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Submission date: 29-May-2023 02:02PM (UTC+0700)
Submission ID: 2104385720
File name: Jurnal_Q1_coauthor_mycoses.pdf (627.62K)
Word count: 6527
Character count: 34732

Received: 3 July 2021 | Revised: 8 December 2021 | Accepted: 11 December 2021

DOI: 10.1111/myc.13414

mycoses | WILEY

ORIGINAL ARTICLE

Mucocutaneous mycoses in people living with human immunodeficiency virus in Indonesia

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Abstract

Background: To date, integrated care for people living with human immunodeficiency virus (PLHIV) has improved. However, although the management of mucocutaneous mycosis cases has improved, disease progression might be different in immunocompromised patients, which leads to variable clinical manifestations.

Objectives: To describe the characteristics of mucocutaneous mycosis cases in the PLHIV population and its associated factors in Indonesia.

Methods: This retrospective study was conducted from January 2014 to December 2018 in four academic hospitals. Data were acquired from medical records with the inclusion of mucocutaneous mycosis patients with concurrent HIV infection. Analysis with the chi-squared test was performed using Statistical Package for the Social Sciences (SPSS) version 20.0.

Results: A total of 1,796 cases of mucocutaneous mycoses were identified in 1782 PLHIV. The most common types of infection were candidiasis (63%), followed by dermatophytosis (35.1%), and malasseziosis (1.9%), which were significantly higher in PLHIV with CD4 level <200 cells/mm^3. The proportions of male gender (78.6% vs. 56.3%, $p < .001$), high level of education (48.0% vs. 64.1%, $p < .001$), office workers (73.8% vs. 64.1%, $p < .001$), combination of topical and systemic antifungal agents (59.1% vs. 48.5%, $p = .006$) and not receiving antiretroviral therapy (63.2% vs. 7.8%, $p < .001$) were significantly higher in PLHIV with a CD4 level <200 cells/mm^3.

Conclusion: In Indonesia, the most common fungal infection in PLHIV is candidiasis. This study also addressed the important matters regarding mucocutaneous mycoses in PLHIV. Education is an important measure to prevent the incidence of cutaneous mycoses in PLHIV, especially in high-risk groups.

KEYWORDS
AIDS, CD4, fungal infection, HIV, mucocutaneous mycosis

1 | INTRODUCTION

Mucocutaneous mycoses are skin infections caused by fungi, consisting of yeasts, dermatophytes and moulds. Fungi can cause infection of the skin, hair and nails with various manifestations depending on the aetiologic agent.[1] The most common causative agent of mucocutaneous mycosis is dermatophytes, followed by *Malassezia* and *Candida*.[2,3] These fungi are often identified as causal agents of

opportunistic infections in human. Several factors which can predispose human to mucocutaneous mycoses are immunosuppression, such as human immunodeficiency virus (HIV) infection, circulatory disorders, keratinisation disorders, genetic mutations etc[1,4] HIV infection, one of the most common immunodeficiency disorders, often presents with opportunistic infections.

Cutaneous fungal infections can be used for clinical indicators of the patient's immune status and they may also affect patient's general condition. Hence, early diagnosis and prompt treatment are necessary.[5] While dermatophytosis is regarded as the most common fungal infection of the skin worldwide, candidiasis accounts for the most common fungal infection in people living with HIV (PLHIV).[6] Unlike *Malassezia* spp. and *Candida* spp., dermatophytes are not part of the normal mucocutaneous microbiome. *Candida* and *Malassezia* exist as harmless organisms in normal individuals; however, they can cause infection under certain conditions. *Candida* is usually found in the digestive tract and *Malassezia* is in sebaceous-rich skin.[7] Dermatophytes are a type of pathogenic fungus transmitted directly from infected people and animals, from the soil or indirectly through fomites.[1] Based on the different nature of the diseases caused by these different fungal species, analysis of their risk factors in PLHIV is necessary.

Of 266,795,000 Indonesian citizens, a total of 640,000 HIV cases were reported from Indonesia in 2019, with only 17% of PLHIV receiving antiretroviral treatment (ART). Most PLHIV are diagnosed with HIV at a late stage and have CD4 cell counts of less than 350 cells/mm^3.[8] In addition, Indonesia, the most populous country in Southeast Asia, is known to have high prevalence of fungal infections. A study in a secondary hospital in Yogyakarta, Indonesia reported that fungal infection was the most common skin infection (42%), consisting of dermatophytosis, pityriasis versicolor and candidiasis.[9] As the prevalence of a disease and its related factors are important data needed to develop strategies for disease management and prevention, this multicentre retrospective study aimed to obtain the prevalence and factors associated with mucocutaneous mycoses among PLHIV in Indonesia.

