals susceptible to opportunistic infections (viral, parasitic, fungal, and bacterial infections<sup>(2)</sup>. Candidiasis is a prevalent opportunistic infection in HIV/AIDS patients which caused by various *Candida* species, especially *C. albicans* , in the mouth, throat, and esophagus<sup>(3)</sup> .

Oral candidiasis (OC) usually develops in HIV-infected patients when the CD4+T-lymphocyte count declines to > 350 CFU/ml . In the HIV patients with CD4 cell counts of  $\leq$  200 CFU/ml, thrush diffuses to the esophagus, there by turning the oral candidiasis to esophageal candidiasis<sup>(4)</sup>. OC remains the most common oral opportunistic infection in human immunodeficiency virus (HIV), positive individuals and individuals with weakened immune system<sup>(5)</sup> Opportunistic infections represent a common complication during HIV pathogenesis and do not only indicate, but also lead to, a progression of acquired immune deficiency syndrome (AIDS) and to a reduction in the survival time of HIV-infected subjects.<sup>(6)</sup> Oral candidiasis is one of the most common AIDS-defining fungal opportunistic infections in HIV-1 positive subjects. Recently discovered the binding of HIV-1 glycoprotein (gp)160/gp14 to *Candida albicans* and its enhancing effect on candida virulence , it was proposed that both viral (HIV) and fungal (*Candida*) disease may be augmented by this direct interaction<sup>(7)</sup> The factors that predispose to oral candidiasis are smoking, age and oral hygiene.<sup>(8)</sup> According to many studies, the presence of

yeasts in the biofilm, mainly *C. albicans*, contribute not only to oral candidiasis, but to dental caries and periodontal disease.<sup>(9)</sup> The prevalence of oral candidiasis varies between 20% and 70% in HIV infected patients, and although a decline in its prevalence has been observed after the antiretroviral therapy (ART) . HIV RNA (viral load ) and CD4 lymphocyte cell count are two surrogate marker of Anti-Retroviral Therapy (ART ) response and HIV progression that have been used for decades to manage and monitor HIV infection .

### **Methods :**

This was a cross sectional descriptive study was carried in the period between October 2018 to October 2020 on patients suffering from AIDS alone and for the presence of *C. albicans* infection. The HIV status (new or old) of all study patients were confirmed at Wad Medani ART center, in Wad Medani teaching hospital. The HIV status was assessed as recommended by the WHO and the Federal Ministry of Health in Sudan. The participants were 100 aged between less than 20–more than 50 years old, Verbal consent and structural questionnaire enquiring their age, marital status, duration of symptoms, comorbidities, signs and symptoms of current condition, stage of pregnancy, and history of antibiotic consumption was obtained from each patient. The participant was ensured of anonymity and that only group finding will be reported, patients on antifungal therapy were excluded.

Oral swabs, were collected from each patient, the swabs were transferred to the microbiology laboratory and processed immediately. All samples were collected under aseptic conditions and transported to the lab for processing. Blood samples collected in EDTA. 2-3ml(refrigerator -80c)

Each swab was streaked on Potato Dextrose agar plates containing rose bengal (0.25g/l) and incubated at 37°C for 48 hours. Phenotypic identification was made using gram stain and germ tube test. Germ tube test was done by incubating one colony in 0.5 ml human serum at 37°C for 3 hours then it was examined under microscope for the formation of germ tube. Colonies suggestive of *C. albicans* were confirmed by this germ tube test. Sub culture on blood agar plates is done and incubated at 37°C for 24 hours to detect hemolytic activity of candida species in blood agar. Chlamydospore formation was done by culture in corn meal (crack line) Incubate for overnight ,examined microscopically in steak line using 40x.

