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NATIONAL INSTITUTE OF MALARIOLOGY, PARASITOLOGY AND ENTOMOLOGY

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NGU THI THAM

CLINICAL AND LABORATORY CHARACTERISTICS OF ORAL CANDIDIASIS IN HIV/AIDS PATIENTS AND TREATMENT OUTCOMES AT NGHE AN GENERAL FRIENDSHIP HOSPITAL (2022-2024)

THESIS SUMMARY

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THE THESIS IS COMPLETED AT THE NATIONAL INSTITUTE OF MALARIOLOGY, PARASITOLOGY AND ENTOMOLOGY

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The thesis will be defended in front of the Institutional Defense Committee at the National Institute of Malariology, Parasitology and Entomology

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The thesis can be found at:

- Vietnam National Library;
- The Library of the National Institute of Malariology, Parasitology and Entomology.

INTRODUCTION

A total of 85.6 million people have been infected with HIV and 40.4 million people have died of AIDS-related diseases worldwide. In Vietnam, the percentage of HIV infection is high. By the end of 2020, the number of HIV infections was 213,724 people, of which 155,973 people were treated with ARV therapy, reaching only 73%, and the cumulative number of deaths by 2020 was 109,446 people. According to Nghe An Center for Disease Control (CDC), nearly 11,000 HIV-infected people were reported from 1996 to 2024 [3], [4].

The most common cause of oral lesions in HIV patients is oral candidiasis [8], [9], [10]. According to a study by Sirun Meng et al. (2024) on 12,612 HIV-infected people, 71.2% of the patients were infected with one or more opportunistic infections, of which the mortality due to opportunistic infections was 9%, and oral candidiasis ranked the third [84]. Therefore, prevention, diagnosis and control of oral health is necessary to be integrated as part of medical treatment for HIV-infected patients [7], [12]. According to Nguyen Ngoc Thien Huong et al. (2007), oral lesions caused by Candida spp were most common in people with HIV (62.7%) [12]. At the Center for Tropical Diseases, Nghe An General Friendship Hospital, the number of HIV patients coming for examination and treatment was about 800 patients in 2023, including a high percentage of HIV/AIDS patients with oral Candidiasis [13]. Determining the characteristics of oral lesions as well as pathogenic species is very important in both prognosis and treatment for HIV/AIDS patients; therefore, we conducted the study: **Clinical and laboratory characteristics of oral candidiasis in HIV/AIDS patients and treatment outcomes at Nghe An General Friendship Hospital, 2022-2024**, with the following objectives:

1. To determine the prevalence, associated factors, and clinical and laboratory characteristics of oral Candidiasis in HIV/AIDS patients in Nghe An from 2022 to 2024.

2. To identify the composition of fungal species causing oral Candidiasis in HIV/AIDS patients in Nghe An from 2022 to 2024

3. To evaluate the treatment outcomes of Fluconazole for oral Candidiasis in HIV/AIDS patients in Nghe An.

NOVELTY AND SCIENTIFIC AND PRACTICAL SIGNFICANCE OF THE THESIS

Studies on oral Candidiasis are being conducted on general subjects, or on subjects with systemic immunodeficiency such as cancer patients, or with local immunodeficiency disorders such as denture wearers; however, there hasn't been any study on oral Candidiasis in HIV/AIDS patients. The study employed molecular biology (PCR, gene sequencing) to determine fungal species composition.

THESIS STRUCTURE

The thesis consists of 115 pages, including: Introduction (2 pages); literature review (32 pages); study subjects and methods (22 pages); study results (34 pages);

discussion (31 pages); conclusion (2 pages); and recommendations (1 page). There are 37 tables, 8 figures, and 119 references.

Chapter 1:
LITERATURE REVIEW

1.1. Oral lesions in HIV/AIDS patients

There are more than 30 oral lesions associated with HIV infection [12]:

Table 1.1: Classification of HIV associated oral lesions

Group 1: Oral lesions are ***strongly associated*** with HIV infection	**Group 2:** Lesions are ***associated*** with HIV infection	**Group 3:** Lesions ***are possibly found*** in HIV infection
Erythematous and pseudomembranous ***candidiasis***	Mycobacterium avium - Cellulare, *M. tuberculosis*	Actinomyces israeli, *E. coli*, Klebsiella; Pneumoniae
Oral hairy leukoplakia	Melanization	Cat scratch disease
Kaposi sarcoma	Necrotizing gingivostomatitis	Drug reaction
Periodontal diseases: marginal gingivitis, necrotizing ulcerative gingivitis, necrotizing periodontitis.	Salivitis: dry mouth, unilateral or bilateral salivary gland enlargement	Increased epithelial cells in blood vessel walls
	Immune thrombocytopenia purpura	Non-Candida spp infection: *Crypyococcus neoformans, Geotrichum, Candidum spp, Histoplasma capsulatum, Aspergillus flavus*
	Ulcer	Neurological disorders such as facial paralysis, trigeminal neuralgia
	Herpes simplex, HPV	Recurrent aphthous stomatitis
		Virus infection: Cytomegalovirus, Molluscum contagiosum

1.2. Oral fungal lesions in HIV/AIDS patients

Any fungus present in the environment has the potential to cause disease in immunocompromised people, but the most common one is *Candida* spp.; other species are less common [23], [24]. *Candida* spp. is highly adaptable to the environment and can live independently in the environment.

- Pathogenicity

Candida can be normally found parasitizing on the skin, in the oral cavity (30%), digestive tract (38%), bronchi (17%), anal folds (46%), vagina... without causing disease.

They live symbiotically and in balance in the normal microflora [27], [28].

Pathogenesis of Candida infections includes three factors: host, fungus, and factors that change the microenvironment. When these factors are out of balance, *Candida* from a symbiotic organism will cause disease by adhering to mucosal epithelial cells, then invading the epithelium thanks to specific protein-degrading enzymes secreted by *Candida*, then multiplying, developing massively and causing disease. For *C. albicans*, the ability to adhere and penetrate the mucosa is higher than other species. This explains why mucosal candidiasis is mainly caused by *C. albicans* [29], [30]. *Candida* spp cause disease in humans when the body is immunocompromised or there are favorable factors. *Candida*-induced diseases often recur. There are more than 300 different strains of *Candida*; however, only a few strains cause disease in humans, of which *C. albicans* is the most common, in addition to *C. glabrata, C. tropicalis, C. crusei, C. parapcilosis, C. dubliniensis, C. pseudotropicalis*... Each species carries different toxicity, so the ability to cause disease and sensitivity to antifungal antibiotics are also different [25], [31], [32].

Candida can cause diseases in many organs from superficial to deep such as: superficial skin, mucous membranes, or penetrate deep into internal organs such as heart, lungs, brain, blood... and even causes death. Their development is controlled by bacteria living in the microflora. *Candida* becomes pathogenic when there are favorable conditions, the body is immunocompromised and the microflora is unbalanced.

- Risk factors for Candida spp infection

Candida spp. infection depends on many factors [33], [34]: Mechanical factors: trauma, local bandages; Physiological factors: newborns, pregnant women, changes in vaginal pH during menstruation; Nutritional factors such as vitamin A, B, C, and D deficiency; iron deficiency diseases (chronic mucosal candidiasis); Pathological factors: diabetes, endocrine diseases such as hypothyroidism or hypoparathyroidism, acute or chronic renal failure (dialysis), malignancy especially leukemia, lymphoma, aplastic anemia, immunosuppression (often associated with patients undergoing cancer treatment, organ transplant, or acquired immunodeficiency syndrome (HIV/AIDS)); and prolonged use of broad-spectrum antibiotics, radiotherapy, other immunosuppressive drugs in the treatment of autoimmune diseases or cancer, contraceptives especially estrogen-dominated... COVID-19 infection is also a factor that can aggravate oral candidiasis in HIV/AIDS patients by reducing host immunity and damaging various tissues in the oral mucosa. Denture-associated candidiasis can aggravate COVID-19 and increase the morbidity and mortality [38], [39].