2 | MATERIALS AND METHODS

2.1 | Design

This was a retrospective study conducted from January 2014 to December 2018 in Indonesia. Four academic hospitals contributed to this study, which were Dr Cipto Mangunkusumo National Central General Hospital (Jakarta), Prof. Dr Kandou General Hospital (Manado), Dr Wahidin Sudirohusodo General Hospital (Makassar) and Dr M. Djamil General Hospital (Padang).

2.2 | Ethics approval

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia.

2.3 | Participants

All patients were diagnosed with mucocutaneous mycosis and HIV infection through serologic tests who visited Dermatology Clinic from January 2014 to December 2018 were included in this study. The diagnosis of mucocutaneous mycoses was established through clinical examination, and diagnostic tests (direct microscopic examination and culture) were also recorded regardless of the results.

2.4 | Data collection

Data were acquired from medical records. The data included patient age, gender, occupation, level of education, distribution of lesion, affected site, results of direct microscopic examination with potassium hydroxide, result of culture, diagnosis, CD4 level, use of ART and the duration and type of antifungal treatment. For the level of education, we divided the data into illiterate, lower education and higher education. Lower education is defined as person who had graduated from primary school, junior high school or senior high school, while higher education is defined as a person who has graduated from university or college.

2.5 | Statistical analyses

The data were analysed with Statistical Package for the Social Sciences (SPSS) version 20.0. Categorical data were presented in frequency, and numerical data were presented in mean (standard deviation) if the distribution was normal and median (range) if the distribution was abnormal. Associations between sociodemographic and clinical factors with the type of fungi were analysed with the chi-squared test. Further analyses on the association between sociodemographic and clinical factors with CD4 level were also conducted with the chi-squared test. A p-value <.05 was considered significant.

3 | RESULTS

A total of 1796 cases of mucocutaneous mycoses was reported in 1782 PLHIV in four academic hospitals. The sociodemographic and clinical characteristics are shown in Table 1. Most of the subjects were male (74.6%) in the age group 31–40 years (36.2%), had a lower education (51.7%) and worked as office workers (69.2%). The lesions were mostly on the oral mucous membrane (59.5%). Among cases that were tested for direct microscopic examination with potassium hydroxide, 82% of subjects showed positive results. A total of 430 subjects were not examined with direct microscopic examination because some subjects were diagnosed at an HIV clinic in which the examination was not available. Hence, the diagnosis was established based on clinical examination. Most subjects received a topical antifungal agent (54.3%) with a duration of treatment less than 1 month (44.3%). In line with the

TABLE 1 Sociodemographic and clinical characteristics of people living with human immunodeficiency virus (PLHIV) with mucocutaneous mycoses in 2014-2018 (number of subjects = 1782)

Characteristics	Frequency (*n*, %)
Age	
0-10 years	78 (4.4%)
11-20 years	53 (3.0%)
21-30 years	571 (32.0%)
31-40 years	645 (36.2%)
41-50 years	322 (18.1%)
51-60 years	95 (5.3%)
61-70 years	18 (1.0%)
Gender	
Male	1329 (74.6%)
Female	453 (25.4%)
Education	
Illiterate	54 (3.0%)
Lower education	994 (51.7%)
Higher education	685 (38.4%)
No data	48 (2.7%)
Occupation	
Office workers	1233 (69.2%)
Wet work (hairdresser, sailor, farmer)	24 (1.3%)
Others (teacher, mechanician, musician, labourer, driver, business owner)	90 (5.1%)
Unemployed	427 (24.0%)
No data	8 (0.4%)
Affected site	
Skin	663 (37.2%)
Oral mucous membrane	1060 (59.5%)
Nail	56 (3.1%)
Hair	3 (0.2%)
Result of direct microscopy examination with potassium hydroxide*	
Positive	1109 (82%)
Negative	228 (16.9%)
Not performed	15 (1.1%)
No resources for direct microscopy examination with potassium hydroxide	430
Type of treatment	
Topical antifungal agent	968 (54.3%)
Systemic antifungal agent	27 (1.5%)
Combination of topical and systemic antifungal agents	785 (44.1%)
No data	2 (0.1%)
Antiretroviral treatment	
Yes	778 (43.6%)
No	1004 (56.4%)

*Percentage was calculated from clinic with resources for direct microscopy examination with potassium hydroxide.