## Results:

Samples of 100 swabs from positive HIV patient were examined for present of *Candida* spp (45 male and 55 female ) , the highest infection of candida in HIV patient in aged 31-41 and lower infection in aged less than 20 and equal infection in aged 20-30 and more than 52 patient with basic education and illiterate have high infection Of HIV 87 (87/100) and lower in other education level , high infection of HIV in stage III and IV of viral stages according to WHO stages (Table 1) . According to material status higher infection between married patient than others (Table 2 and Figure 1) . 21(21/100) samples of cultured swab were showed positive growth(Table 3), all positive growth sample (21% ) positive for gram stain (violet budding cell ) and forming germ tube (100%) (Table 4and Figure 3) . 18 samples of positive growth forming chlamyospore 85.7% (18/21) (Table4 and Figure 3) . All positive growth have hemolytic activity (beta hemolysiss ) .Chi square test showed that no association between aged group and culture ( p. value 0.423 )(Table 6) while gender has significant relation (p .value 0.023) (Table 7). Stage of HIVand viral load showed insignificant relation in occurrence of oral candidiasis (p. value 0.431) (Table 8).

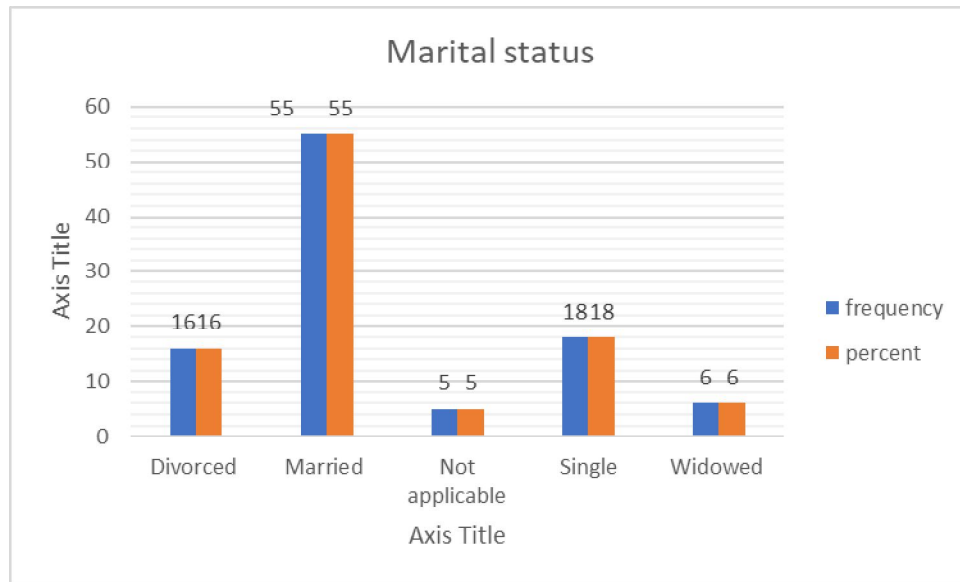
Table (1): Demographic characteristics of patients infected with HIV/AIDS with oral candidiasis

		Negative		Positive		p. value
		Frequency	Percentage	Frequency	Percentage	
<b>Age Group</b>	less than 20	5	6.3	2	9.5	<b>0.423</b>
	20-30	15	19.0	4	19.0	
	31-41	39	49.4	8	38.1	
	42-52	15	19.0	3	14.3	
	more than 52	5	6.3	4	19.0	
	Total	79	100.0	21	100.0	
<b>Gender</b>	Female	48	60.8	7	33.3	<b>0.023</b>
	Male	31	39.2	14	66.7	
	Total	79	100.0	21	100.0	
<b>Education</b>	NO	37	46.8	1	4.8	<b>30.55</b>

<b>Level</b>	Basic	34	43.0	8	38.1	
	Higher	3	3.8	2	9.5	
	Secondary	5	6.3	10	47.6	
	Total	79	100.0	21	100.0	
<b>Stage</b>	Stage 1	15	19.0	1	4.8	<b>0.431</b>
	Stage 2	4	5.1	1	4.8	
	Stage 3	43	54.4	14	66.7	
	Stage 4	17	21.5	5	23.8	
	Total	79	100.0	21	4.8	
<b>Viral Load</b>	<40	55	69.6	11	52.4	<b>0.08</b>
	>40	0	0.0	6	28.6	
	Not Detected	4	5.1	4	19.0	
	Total	79	100.0	21	4.8	