Chapter 2:
STUDY SUBJECTS AND METHODS

2.1. Study subjects and methods for objective 1*: Prevalence, associated factors, clinical and laboratory characteristics of oral candidiasis in HIV/AIDS patients*

- Study subjects: HIV/AIDS patients diagnosed with oral Candidiasis. The patients were diagnosed with HIV infection according to the criteria in Decision No. 5968/QĐ-BYT of the Ministry of Health in 2021) [4], and were being treated as an outpatient or inpatient at the Center for Tropical Diseases, Nghe An General Friendship Hospital. The patients were diagnosed with oral Candidiasis according to Decision No.75/QĐ-BYT of the Ministry of

Health in 2015 on diagnosis and treatment of dermatological diseases). ***Exclusion:*** Patients under 18 years old; Patients who had used systemic or topical antifungal medications in the oral area within 1 month

- ***Study location:*** The Center for Tropical Diseases, Nghe An General Friendship Hospital

- ***Study duration:*** From January 2022 to May 2024.

- ***Study design:*** Descriptive research method.

- ***Sample size:*** We applied the formula for calculating minimum sample size for prevalence:

$$n = Z^2_{1-\alpha/2} \frac{1-p}{p\varepsilon^2}$$

Where: n is the minimum sample size; p: is the estimated proportion of the population, choose p = 0.5 (there had been no research on this topic in Vietnam, therefore choose p = 0.5.), $Z_{1-\alpha/2}$: With a 95 percent confidence interval, the value of $Z_{1-\alpha/2}$ is 1.96; ε: Desired relative error, choose ε = 0.1). With the selected values, the sample size is 385. In fact, we studied 393 patients.

- ***Research content***

Describe general information about the study subjects: demographic characteristics (age, gender, occupation, education), eating habits, oral hygiene, history of HIV/AIDS infection and treatment, and associated diseases.

- Determine the prevalence, distribution of the prevalence by some information of the subject. Determine some factors related to oral candidiasis: demographic characteristics, habits, behaviors, history of HIV/AIDS and accompanying diseases.

- Determine clinical characteristics: basic lesions, location, number, clinical form. Determine laboratory characteristics of the subjects with oral candidiasis.

- ***Techniques used in the study:*** Patient interview; Clinical examination; Oral sample collection; Direct potassium hydroxide (KOH) testing; Fungal culture on Sabouraud Dextrose Agar

- ***Research indicators:*** The overall prevalence of oral candidiasis; Prevalence by age, education level, ethnicity, place of residence, occupation, income; Some related factors such as eating habits, oral hygiene, history of HIV/AIDS infection and treatment, and accompanying medical conditions; Percentage of functional symptoms, physical symptoms, clinical form, biochemical test results, and viral load among the infected subjects.

2.2. Study subjects and methods for objective 2: *Identification of Candida species in HIV/AIDS patients*

- ***Study subjects:*** Positive samples with direct examination or fungal culture.

- ***Study location:*** At the High-Technology Analysis Laboratory, Department of Parasitology and Entomology, Military Medical Academy.

- ***Study duration:*** From January 2022 to May 2024.

- ***Study design:*** Descriptive laboratory study.

- ***Sample size:***

Species identification by Morphology: All positive samples with direct examination

and/or fungal culture.

Species identification by PCR - RFLP: All fungal isolates.

Species identification by gene sequencing: Sequencing of a representative sample for each species; samples that couldn't be identified using the above two methods; samples with inconsistent results. The identification result was confirmed by sequencing.

- ***Research content***: Fungal samples were cultured on Sabouraud Dextrose Agar; Species identification was performed using morphology and gene sequencing. The obtained gene sequences were compared with the international gene bank.

- ***Techniques used in the study:*** *Fungal culture on CHROMagar^{TM} Candida agar*; *Serological testing*; *PCR-RFLP.*

Table 2.3. Details of forward and reverse primers used for PCR-RFLP:

Primer	Sequence (5'-3')	Primer length	Position of primer attachment
ITS1	TCC GTA GGT GAA CCT GCG G	19	Varying by species
ITS4	TCC TCC GCT TAT TGA TAT GC	20	

Identification of fungal species based on PCR products and restriction digestion

Table 2.5. PCR product size and cutting with MspI enzyme

Species	Sizes of PCR products with ITS1-ITS4 primers	Sizes of PCR products with MspI restriction enzyme
C. albicans complex	535	297, 238
C. glabrata complex	871	557, 314
C. tropicallis	524	340, 184
C. krusei	510	261, 249
C. guilliermondii	608	371, 155, 82
C. parapsilosis complex	520	520

- ***Agarose gel electrophoresis***

- ***Gene sequencing***

- ***Research indicators*****:** Percentage and species composition using fungal culture and morphology, PCR-RFLP, gene sequencing; Percentage of mono-infection and co-infection.

2.3. Study subjects and methods for objective 3: Evaluation of the treatment outcomes for oral candidiasis with Fluconazole 150mg in HIV/AIDS patients.

- ***Study subjects:*** HIV/AIDS patients diagnosed with oral Candidiasis according to Decision No. 75/QĐ-BYT of the Ministry of Health in 2015. ***Exclusion:*** Patients with contraindications to Fluconazole; Hypersensitivity to fluconazole, or the same group of antifungals (i.e. imidazole), or to any ingredient of the drug; Currently taking other drugs such as terfenadine or astemizole, cisapride pimozide and quinidine, acute porphyria

- ***Study location:*** The Center for Tropical Diseases, Nghe An General Friendship Hospital

- ***Study duration:*** From January 2022 to May 2024

- ***Study design:*** Non-controlled intervention study.

- ***Sample size:*** All patients diagnosed with oral Candidiasis, including HIV/AIDS

inpatients and outpatients.

- ***Research content:*** Patients with confirmed oral candidiasis were selected for treatment of oral candidiasis. The treatment regimen followed the HIV/AIDS treatment and care guidelines (Decision No. 5968/QĐ-BYT dated December 31, 2021 of the Ministry of Health [4]):

+ Adults: Fluconazole 100 - 200mg/day x 7 - 14 days.

+ Children: 3 - 6 mg/kg x 1 time/day x 7 - 14 days.

+ Patient follow-up; Evaluation of treatment outcomes and adverse effects on the research subjects after 4 weeks of treatment.

- ***Techniques used in the study***

Use the treatment regimen for oral candidiasis in HIV-infected patients according to the Ministry of Health's guidelines in 2021 as follows: Adults: Fluconazole 100 - 200mg/day x 7 - 14 days.

In this study, we used fluconazole 150mg tablets (brand name: Salgad 150mg) for 7 days for all patients.

+ *About Salgad 150 mg:*

Ingredients: Each Salgad 150mg tablet contains Fluconazole: 150mg. Excipients (Microcrystalline cellulose M112, magnesium stearate, sodium starch glycolate, sodium lauryl sulfate): just enough for 1 tablet. Dosage form: Hard capsule. *Manufacturer:* Registration number: VD-28483-17. Manufacturer: Dat Vi Phu Pharmaceutical Company Limited. Packing: Box of 1 blister x 1 tablet.