Indonesian guidelines for HIV treatment in 2011,[10] more than half of the subjects did not receive ART (56.4%). Also, several subjects had comorbidities, such as tuberculosis. Hence, ART was delayed to prevent the occurrence of immune reconstitution inflammatory syndrome (IRIS). The median CD4 level was 0 cells/mm^3, ranging from 0 to 1426 cells/mm^3.

The most common infections identified in PLHIV were candidiasis (63%), followed by dermatophytosis (35.1%) and malassezi-osis (1.9%). The frequency of mucocutaneous mycosis is shown in Table 2. We only acquired data for oral candidiasis, since candidiasis at other mucosal sites, such as the genitals, is treated at sexually transmitted infection (STI) clinics. The number of cases was higher than the number of subjects because 14 subjects were infected with several infections. A total of 12 subjects were infected with tinea cruris and tinea corporis, while one subject was infected with tinea facialis and tinea cruris, and another subject was infected with tinea capitis and tinea corporis. Out of these 14 subjects, seven subjects had CD4 <200/mm^3, four subjects had CD4 ≥200/mm^3 and three subjects did not have CD4 data. All of these subjects had received ART.

The association between sociodemographic factors and type of fungi infecting PLHIV is shown in Table 3. The occurrence of mucocutaneous fungal infection was significantly associated with the level of education, occupation and ART. Based on the diagnosis, the duration of treatment ranged from 1 week to 24 weeks. Most of the subjects with skin involvement were treated for less than 1 month (59.1%), while the rest were treated for more than 1 month. For subjects with hair involvement, two subjects were treated for more than 1 month and one subject was treated for less than 1 month. For subjects with oral mucous membrane involvement, most of the subjects were treated for less than 1 month (59.3%). As for subjects with nail manifestations, most of them were treated for more than 1 month (58.9%).

Subjects with dermatophytosis had a median CD4 level of 28 cells/mm^3, ranging from 0 to 1426 cells/mm^3. Subjects with candidiasis had a median CD4 level of 0 cells/mm^3, ranging from 0 to 535 cells/mm^3. Subjects with malasseziosis had a median CD4 level of 0 cells/mm^3, ranging from 0 to 947 cells/mm^3. Among 1346 subjects whose CD4 levels were available, analysis of the association between sociodemographic and clinical factors with CD4 level was conducted, with the results shown in Table 4. The proportions of male gender (78.6% vs. 56.3%, $p < .001$), high level of education (48.0% 64.1%, $p < .001$), office workers (73.8% vs. 64.1%, $p < .001$), combination of topical and systemic antifungal agents (59.1% vs. 48.5%, $p = .006$) and not receiving antiretroviral therapy (63.2% vs. 7.8%, $p < .001$) were significantly higher in PLHIV with a CD4 level <200 cells/mm^3.

4 | DISCUSSION

This study found that the 31–40- and 21–30-year-old males were the most common group of PLHIV with mucocutaneous mycoses

TABLE 2 Frequency of mucocutaneous mycoses in people living with human immunodeficiency virus (PLHIV) in 2014-2018 (number of cases = 1796)

Type of infection	Frequency (*n*, %)
Candidiasis	**1132 (63.0%)**
Oral candidiasis	1078 (95.2%)
Cutaneous candidiasis	14 (1.2%)
Onychomycosis	40 (3.5%)
Dermatophytosis	**630 (35.1%)**
Tinea corporis	439 (69.7%)
Tinea cruris	125 (19.8%)
Tinea facialis	24 (3.8%)
Tinea pedis	18 (2.9%)
Tinea manum	17 (2.7%)
Tinea capitis	6 (1.0%)
Tinea unguium	1 (0.2%)
Malasseziosis	**34 (1.9%)**
Pityriasis versicolor	29 (85.3%)
Malassezia folliculitis	5 (14.7%)

despite no significant association with the type of fungal infection. However, males had a significantly higher proportion of CD4 counts less than 200 cells/mm^3. A similar result was reported by Otike-Odibi et al, who stated that the highest prevalence of dermatophytosis was observed in the second to the fourth decades in PLHIV, and males had a higher prevalence than females.[10] Additionally, Maheshwari et al reported that *Candida* infection in PLHIV occurred most in the age group of 21–45-year-old age and sexually active age, with a male-to-female ratio of 2.2:1.[11] Hence, these two studies support our findings that the age and gender of patients with mucocutaneous mycosis are in line with those of PLHIV, which are the most active age population; in addition, males have a higher risk of HIV due to frequent sexual activities and lack of condom use.[10–12]