(Table 2): Distribution of the study population according to marital status

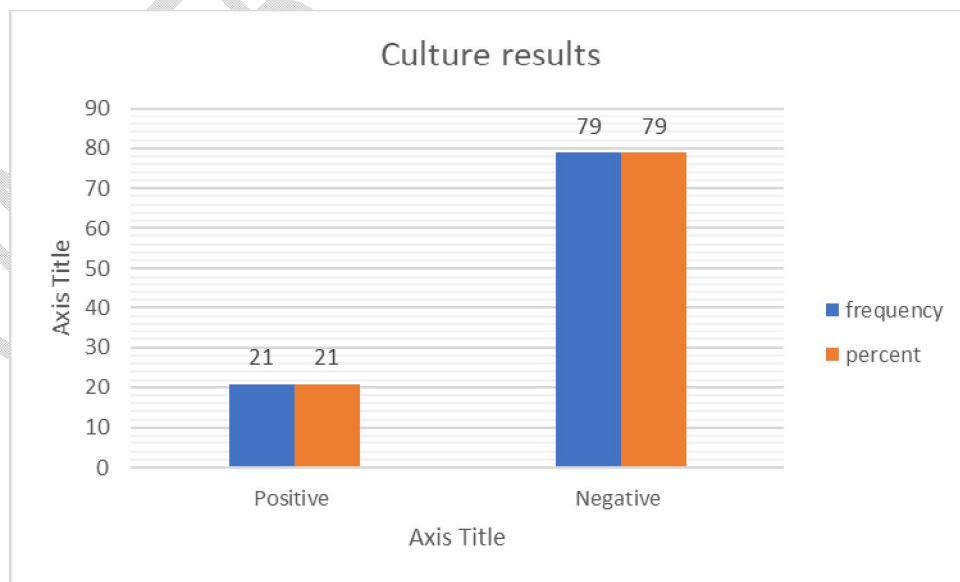
<b>Marital status</b>	<b>Frequency</b>	<b>Percent</b>
Divorced	16	16.0
Married	55	55.0
Not applicable	5	5.0
Single	18	18.0
Widowed	6	6.0
<b>Total</b>	<b>100</b>	<b>100.0</b>



(Figure 1): Distribution of the study population according to marital status

(Table 3): Distribution of the study population according to culture results

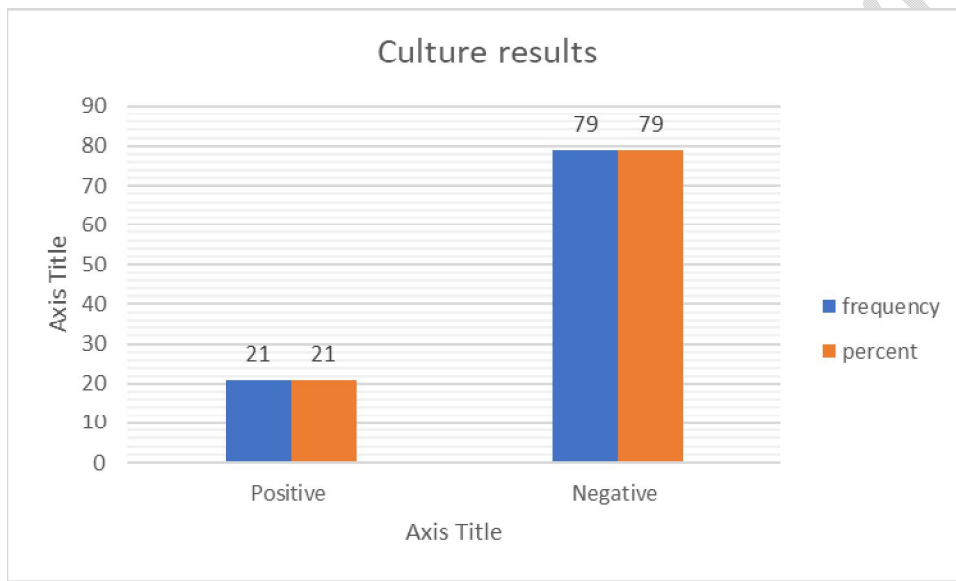
Culture results	Frequency	Percent
Positive	21	21.0
Negative	79	79.0
<b>Total</b>	<b>100</b>	<b>100.0</b>