+ *Evaluation of treatment outcomes*: Clinically cured, lesions gone 100%; Clinically uncured, lesions persistent 100%; Percentage of completely cured patients. When the disease was clinically cured, all functional and physical symptoms were gone and the fungal test was negative. Interviews were conducted to assess adverse reactions.

- ***Research indicators***: The cure rate and treatment failure after 4 weeks of treatment.

2.4 Data processing and analysis

The data were compiled and calculated using Excel 2010 and statistical analysis was performed using SPSS version 20.0.

2.5. Errors and elimination of errors

The study complied with the selection criteria for screening research subjects. Data were double checked. Investigators had been thoroughly trained on the evaluation criteria and data collection methods. During the interview, the investigator had to clearly explain the purpose of the study and encourage the subjects to answer honestly. During the investigation, information collection was supervised for promptly error correction. Questionnaires and examination forms were re-checked, completed and cleaned before analysis.

2.6. Ethics in research

The study strictly complied with regulations in biomedical research. Before interviewing and examining, the study subjects were well informed. The health status of the participants was also kept confidential. The study had been approved by the Scientific and Ethical Review Board at Decision No. 303/QĐ-VSR dated March 26, 2019 by the National

Institute of Malariology, Parasitology and Entomology.

Chapter 3:
STUDY RESULTS

Of 393 HIV/AIDS patients who had been examined and treated as inpatients and outpatients, 42 patients were found to have oral candidiasis. Clinical and laboratory results were as follows:

3.1. Prevalence, associated factors and clinical and laboratory characteristics of oral Candidiasis in HIV/AIDS patients

- Prevalence and some associated factors of oral Candidiasis in HIV/AIDS patients

Figure 3.1: Prevalence of oral Candidiasis in HIV/AIDS patients

The prevalence of oral Candidiasis in HIV/AIDS patients in the study was 10.7% (42/393).

- Distribution of HIV/AIDS patients with oral Candidiasis by demographic characteristics

Table 3.5. Some demographic characteristics of the study subjects (n=42)

		Number	Percentage (%)
Gender	Male	28	66.7
	Female	14	33.3
Ethnicity	Kinh	37	88.1
	Others	5	11.9
Education	Primary school	9	21.4
	Secondary school	16	38.1
	High School	16	38.1
	College-University	1	2.4
Place of residence	Urban	13	31.0
	Rural	22	52.4
	Mountainous	7	16.6
Occupation	Student	1	2.4
	Civil servant	0	0
	Worker	16	38.0
	Farmer	6	14.2
	Self-employed	15	35.7

	Unemployed	2	4.8
	Others	2	4.8
Income	≥5 million	19	45.2
	>5 million - ≤ 10 million	21	50.0
	> 10 million	2	4.8
Obesity		4	9.5

Among 42 infected persons, males outnumbered females by two to one; the number of Kinh patients was 7.4 times higher than that of other ethnic groups; the disease was common in patients with secondary and high school education (76.2%), patients living in rural areas (53.4%), patients working for themselves and workers (73.8%), and patients with incomes under 10 million (95.2%). The proportion of patients with obesity was 9.5%.

- Some factors related to oral candidiasis in HIV/AIDS patients

Multivariate analysis showed that:

Table 3.15. Results of multivariate analysis of factors associated with the presence of oral Candidiasis in HIV/AIDS patients

Research variables	**p**	**OR, 95%CI:**
Ethnicity	0.945	0.763 (0.000-1.577)
Education	0.392	0.457(0.076-2.739)
Place of residence	0.747	0.363(0.001-170.988)
Income	0.296	2.378(0.468-12.084)
Smoking	0.160	3.820(0.590-24.747)
Toothbrushing frequency	**0.032**	**9.057(1.205-68.075)**
Eating and drinking sweets	0.173	7.246(0.420-12.497)
Drinking alcohol	0.145	0.158(0.013-1.891)
Oral sex	0.758	2.307(0.011-46.931)
Wearing dentures	**0.001**	**15.104(2.840-80.339)**
Tooth loss	0.091	6.656(0.739-59.981)
Accompanying diseases	0.611	0.574(0.068-4.869)
Antibiotic use	0.219	0.081(0.001-4.471)
HIV/AIDS inpatients	**0.006**	**11.970(3.855-37.145)**
Stage of HIV infection	**0.001**	**8.363(2.217-31.552)**
ARV therapy	0.001	1.214(0.906-12.314)
Adherence to ARV therapy	**0.001**	**8.261 (4.916 – 14.094)**

Results of multivariate analysis of some factors associated with oral Candidiasis in HIV/AIDS patients were as follows: Number of toothbrushing times ≤ 1 time/day [9.057(1.205-68.075), $p < 0.05$], wearing dentures [15.104(2.840-80.339), $p < 0.01$], inpatient treatment [11.970(3.855-37.145, $p < 0.05$], stage of HIV infection [8.363(2.217-31.552), p <

0.01], and adherence to ARV therapy [8.261(4.916 - 14.094), p < 0.01].

- Clinical features of oral candidiasis in HIV/AIDS patients

Table 3.16. Percentage of patients having functional symptoms and fever (n = 42):

	Number	Percentage %
Having functional symptoms	32	76.2
Having a fever	18	42.9
Total	42	100.0

In a total of 42 HIV/AIDS patients with oral Candidiasis, 76.2% (32/42) had functional symptoms, and 42.9% (18/42) had a fever.

- Physical symptoms of oral candidiasis

In a total of 45 patients with suspicious oral lesions, 42 patients (93.3%) were diagnosed with oral candidiasis.

Table 3.18. Distribution of oral fungal lesions (n=42):

Description of oral lesions	**Number**	**Percentage (%)**
Pseudomembrane	26	61.9
Red mucous membranes	19	45.2
Red gums	14	33.3
Atrophy of the tongue papillae	7	16.7
Cracked corners of the mouth on both sides	1	2.4
Mouth ulcers	1	2.4
Cracked corners of the mouth on one side	1	2.4
Red papules or nodules	0	0.0
Necrosis	0	0.0
Geographic tongue	0	0.0

The most common lesion was pseudomembrane (61.9%), followed by red mucosa (45.2%) and red gums (33.3%). Other lesions such as atrophy of the tongue papillae, cracked corners of the mouth, and mouth ulcers were less common.

Table 3.20. Distribution of oral clinical forms

Clinical form	**Number**	**Percentage %**
Pseudomembranous	25	51.0
Erythematous	13	26.5
Angular Cheilitis	4	8.2
Rhomboid glossitis	7	14.3
Leukoplakia	0	0.0
Others	0	0.0
Total	49	100.0

The most common clinical form was pseudomembranous (51%), followed by

erythematous (26.5%), rhomboid glossitis (14.3%), and angular cheilitis (8.2%).

- Laboratory characteristics of oral candidiasis

Table 3.21. GOT/GPT test results (n=42)

	SGOT (U/L)	SGPT (U/L)
Average	52.5	39.2
Median	29.0	27.0
Standard deviation	91.7	32.3
Minimum	15.0	10.0
Maximum	616.0	191.0

The results showed that the mean value of GOT/GPT was 52.5/39.2 U/L, with the minimum value being 15/10 U/L, the maximum value being 616.0/191.0 U/L, respectively, and the standard deviation was 91.7/32.3.