More than half of the highly educated subjects were infected with dermatophytes; on the other hand, most subjects with lower education were infected with *Candida* and *Malassezia*. There was a significant association between educational level and the type of fungal infection. Contradictory to these results, Otike-Odibi et al found that dermatophytosis in HIV-infected patients is often encountered in people with a secondary educational level, and Bragine-Ferreira et al found only a small proportion of dermatophyte infection in PLHIV with a high educational level.[10,13] However, there is a record of similar results with this study, found by Krzyściak et al, who reported that a majority of the population with a lower education is infected with *Malassezia*.[14] Malassezia infections can be triggered by several factors, such as a hot and humid environment and overcrowded areas.[15] The number of *Malassezia* infections in individuals with lower education is thought to be related to their activities that can cause excessive sweating. On the contrary, *Candida* infection, which is mainly dominated by oral candidiasis, can cause eating disorders. Oral infections that are acute, chronic or systemic can affect an individual's functional ability to chew properly. This might be the reason for an individual to seek treatment, regardless of their educational level.[16] This difference might be explained by different classifications of education levels in each country.[14] However, in general, the level of education influences knowledge and awareness of diseases. The higher the level of education of an individual, the better their understanding and awareness of diseases.[17] As fungal infection causes disturbances and discomfort, it leads patients with a higher educational level to seek treatment. Similarly, a higher educational level was also associated with a CD4 level <200 cells/mm^3 because the patients with higher education tend to seek treatment at this stage of disease.

There was a significant association between the type of occupation and the type of fungal infections. The majority of subjects infected with dermatophytes, *Candida* and *Malassezia* were office workers. Office workers also had significantly higher proportions of a CD4 level <200 cells/mm^3. *Candida spp*. and *Malassezia spp*. are commensal fungi that can induce opportunistic infections in immunosuppressed patients. While occupation can possibly play a role in fungal infection, HIV infection is a more prominent risk factor in developing fungal infection due to the immunosuppression status of the host.[18] Office workers are more prone to stressful jobs and the psychosocial effects from the job. Hence, this could impair their immune system.[19] Stress is also associated with lower CD4 cell counts and more progressive HIV infection, which might predispose PLHIV to opportunistic infections.[20] In addition, office workers are likely to smoke. Indonesia is the biggest contributor of smoking worldwide, with prevalence varying from 9% to 81% in males and 0 to 41% in females between districts.[21] Smoking is a known risk factor for oral candidiasis in PLHIV with an incidence rate ratio of 1.9 (95% confidence interval: 1.1–3.8).[22] As for malasseziosis, office workers usually wear long sleeve shirts, which will increase moisture on the skin, particularly in areas with high number of eccrine glands. *Malassezia* is known to grow best at temperatures of 32–34°C, especially in moist environments.[2] Therefore, office workers are predisposed to mucocutaneous mycosis, especially when immunosuppressed.

Our study found that the most common mucocutaneous mycosis in PLHIV was candidiasis, and the proportion of candidiasis was significantly higher in PLHIV with CD4 cell counts less than 200 cells/mm^3. Candidiasis is a well-known opportunistic fungal infection in PLHIV, as *Candida* is part of the normal flora of human skin and mucosa. HIV infection makes humans a favourable host for *Candida* infection, which is shown by enhanced secreted aspartyl proteinases (Saps) production and faster hyphal growth.[23] Oropharyngeal candidiasis is one of the indicators of the progression of HIV infection. It is usually identified in patients with CD4 cell counts less than 200 cells/mm^3. Similarly, Vasudevan et al also reported that candidiasis is the most prevalent skin infection in PLHIV.[24] On the other hand, there are several contradicting results regarding the prevalence of dermatophytosis in PLHIV. While several studies have reported low prevalence, other studies reported a high prevalence of dermatophytosis in PLHIV.[24–26] Our study

TABLE 3 Association between sociodemographic and clinical characteristics with the type of infection in people living with human immunodeficiency virus infection in Indonesia (number of cases = 1796)