**(Figure 2): Distribution of study population according to culture results**

**(Table 4): Distribution of the study population according to gram stain result**

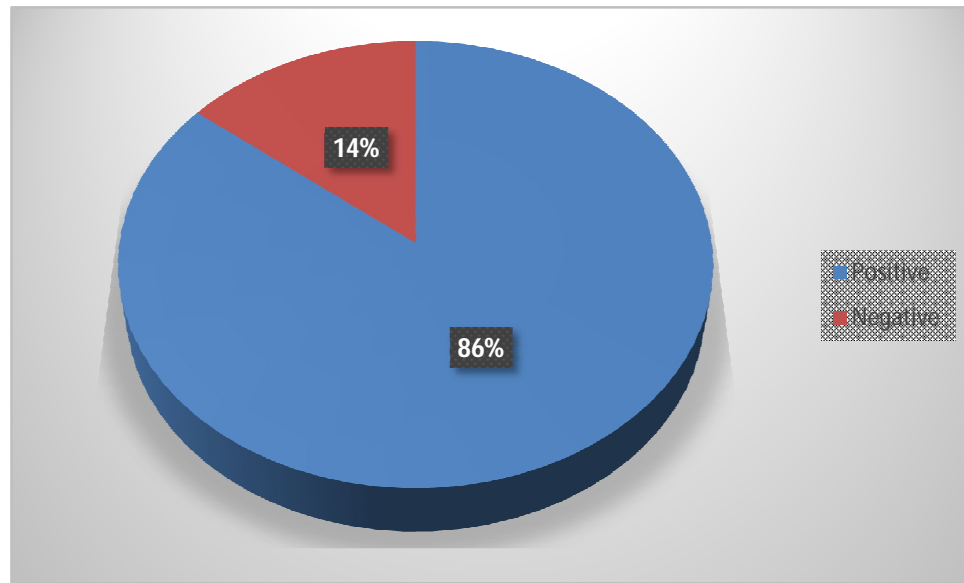
<b>Gram stain results</b>	<b>Frequency</b>	<b>Percent</b>
Positive	21	21.0
Negative	79	79.0
<b>Total</b>	<b>100</b>	<b>100.0</b>



**(Figure3):Distribution of study population according to gram stain result**

**(Table 5): Distribution of the study population according to Chlamydo spore formation**

<b>Chlamydo spore</b>	<b>Frequency</b>	<b>Percent</b>
Positive	18	85.7%
Negative	3	14.3%
<b>Total</b>	<b>21</b>	<b>100.0</b>



**(Figure4): Distribution of study population according to chlamydo spore formation**

**(Table 6): Distribution of the study population according to blood agar**

Blood AGAR	Frequency	percent
Positive	21	21.0
Negative	79	79.0
<b>Total</b>	<b>100</b>	<b>100.0</b>