Table 3.22. Percentage of patients with elevated liver enzymes (n=42)

Elevated liver enzymes ≥40 (U/L)	Number	Percentage %
SGOT	18	42.9
SGPT	16	38.1

Results showed that 42.9% (18/42) and 38.1% (16/42) of the patients had elevated liver enzymes corresponding to SGOT and SGPT. This elevation was caused by liver diseases such as hepatitis B/C, cirrhosis or use of ARV therapy or other treatment drugs.

Table 3.24. Viral load results (n = 42)

Viral load	**Number**	**Percentage (%)**
Group 1 (≤20 copies/ml)	15	35.7
Group 2 (>20 copies/ml)	27	64.3
Total	42	100.0

Results showed that the patients with viral load above 20 copies/ml accounted for the highest percentage of 63.4% (18/42), followed by viral load ≤20 copies/ml at 35.7%. The viral load in group 2 was mainly found in newly discovered HIV or treatment abandonment inpatients. The viral load in group 1 was mainly found in outpatients with ARV therapy and ARV therapy adherence.

- Association between viral load and oral candidiasis

According to the World Health Organization (WHO), viral load assessment is a valuable tool for monitoring HIV/AIDS patients. Viral load helps clinicians predict the risk of opportunistic infections, including oral candidiasis.

Table 3.25. Association between viral load and oral candidiasis

Viral load		Oral candidiasis		Total	p	OR, 95%CI:
		Yes	No			
Group	Group 1 (≥ 20 copies/ml	27	3	30	0.0001	208.6 (102 – 300)
	Group 2 (< 20 copies/ ml	15	348	363		
	Total	42	351	393		

The results in Table above showed that the patients with viral load ≥ 20 copies/ml had a statistically significantly higher risk of oral candidiasis with OR, 95%CI, $p < 0.05$.

3.2. Species composition of oral Candida spp.

3.2.1. Results of morphological species identification

Table 3.26. Results of morphological species identification

No.	Species	Number	Percentage (%)
1	*C. albicans*	36	65.5
2	*C. tropicalis*	7	12.7
3	*C. glabrata*	4	7.3
4	*C. krusei*	2	3.6
5	*Candida* spp.	6	10.9
Total		55	100,0

A total of 55 species were isolated, of which:

C. albicans accounted for the highest percentage of 65.5% (36/55), followed by *C. tropicalis* of 12.7% (7/55). *C. glabata* and *C. krusei* were less common with the rate of 7.3% (4/55) and 3.6% (2/55) respectively. Up to 10.9% (6/55) of *Candida* spp could not be identified by morphology.

- Results of fungal culture in CHROMagar™ Candida and germ tube formation:

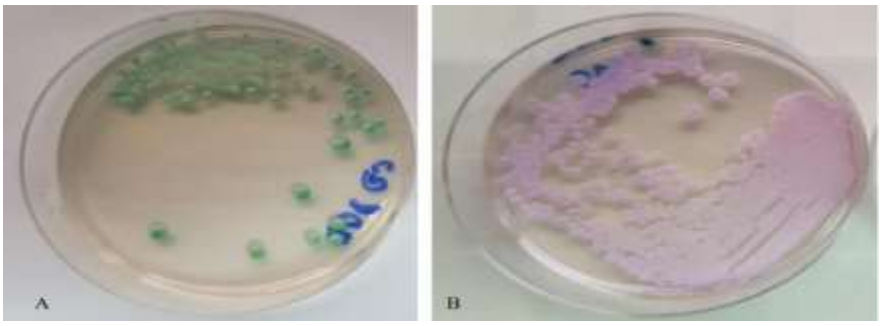

Figure 3.3. Results of fungal culture in CHROMagar™ Candida

Figure 3.3.A showed green colonies of *C. albicans*, Figure 3.3.B showed pink colonies of *C. krusei*.

3.2.2. Results of species identification by PCR – RFLP

Table 3.27. Results of species identification by PCR – RFLP

No.	Species	Number	Percentage (%)
1	*C. albicans*	35	63.6
2	*C. tropicalis*	11	20.0
3	*C. glabrata*	1	1.8
4	*C. krusei*	1	1.8
5	*C. parapsilosis*	2	3.6
6	*C. guilliermondii*	1	1.8
7	*Candida* spp.	4	7.3
Total		55	100.0

PCR – RFLP results were similar with results obtained from morphology. Among 55

isolated species, *C. albicans* accounted for the highest percentage (63.6%), followed by *C. tropicalis* (20%), *C. parapsilosis* (3.6%), and less common species such as *C. glabata, C. krusei* and *C. guilliermondii* (each 1.8%).

There were 4 samples (7.3%) that could not be identified by PCR-RFLP method.

- PCR results

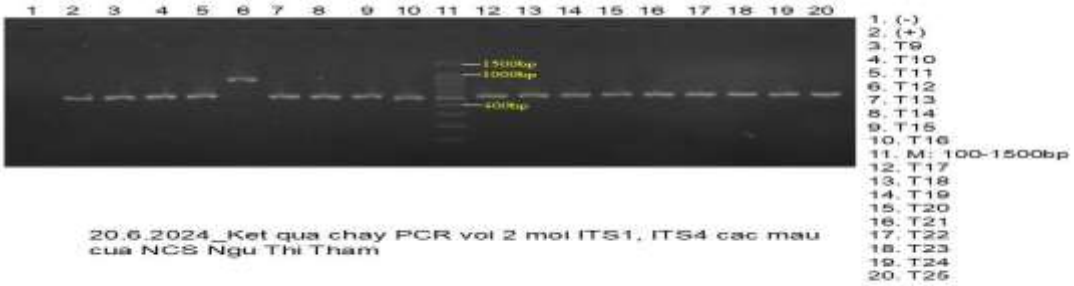

Figure 3.5. PCR products with primers ITS1 and ITS4

In the above Figure, well no.1 was the negative control; well no.2 was the positive control; wells no.3 to 10 corresponded to the samples from T9 to T16; well no.11 was the standard DNA ladder; wells no.12 to 20 corresponded to the samples from T17 to T25.

- PCR products with restriction enzyme

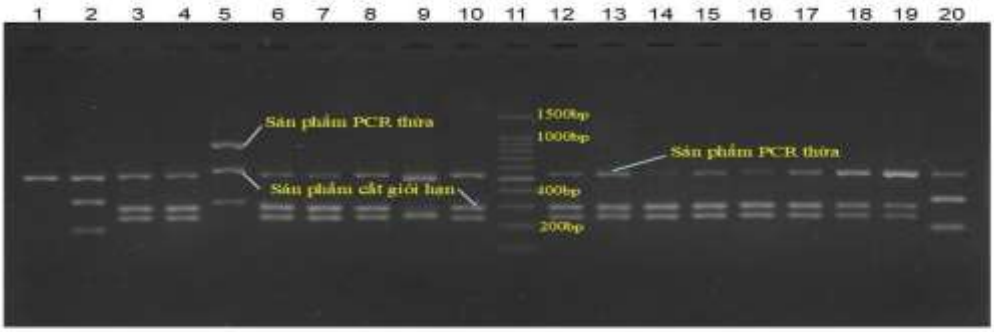

Figure 3.6. PCR products with MspI restriction enzyme

In the Figure above, well no.1 was the positive control (*C. parapsilosis*), wells no.2-10 corresponded to the samples T9 to T17; well no.11 was the standard DNA ladder (100-1500bp); wells no.12 to 20 corresponded to the samples from T18 to T25. Clear brighter bands appeared in gel electrophoresis, which was consistent with the genebank.