	Dermatophythosis	Candidiasis	Malasseziosis	*p*-value[a]
Age				
0–10 years	32 (5.2%)	45 (4.0%)	1 (2.9%)	.292
11–20 years	17 (2.8%)	36 (3.2%)	0 (0.0%)	
21–30 years	190 (30.8%)	368 (32.5%)	13 (38.2%)	
31–40 years	237 (38.5%)	392 (34.6%)	16 (47.1%)	
41–50 years	108 (17.5%)	212 (18.7%)	2 (5.9%)	
51–60 years	24 (3.9%)	69 (6.1%)	2 (5.9%)	
61–70 years	8 (1.3%)	10 (0.9%)	0 (0.0%)	
Gender				
Male	466 (75.6%)	834 (73.7%)	29 (85.3%)	.232
Female	150 (24.4%)	298 (26.3%)	5 (14.7%)	
Education				
Illiterate	23 (3.7%)	31 (2.7%)	0 (0.0%)	<.001*
Lower education	192 (31.2%)	787 (69.6%)	15 (44.1%)	
Higher education	380 (61.7%)	292 (25.8%)	13 (38.2%)	
Occupation				
Office workers	437 (70.9%)	776 (68.6%)	20 (58.8%)	<.001*
Wet work (hairdresser, sailor, farmer)	1 (0.2%)	22 (1.9%)	1 (2.9%)	
Others (teacher, mechanician, musician, labourer, driver, business owner)	14 (2.3%)	70 (6.2%)	6 (17.6%)	
Unemployed	162 (26.3%)	257 (22.7%)	7 (20.6%)	
Type of treatment				
Topical antifungal agent	60 (9.7%)	896 (79.2%)	12 (35.3%)	<.001*
Systemic antifungal agent	20 (3.2%)	7 (0.6%)	0 (0.0%)	
Combination of topical and systemic antifungal agents	535 (86.9%)	229 (20.2%)	21 (61.8%)	
Antiretroviral treatment				
Yes	323 (52.4%)	438 (38.7%)	17 (50.0%)	<.001*
No	293 (47.6%)	694 (61.3%)	17 (50.0%)	

*Statistically significant

[a]Chi-squared test

reported a high prevalence of candidiasis and dermatophytosis in Indonesia. The occurrence of candidiasis and dermatophytosis are highly influenced by cell-mediated immunity (CMI).[27,28] The occurrence of malasseziosis is not solely influenced by CMI but more complex mechanisms.[29] Since CMI is disrupted in HIV, both candidiasis and dermatophytosis are more prevalent, especially in subjects with lower CD4 cell counts.[30]Most of the subjects had clinical manifestations on the mucous membranes, with oral candidiasis as the most common diagnosis. Skin manifestations were exhibited by patients with dermatophytosis and malasseziosis. The results are supported by Goulart et al, who reported that more than 50% of PLHIV experience oral candidiasis.[31] Also, Anwar et al found that 71.25% of oral candidiasis cases were experienced by PLHIV.[32] The proportion of mucous membrane lesions is significantly higher in patients with a CD4 level <200 cells/mm^3. This is in line with the literature stating that oropharynx candidiasis is one of the very first

TABLE 4 Association between sociodemographic and clinical factors with CD4 level people living with human immunodeficiency virus infection in Indonesia (number of subjects = 1346)

	CD4 level		
	<200 cells/mm^3	≥200 cells/mm^3	*p*-value[a]
Age			
<20 years	81 (6.5%)	4 (3.9%)	.352
20–50 years	1096 (88.2%)	91 (88.3%)	
>50 years	66 (5.3%)	8 (7.8%)	
Gender			
Male	977 (78.6%)	58 (56.3%)	<.001*
Female	266 (21.4%)	45 (43.7%)	
Education			
Illiterate	40 (3.2%)	2 (1.9%)	<.001*
Lower education	580 (46.7%)	15 (14.6%)	
Higher education	597 (48.0%)	66 (64.1%)	
Occupation			
Office workers	917 (73.8%)	66 (64.1%)	<.001*
Wet work (hairdresser, sailor, farmer)	0 (0.0%)	4 (3.9%)	
Others (teacher, mechanician, musician, labourer, driver, business owner)	39 (3.1%)	8(7.8%)	
Unemployed	284 (22.9%)	25 (24.3%)	
Affected site			
Skin	593 (47.7%)	67 (65.0%)	<.001*
Oral mucous membrane	601 (48.4%)	103 (26.2%)	
Nail	46 (3.7%)	9 (8.7%)	
Hair	3 (0.2%)	0 (0.0%)	
Type of fungi			
Candida	658 (52.9%)	39 (37.9%)	.012*
Dermatophytes	555 (44.7%)	60 (58.3%)	
Malassezia	30 (2.4%)	4 (3.9%)	
Result of direct microscopy examination with potassium hydroxide			
Positive	1005 (80.9%)	101 (98.1%)	<.001*
Negative	228 (18.3%)	0 (0.0%)	
Type of treatment			
Topical antifungal agent	487 (39.2%)	47 (45.6%)	.006*
Systemic antifungal agent	19 (1.5%)	6 (5.8%)	
Combination of topical and systemic antifungal agents	735 (59.1%)	50 (48.5%)	
Antiretroviral treatment			
Yes	457 (46.8%)	95 (92.2%)	<.001*
No	786 (63.2%)	8 (7.8%)	