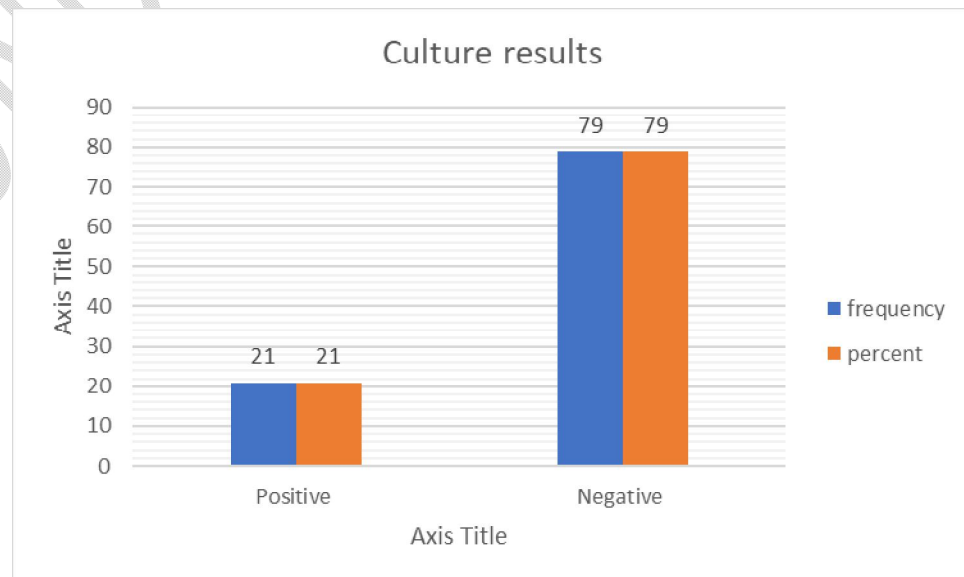


Fig.5 : culture results

(Table 7): Association between age group and culture results :

Age group	Culture results			p. value
	Negative	Positive	Total	
less than 20	5	2	7	0.423
20-30	15	4	19	
31-41	39	8	47	
42-52	15	3	18	
more than 52	5	4	9	
Total	79	21	100	

(Table 8): Association between gender and culture results

Gender	Culture results			p. value
	Negative	Positive	Total	
Female	48	7	5	0.023
Male	31	14	30	
Total	79	21	100	

(Table 9): Association between viral load and stage of disease

Stage of disease	Viral load			p. value
	less than 40	more than 40	not detected	
Stage 1	13	3	0	0.431
Stage 2	5	0	0	
Stage 3	34	17	6	

Stage 4	14	6	2	
<b>Total</b>	66	26	8	

## Discussion

The acquired immune deficiency syndrome (AIDS) is caused by the human immunodeficiency virus (HIV) and is characterized by progressive damage to the immune system, is the most important public health problem of the 20th century, HIV/AIDS continues to spread globally and remains a worldwide pandemic affecting about 36.7 million people <sup>(10)</sup>. Oral candidiasis (OC) is the most common fungal infection in immune compromised patients, infecting approximately 90% of patients with acquired immunodeficiency syndrome (AIDS) <sup>(11)</sup>.

In the present study results showed that 21% had positive candida culture of swabs collected from the oral cavity of HIV/AIDS patients. This result is lower than rates documented in Brazil with percentage of 41.87% and 42% <sup>(12)</sup>. Also is more lower than reported by <sup>(13)</sup>, whom found the frequency was 60% . These differences could probably be due to the fact that not all participants in these studies were on HAART (highly active antiretroviral treatment) and the advent of HAART has allowed for the suppression of viral replication to very low levels and a partial recovery of CD4 cells in patients with HIV, which has consequently reduced opportunistic infections <sup>(14)</sup>.

The present study found that there is slight different in frequency between women (55%) and men (45%), but the higher infection in male (66.7%) may be due to lack of personal hygiene and hormonal change , the result considered statistically significant (P=0.023). This result was lower than studies carried out in Cameroon <sup>(14)</sup> and Mexico <sup>(15)</sup> whom found that high rate of infection in male 74%. This difference is probably because most men rarely go for routine checkups until the disease has reached symptomatic stage and at the time of this study only a few women consented. Also, we found Participants around the age group of 31-41 year accounted for the highest frequency rate (47%), this result is agree with a study carryout in Cameroon but contrary to study carried out in Mexico which shows that *Candida* colonization was age dependent. This highest frequency rate between these age group (31-41 year) is probably due to the majority of the study participants at the highest active sex group which may

also spread oral candidiasis exogenously . The study represent that the high infection of HIV in patient with basic education and illiterate (87%).

Most positive result mainly in stage III and IV followed by stage I and II .There is in significant relation with viral load and Candida infection in patient under ART (p. value 0.08), the result was agree with <sup>(16)</sup> whom found that stage III and IV count high frequency of infection but was significant in present of candidiasis in HIV patient (p .value 0.024).The differ may related to small sample size (34) and all HIV patient had clinical manifestation of oral candidiasis .

### **Conclusion:**

Candida species were isolated from 21% (21/100) of HIV positive subjects, and *Candida albicans* was predominated with percentage of 85.7% (18/21), and there was no significant association between HIV stages and viral load among participants with oral candidiasis (*p. value* 0.431). To ensure good management, the early detection of HIV patients and continuous availability of ART in AID centers are recommended.

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