3.2.3. Results of sequence-based identification

Table 3.29. Results of sequence-based identification

No.	Species	Number	Percentage (%)
1	*C. albicans*	33	60.0
2	*C. tropicalis*	11	20.0
3	*C. glabrata*	1	1.8
4	*C. krusei*	1	1.8

5	*C. parapsilosis*	1	1.8
6	*C. dubliniensis*	2	3.6
7	*C. metapsilosis*	1	1.8
8	*C. mesorugosa*	2	3.6
9	*Kodamaea ohmeri*	2	3.6
10	*Meyerozyma caribbica*	1	1.8
Total		55	100.0

Results of sequence-based identification showed 10 fungal species, of which *C. albicans* accounted for the highest percentage of 60% (33/55), followed by *C. tropicalis* 20% (11/55). Less common species including *C. glabrata, C. krusei, C. parapsilosis, C. metapsilosis*, and *Meyerozyma caribbica* each accounted for a small proportion of 1.8% (1/55); *C. dubliniensis, C. mesorugosa* and *Kodamaea ohmeri* each made up 3.6% (2/55). Some rare pathogenic species such as *Kodamaea ohmeri* 3.6% (2/55) and *Meyerozyma caribbica* 1.8% (1/55) were also detected in the study.

3.2.4. Percentage of mono-infection and co-infection

Table 3.30. Percentage of mono-infection and co-infection

Infection	Species	Number	Percentage (%)
Mono-infection	*C. albicans*	25	45.5
	C. tropicalis	5	9.1
	C. mesorugosa	1	1.8
Co-infection	*C. albicans + C. tropicalis*	4	7.3
	C. albicans + C. glabrata	1	1.8
	C. tropicalis + C. dubliniensis	1	1.8
	C. krusei + C. dubliniensis	1	1.8
	C. parapsilosis + C. mesopsilosis	1	1.8
	C. albicans + Kodamaea ohmeri	1	1.8
	C. albicans + C. tropicalis + Meyerozyma caribbica	1	1.8
	C. albicans + C. mesorugosa + Kodamaea ohmeri	1	1.8
	Total	42	76.2

There were 31 patients with mono-infection (73.8%) and 11 patients with co-infection (26.2%). Among 11 co-infections, 9 (21.4%) patients got infected with two species, and 02 (4.8%) patients got infected with 3 species.

3.3. Oral candidiasis treatment outcomes and adverse effects

A total of 42 HIV/AIDS patients with oral Candidiasis underwent treatment according to the Ministry of Health's antifungal regimen combined with ARV therapy. Results were as follows:

3.3.1. Oral candidiasis treatment outcomes

Table 3.31. Results of re-examination after 4 weeks of treatment (n= 42)

Clinical examination results	**Number**	**Percentage (%)**
No more lesions	33	78.6
Lesions persisting	6	14.3
No follow-up examination	3	7.1
Total	42	100.0
Test results		
Negative	33	78.6
Positive	6	14.3
No follow-up test	3	7.1
Total	42	100

78.6% (33/42) of the patients saw no clinical lesions after 4 weeks of treatment, corresponding to the negative rate of 78,6%. 7.1% (3/42) of the patients did not return for follow-up examination.

Table 3.32. The cure rate of oral candidiasis after 4 weeks of treatment (n = 39)

Treatment outcomes after 4 weeks	Number	Percentage %
No more clinical lesions and negative test results	33	84.6
Persistent lesions and positive test results	6	15.4
Total	39	100.0

The patients with the presence of clinical symptoms and positive test results were considered not cured. After 4 weeks of treatment, 39/42 patients returned for a follow-up examination, and the cure rate was 84.6% (33/39).

Table 3.33. Viral load results before and after treatment

	Viral load results	**Number**	**Percentage (%)**	**p**
Before treatment (1)	Undetectable (≤ 50 copies/mL)	15	38.5	0.001
	Positive (> 50 copies/mL)	24	61.5	
	Total	39	100.0	
After treatment (2)	Undetectable (≤ 50 copies/mL)	24	61.5	
	Positive (> 50 copies/mL)	15	38.5	
	Total	39	100.0	

The percentage of patients with viral load (> 50 copies/mL) dropped from 61.5% (24/42) before treatment to 38.5% (15/42) after treatment, the difference was statistically significant, with $p < 0.01$.

3.3.2. Adverse effects

Table 3.36. Percentage of adverse effects

Adverse effects	Number	Percentage (%)
No	33	78,6
Yes	9	11,4
Total	42	100,0

The proportion of adverse effects was 11.4% (9/42).

Chapter 4:
DISCUSSION

4.1. Prevalence and associated factors of oral candidiasis in HIV/AIDS patients

Opportunistic infections only appear in HIV/AIDS patients when the body's immune system is severely impaired due to the patient's failure to comply with the ARV therapy. Common opportunistic infections include bacterial and viral pneumonia, tuberculosis, cryptococcal meningitis, sepsis, and even death. Opportunistic infections often appear when CD4+ T cell count drops below 200 cells/μL. Among opportunistic infections, oral candidiasis also accounts for a very high percentage. Oral lesion is one of the manifestations of human immunodeficiency virus (HIV) infection. During HIV infection, 95% of HIV-infected people have one or more lesions in the oral cavity [64].

In China, Sirun Meng et al. conducted a study on 12,612 HIV, of whom 8982 (71.2%) of the patients had one or more opportunistic infections, including 35.6% mono-infections and 64.4% co-infections. The overall in-hospital mortality rate was 9.0%. More than 60.6% of the patients had CD4+ T cell counts below 200 cells/μL. Pneumonia (39.8%), tuberculosis (35.3%), and candidiasis (28.8%) were the most common opportunistic infections among the patients. Co-infection of cryptococcal meningitis and co-infection of dermatitis were the most prevalent. The morphology of mucosal lesions in the patients with oral Candidiasis was very typical such as white patches on the oral mucosa, pain, bleeding, difficulty swallowing... [89], which was further confirmed by a study on 177 patients by Marco Tarozzi (2023). Among 177 patients enrolling in the study, 30 (16.9%) patients had manifestations of HIV-related diseases on the oral mucosa, mainly found in the patients above 35 years old, being treated with combination antiretroviral therapy (cART) and having CD4+ cell count below 500/μL. Early diagnosis and management of oral lesions in HIV patients should be part of the regular monitoring process [10].

Giới tính nam hay gặp hơn nữ gấp 2 lần; Ethnicity Kinh hay gặp hơn các Ethnicity khác gấp 7,4 lần; hay gặp ở người có trình độ Education THCS đến THPT với Percentage 76,2%; hay gặp người sống ở nông thôn với 53,4%; nghề nghiệp chủ yếu là công nhân và buôn bán tự do với 73,8%; Income chủ yếu dưới 10 tr với 95,2%; Percentage bệnh nhân béo phì là 9,5%.

The prevalence of oral candidiasis in HIV/AIDS patients in this study was 10.7% (42/393), which is similar to many studies in the world such as: 10.2% in Chad [9], 11% in Cameroon [85], 9.7% in Senegal [90], 12% in Tanzania [91]. The prevalence of oral candidiasis depends on many factors, including stage of HIV/AIDS, oral hygiene, the patient’s adherence to ARV therapy combined with nutrition, physical exercises, timely

examination and treatment of opportunistic infections, the quality of health care, and government policies in the management and taking care of HIV/AIDS patients. Among 42 patients infected, the mean age was 44.6 ± 8.8 years old with the most common age of 40 – 49; no patients under 20 years old and over 70 years old were found. Males outnumbered females by two to one. Kinh patients were 7.4 times higher than that of other ethnic groups. The disease was common in patients with secondary and high school education (76.2%), patients living in rural areas (53.4%), patients working for themselves and workers (73.8%), and patients with incomes under 10 million (95.2%). The proportion of patients with obesity was 9.5%.

4.1.3. Some associated factors of oral candidiasis in HIV/AIDS patients

Some factors related to oral candidiasis included tooth brushing frequency ≤1 time/day, wearing dentures, inpatient treatment, and HIV/AIDS stage.

The study results showed that patients with income ≤7 million/month had a higher risk of getting the disease, with OR > 1, $p < 0.05$. This finding is also consistent with the fact that most HIV/AIDS patients are poor, have low education, low income and mostly live in rural and mountainous areas with poor socio-economic conditions. When functional symptoms appear, the infected person often neglects, and they do not go to medical facilities for timely examination and treatment.

Currently, scientists have determined that oral Candidiasis, in addition to favorable factors in HIV/AIDS patients, is associated with lifestyle factors such as smoking, eating/drinking sweets regularly, drinking alcohol daily/alcoholism, and oral sex. In this study, smoking, eating/drinking sweets regularly, drinking alcohol daily/alcoholism, and oral sex had corresponding OR 95%CI and p value to oral candidiasis as follows: [4.162:2.150 -8.054, $p < 0.01$]; [11.533:3.353-39.674, $p < 0.01$]; [3.889:1.663-9.097, $p < 0.01$]; [6,673:1,440 – 30,913, $p < 0.05$]. This result suggests that oral candidiasis is an opportunistic infection in HIV/AIDS patients with pre-existing immunodeficiency, combined with poor oral hygiene knowledge and practices, and unhealthy sexual activity. Our findings are also completely consistent with domestic and foreign studies [3], [8], [9].

Factors like wearing dentures, tooth loss, bleeding gums, and toothbrushing frequency ≤1 time/day increased the risk of oral candidiasis, with corresponding OR 95%CI, p values as follows: [3.082:1.517- 6.262, $p < 0.01$]; [7.044:3.200- 15.506, $p < 0.01$], [40.596: 15.483-106.442, $p < 0.01$], [31.474: 13.831 – 71.621, $p < 0.01$. According to some studies, the possibility of developing oral candidiasis in patients wearing dentures was 6.9 times higher than that in older people without wearing dentures. Wearing dentures causes mechanical irritation, leading to pathological conditions like oral candidiasis. The prevalence of denture-related stomatitis was 11%-67% [60], [61], [62], [63].

Many scientists in the world and Vietnam have also reported an increase in oral Candidiasis in patients with underlying medical conditions or use of antibiotics. Our findings confirmed that the risk of getting the disease in patients with underlying medical conditions or use of antibiotics was higher than that in patients without underlying medical conditions or antibiotic use with the corresponding OR, 95%CI, and p value as follows: [7.575: 3.835-14.959, $p < 0.01$]; [31.391: 12.782- 77.093, $p < 0.01$].

HIV/AIDS is essentially an infectious disease that causes immunodeficiency. The patient's immune system gradually declines by stages 1, 2, 3, and 4 of HIV/AIDS. At each stage, TCD3 and TCD4 cell count drops accordingly, leading to gradually lost immune capacity of the body and the body no longer being resistant to pathogens, especially *Candida* spp. Treatment and compliance with the treatment regimen for oral Candidiasis play an important role. The findings of this study once again confirmed the above statement, i.e. Inpatients or non-adherents to treatment had a higher risk of oral Candidiasis than outpatients or adherents, with the corresponding OR, 95%CI, p values as follows: [41.212:17.496 – 97.074, $p < 0.01$]; [16.217:10.916 – 24.094, $p < 0.01$].

The percentage of inpatients with oral Candidiasis was 68.6%, 13.7 times higher than that of outpatients; the difference was statistically significant. This finding can be explained by the fact that the inpatients were mainly in stages II, III, IV of HIV/AIDS while the outpatients were mainly in stage I; the inpatients poorly adhered to ARV therepy while the outpatients mostly complied with ARV treatment.

Each factor related to oral Candidiasis in HIV/AIDS patients played a different role, therefore we employed multivariate correlation analysis to find out the most important factors causing oral Candidiasis in the study subjects. Results showed 4 most associated factors, including: toothbrushing frequency ≤1 time/day, wearing dentures, inpatient treatment, and HIV/AIDS stage with the corresponding OR, 95%CI, p as follows: [9.057: 1.205- 68.075, $p < 0.05$], [15.104: 2.840-80.339, $p < 0.01$], [11.970:3.855 - 37.145, $p < 0.01$], [8.363:2.217 - 31.552, $p < 0.01$]. In fact, many patients with HIV/AIDS stage III and IV were poor, lonely or homeless elderly people living in the mountainous areas of Nghe An. Many of them were involved in drug trafficking on the Vietnam-Laos border. A large proportion of patients had a duration of serving a prison sentences in Nghe An province.

In addition to oral hygiene factors, scientists in the world have demonstrated that COVID-19 infection aggravates oral Candidiasis in HIV/AIDS patients because COVID-19 can cause leukopenia, further reducing the host's ability to fight pathogens. SARS-CoV-2 virus can also directly attack various tissues on the oral mucosa, contributing to the severity of oral candidiasis in HIV/AIDS patients. This is demonstrated by the study of M Hasan Hapid (2023), which reported a case of a 56-year-old male patient with symptoms of mouth pain, discomfort due to white patches covering the surface of the tongue who had been consulted from the Covid-19 isolation area to the Department of Dentistry. The patient was diagnosed with HIV/AIDS and Covid-19 infection. He was instructed for oral hygiene, use of antifungal medicines such as nystatin and fluconazole oral suspension, chlorhexidine gluconate 0.2% mouthwash, and Vaseline [38], [39].

4.2. Clinical and laboratory characteristics of oral candidiasis in HIV/AIDS patients

In a total of 42 HIV/AIDS patients with oral Candidiasis, 76.2% (32/42) had functional symptoms, and 42.9% (18/42) had a fever.

Among 32 patients with functional symptoms, the most common symptoms were dry mouth, loss of appetite (84.4%), followed by decreased or loss of taste (81.9%) and bitter taste in the mouth (43.8%), in addition to some other less common symptoms such as burning pain in the mouth, burning pain when opening the mouth, difficulty swallowing, and painful

swallowing. The oral cavity is the entrance to the body, regularly exposed to food, drink and air; when people have human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) they are at a higher risk of oral diseases. Our findings on functional symptoms are consistent with many studies in the world [29], [31], [33].

The percentage of patients with suspicious oral lesions diagnosed with oral Candidiasis was 93.3% (42/45). Most common lesions included pseudomembrane (61.9%), red mucosa (45.2%), and red gums (33.3%), and other less common lesions such as atrophy of the tongue papillae, cracked corners of the mouth, and mouth ulcers.

Lesions were mostly found on the tongue surface (57.1%). Other locations such as buccal mucosa, corners of the mouth, palatal area, mucosal area, and the pharynx were less common (42.9% - 7.1%).

The most common clinical form was pseudomembranous (51%), followed by erythematous (26.5%), rhomboid glossitis (14.3%), and angular stomatitis - the least common form (8.2%).

According to the above results, our study finding is also consistent with many studies in the world showing that the most common clinical form of oral Candidiasis in HIV/AIDS patients was pseudomembranous form, followed by erythematous form [59], [86], [87]. Meanwhile, another study showed that the most common clinical form was atypical oral candidiasis, followed by rhomboid glossitis [9]. Although the prevalence of oral Candidiasis in our study is similar, the clinical form is different from the study by Joseph Fokam et al. (2023), which was 11%, including 28% pseudomembranous form and 72% erythematous form [85].

Clinical symptoms of oral Candidiasis cause pain, bleeding, difficulty swallowing and inconvenience in daily life for patients, and lesions caused by oral Candidiasis only appear when patients have poor oral hygiene and decreased immunity, which is confirmed by Yessy Novianti (2023). He described a series of 5 cases and found white patches in the mouth and pain when swallowing; 3 patients had their lymphocyte count (TLC) <1,170 cells/mm3; 02 patients stopped ARV therapy with CD4 count < 40 cells/mm3. The patients' simplified oral hygiene index (OHI-S) was moderate to poor [21].

Joseph Fokam (2023) studied the characteristics of oral Candidiasis according to antiretroviral treatment status in 18 HIV-infected patients at two health facilities in Yaoundé Cameroon. Results showed 13 cases of erythematous form and 5 cases of pseudomembranous form; 77.8% (14/18) and 22.2% (4/18) of cases were identified among participants with CD4<200 cells/mm3 and CD4>200 cells/mm3, respectively ($p<0.0001$). In the light of viral load, the occurrence of oral Candidiasis was largely observed among subjects with VL≥1000 copies/ml, 83.3% (15/18), against 16.7% (3/18), with VL<1000 copies/ml, irrespective of the Candidiasis form ($p<0.0001$). He recommended that in people living with HIV, erythematous and pseudomembranous Candidiasis were commonly found in the absence of ART, driven by immunodeficiency and active viral replication. In spite of the protective role of ART, people living with HIV experiencing immuno-virological failure should be referred for management of oral Candidiasis.

In Vietnam, our study finding is similar to the study by Le Huu Doanh and Ha Minh

Tuan in that the most common clinical form is pseudomembrane (82.6%), but this study was conducted on all patients with oral Candidiasis, including HIV/AIDS [67].

Currently, many scientists around the world believe that *Candida albicans* infection in HIV patients promotes intestinal dysbiosis and systemic inflammation. HIV-infected people, including those on antiretroviral therapy, are characterized by CD4 + T cell depletion and intestinal dysbiosis, with frequent *C. albicans* invasion, causing a high prevalence. Intestinal barrier damage and high levels of bacterial translocation are also quite common in this group of subjects [11].

The results of liver enzyme tests showed that the average value of GOT/GPT was 52.5/39.2 U/L with a corresponding standard deviation of 91.7/32.3. There were 18/42 (42.9%) and 16/42 (38.1%) patients with elavated liver enzymes.

This elavation of liver enzymes has two main causes: patients with liver diseases such as hepatitis B/C, cirrhosis or taking ARV drugs or other treatment drugs. The average creatinine was 93.7 mmol/l with a standard deviation of 37.5; 9/42 (21.4%) of the patients had increased blood creatinine. This condition is due to concomitant renal dysfunction or taking ARV drugs or other treatment drugs. Viral load results showed that the percentage of patients with group 2 viral load (>20 cps/ml) was the highest, accounting for 64.3% (27/42), followed by group 1 viral load (≤20 cps/ml) at 35.7% (15/42). Viral load is the amount of HIV virus measured in the patient's blood (unit: copy/ml). If in the past, studies and guidelines on HIV/AIDS diagnosis and treatment used T-CD4 index, people today use viral load to assess the immune status before and during ARV treatment, and to monitor the response or failure of ARV treatment. The reason why viral load is used today is because this index shows that the amount of HIV virus in the blood will appear earlier than the decrease in the T-CD4 count. The viral load ≤ 20cps/ml is considered to be undetectable.

4.3. Species composition of *Candida* spp.

By morphological and molecular identification, we detected 10 fungal species from 55 isolates, including *C. albicans* (60%), *C. tropicalis* (20%), and other less common species such as *C. dubliniensis, C. glabrata, C. krusei, C. parapsilosis, C. metapsilosis, C. mesorugosa* ranging from 1.8% - 3.6%. The predominance of *C. albicans* may be related to its ability of yeast-to-hyphae transition, formation of hydrolytic enzymes, biofilms and adhesion necessary for pathogenicity. The transition to non-*C.albicans* in HIV-infected people may be due to significant immunosuppression that promotes the growth of non-*C. albicans* [99], [100], [101].

Our study results are consistent with the previous study conducted in Ethiopia [102] and lower than those conducted in Cameroon by Miguel et al. [103], in South Africa by Owotade and Patel [104], and in Ghana by Kwamin et al. [93]. However, Enwuru [105] and Anbesa et al. [106] reported a lower prevalence of *C. albicans* compared to our study. Additionally, Agwu et al. [97], Taverne-Ghadwal et al. [94], and Berberi et al. [107] reported a higher prevalence of *C. albicans* and lower non-*C. albicans* isolates in southwestern Uganda, Chad, and Lebanon, expressing a growing trend in oropharyngeal Candida toward non-*C. albicans*. The discrepancies in the distribution of Candida species may be due to differences in the study population in terms of geographical location, demographics, clinical

characteristics, immune status, use of ARV therapy and antifungal medicines [96]. With gene sequencing, we detected some very rare pathogenic species in Vietnam such as *Kodamaea ohmeri* (3.6%) and *Meyerozyma caribbica* (1.8%). To confirm the pathogenic role of these species, a further and broader study is neded. Of 42 HIV/AIDS patients with oral Candidiasis, 31 (56.4%) patients were infected with a single species, and 11 (19.8%) patients got infected with mixed infections, mainly infected with two species, and 2 patients infected with three species.

Hamid Morovati (2023) employed molecular tools for 169 HIV-infected patients with culture and polymerase chain reaction-restriction fragment length polymorphism (RFLP-PCR). Disk diffusion was used to determine the sensitivity of isolated yeasts to common antifungal medicines according to CLSI M44-A2 procedure. Results showed 81 participants (47.92%) positive for OC and *Candida albicans* which is the most common yeast (53.98%). The median age of patients was 36 years old (IQR=10.5; 17-59). The patients treated with antifungal medicines had a 97.3% reduced risk of OC (OR: 0.027; 95% CI: 0.008-0.091; p-value: 0.000). Antifungal treatment reduced the risk of OC by 97.3% (OR=0.027; 95%CI=0.008-0.091; p=0.000), and antiviral treatment reduced the risk of OC by 4.42 times (OR=4.423; 95%CI=1.697-11.528; p = 0.002). The percentage of resistance to fluconazole, ketoconazole, itraconazole, amphotericin B and nystatin was 15.93%, 8.85%, 7.96%, 5.31% and 4.42%, respectively [110].

4.4. Treatment outcomes and adverse effects

The selection of antifungal agents should ensure the followings: its ability to penetrate the fungal cell wall; non-toxicity or less toxicity to users; high effectiveness; and reasonable price. There are currently many studies on the effectiveness of antifungal agents in the world such as Ekwealor (2023), which employed the Kirby-Bauer disk diffusion susceptibility test for fluconazole, clotrimazole, ketoconazole and nystatin. Results showed that 98 (65.3%) of the HIV-infected participants were positive for oral candidiasis, with 4 Candida species isolated: Candida albicans (62.2%), Candida glabrata (18.4%), Candida tropicalis (12.2%) and Candida krusei (7.1%). Fifty-nine (60.2%) of the 98 participants had a CD4+ cell count below 200 cells/µL, 33 (33.7%) had a CD4+ cell count between 200 and 399 cells/µL, and 6 (6.1%) had a count in the range of 400 and 499 cells/µL (p=0.001). Candida infection was not significantly different between females (67.0%, 65/97) and males (62.3%, 33/53) (p=0.6598), but the prevalence was significantly higher ($p<0.05$) in participants age group 21-30 years (80.7%, 42/52), divorced (100%, 1/1) and married (75%, 45/60), those with primary school level education (73.7%, 42/57), civil servants (85.7%, 18/21), and those who performed mouth hygiene once daily (71.9%, 69/96). Nystatin (77.6%, 76/98) showed the highest while fluconazole and ketoconazole (68.4%, 62/98) showed the lowest in vitro antifungal activity. He concluded that Oral Candidiasis is prevalent among HIV-infected patients in the study population, with evidence of in vitro resistance of the Candida isolates to available antifungal drugs. Proper diagnosis, susceptibility testing and treatment of infection will be helpful in managing oral Candidiasis infection among HIV infected patients [111].

With the seletion criteria for antifungals, fluconazole 150 mg was suitable for the actual situation in Nghe An.

The cure rate in our study was 84.6% (33/39). This result is similar to previous studies conducted to evaluate the clinical and mycological efficacy of fluconazole 150 mg in the treatment of oral Candidiasis in HIV/AIDS patients, showing an efficacy of 87% – 100% [112], [113], [114], but these studies had a treatment duration of 14 days compared to 7 days as in our study.

The undetectable viral load after treatment (viral load ≤ 20 cps/ml) was 61.5% (24/39), showing the effectiveness of combining early ARV therapy and antifungal treatment in boosting the immune system.

The proportion of adverse effects in the study was 11.4% (9/42), much higher than that in the study by Omar Jm Hamza et al. [109]. *C. albicans* was the most common in patients with treatment failure, which maybe resulted from the fact that *C. albicans* was the most common species in the study (60%), therefore the probability of treatment failure was also proportional to this rate, or it may be due to the increasing resistance of *C. albicans* resulting from the widespread use of fluconazole 150mg. For better patient management and improved treatment outcomes, it is necessary to combine antiviral drugs according to the ARV treatment regimen of the Ministry of Health.

CONCLUSION

1. Prevalence, associated factors, and clinical and laboratory characteristics of oral Candidiasis in HIV/AIDS patients

Among 393 HIV/AIDS patients enrolled into the study, 42 patients got infected with oral Candidiasis, accounting for 10.7% (42/393). Some factors related to oral Candidiasis included toothbrushing frequency, wearing dentures, HIV/AIDS inpatient treatment, HIV/AIDS stage, ARV therapy and adherence to ARV therapy. 76.2% (32/42) of the patients had functional symptoms and 42.9% (18/42) of the patients had a fever. Most common symptoms were dry mouth, loss of appetite (84.4%), decreased or loss of taste (81.3%) and a bitter taste in the mouth (43.8%), in addition to some other less common symptoms such as burning pain in the mouth, burning pain when opening the mouth, difficulty swallowing, and painful swallowing. The percentage of patients with suspicious oral lesions diagnosed with oral Candidiasis was 93.3% (42/45). Most common lesions included pseudomembrane (61.9%), red mucosa (45.2%), and red gums (33.3%), and other less common lesions such as atrophy of the tongue papillae, cracked corners of the mouth, and mouth ulcers. Lesions were mainly found on the surface of the tongue (57.1%), gums (54.8%), and the upper jaw (1.5 times higher than in the lower jaw). Other lesion sites such as the buccal mucosa, corners of the mouth, the palatal area, the mucosal area, and the pharynx were less common (42.9% - 7.1%).

The most common clinical forms were pseudomembranous (51%), erythematous (26.5%), fusiform glossitis (14.3%), and angular stomatitis (8.2%). Leukoplakia, black hairy tongue, and Candida-associated cheilitis were not found in the study.

With regard to laboratory characteristics: 42.9% (18/42), 38.1% (16/42) of the patients had elevated liver enzymes with the corresponding SGOT and SGPT. 21.4% of the patients had increased blood creatinine. Viral load results showed that the patients with viral load over

1000 copies/ml made up the highest rate of 42.9% (18/42), followed by those with viral load ≤ 20 copies/ml (35.7%) and those with viral load in the range of 20 to < 1000 copies/ml (24.1%). The viral load over 1000 copies/ml was mainly found in HIV/AIDS outpatients who were on the ARV therapy and adhered to the ARV therapy.

2. Species composition of *Candida* spp.

Results of morphological and molecular identification showed 10 fungal species, of which *C. albicans* accounted for the highest percentage of 60% (33/55), followed by *C. tropicalis* 20% (11/55). Less common species including *C. glabrata, C. krusei, C. parapsilosis, C. metapsilosis*, and *Meyerozyma caribbica* each accounted for a small proportion of 1.8% (1/55); *C. dubliniensis, C. mesorugosa* and *Kodamaea ohmeri* each made up 3.6% (2/55). Some rare pathogenic species such as *Kodamaea ohmeri* 3.6% (2/55) and *Meyerozyma caribbica* 1.8% (1/55) were also detected in the study.

3. Treatment outcomes and adverse effects

Among 42 patients enrolled for treatment, 39 patients returned for follow-up examinations, and the cure rate was 84.6% (33/39). The undetectable viral load (≤20 copies/mL) after treatment was 61.5% (24/39), 1.6 times higher than that before treatment.

Treatment failure was mainly found in male patients at 83.3% (5/42). *Candida albicans* was present in 100.0% (6/6) of the uncured cases. The proportion of adverse effects was 11.4% (9/42), mainly manifesting in the digestive tract, of which nausea accounted for the highest rate of 16.7%, followed by diarrhea, abdominal pain, and flatulence at 9.5%, 4.8%, and 4.8%, respectively.

RECOMMENDATIONS

For patients: In addition to regular check-ups and adherence to the ARV therapy, patients need regular screenings to prevent opportunistic infections, especially regular dental check-ups for denture wearers or when there are signs of inflammation. Tooth brushing should be at least twice a day.

For healthcare workers: Oral Candidiasis remains a strong indicator of HIV/AIDS and ARV treatment failure. Oral Candidiasis is also common in denture wearers despite viral loads <20 cps/ml.

Some factors associated with oral Candidiasis such as frequency of tooth brushing, denture wearing, HIV/AIDS inpatient treatment, HIV/AIDS stage, lack of the ARV therapy, and non-adherence to the ARV therapy should be noted.

For research: It is necessary for further research and monitoring the recurrence rate after 4 weeks of treatment with Fluconazole to have timely preventive measures. Also, a study on antifungal drug maps should be conducted for selection of an appropriate regimen at each health center/facility.

LIST OF PUBLICATIONS

1. Ngu Thi Tham, Vu Van Du, Que Anh Tram (2024), The prevalence and related factors for oral candidiasis in HIV/AIDS patients at the Center For Tropical Diseases, Nghe An General Friendship Hospital (2020-2022). *Journal of Community Medicine*, Volume 65(6), pp.153-163
2. Ngu Thi Tham, Vu Van Du, Que Anh Tram (2024), Determination of Candida species in HIV/AIDS patients with oral candidiasis at the Center For Tropical Diseases, Nghe An General Friendship Hospital (2020-2022). *Journal of Community Medicine*, Volume 65(5), pp.164-172
3. Ngu Thi Tham, Vu Van Du, Que Anh Tram (2024), Evaluation of treatment outcomes for oral candidiasis in HIV/AIDS patients at the Center For Tropical Diseases, Nghe An General Friendship Hospital (2022-2024). *Journal of Community Medicine*, Volume 65(5), pp.173-179