*Statistically significant

[a]Chi-squared test

clinical signs of AIDS, occurring in 50 to 95% PLHIV.[31] The oropharynx is the most common site of mucous candidiasis and can extend to the oesophagus and/or tracheobronchial tree in advanced stages of HIV infection. Vulvovaginal candidiasis is often found in HIV-infected females and can be identified as an early sign of immunodeficiency. On the other hand, intertrigo candidiasis, which is more common than mucous candidiasis, is uncommon in PLHIV.[33] In our study, vulvovaginal candidiasis was not reported since genital cases are treated at the STI clinic.

More than half of the cases were diagnosed with a positive direct microscopic examination with potassium hydroxide. The results are similar to those of Ali et al, who found an 86.84% incidence of fungal elements (hyphae and arthrospores) from # skin scrapings of PLHIV.[34] The diagnosis of superficial fungal infections can be established by direct examination through skin scraping. Using KOH, the fungal hyphae, spores and/or pseudohyphae can be observed.[30] This is a common practice, especially in developing countries with limited resources and funding. Our study did not report on culture results because culture is not always performed at our institutions as it is not covered by national health insurance.

Combinations of topical and systemic antifungal agents were the most used regimen for dermatophyte and *Malassezia* infections, while most *Candida* infections were treated by topical antifungal therapy. Most of the PLHIV with a CD4 level <200 cells/mm^3 received a combination of topical and systemic antifungal agents. Localised superficial fungal infections should be treated with topical antifungal therapy first then with systemic therapy in case of lack of efficacy,[30] although in extensive cases, oral medication is recommended from the onset. As HIV infection alters the immune system, inflammatory lesions might be suppressed, leading to atypical lesions. This can have an impact on the effectiveness of topical antifungal agents. Hence, a combination of topical and systemic antifungal agents should be considered in PLHIV, especially in the AIDS population in which the CD4 level is much lower.[35] In our settings, oral antifungal agents are administered for several cases, such as tinea capitis and nail involvement. In addition, oral antifungal agents are also administered to PLHIV for oral candidiasis with a CD4 level <200 cells/mm^3.

The duration of treatment in our study ranged from 1 week to 24 weeks. Most subjects were treated for less than 1 month, except in the cases of nail and hair involvement. Nail and hair involvement needs to be treated longer than skin or mucosa because it is more difficult for the drugs to reach the nails and hair.[36] This shows that the subjects responded positively to the treatments that were given. Oral candidiasis in PLHIV also responds readily to antifungal agents. The previously common azole-resistant *Candida* spp. has been reduced significantly since the commencement of ART.[37] Since 43.6% subjects in our study took ART, this helped improve the outcome of treatment with antifungal agents. In addition, the drugs used for oral candidiasis in Indonesia, which are topical nystatin or oral fluconazole, are known to have a high cure rate and short duration of treatment.[38] Elmets et al stated that the majority of mucocutaneous mycoses respond well to topical antifungal agents despite a low CD4

level. While mucocutaneous mycoses are easily treated, the main problem in the HIV/AIDS population is their recurrence.[39]

More than half of the subjects with dermatophyte infections had been treated with ART. In contrast, more than 50% of the subjects with *Candida* infections had not been with ART. Subjects with *Malassezia* infections showed an equal ratio of those who had and had not been on ART. This study also found that there was a significant association between ART and the type of fungal infection. The proportion of PLHIV not getting ART was significantly higher in the group with a CD4 level <200 cells/mm^3. ART administration will progressively increase the number of immune cells. If given to patients with a CD4 cell count above 100 cells/mm^3, dermatophyte infection will improve or even disappear without a specific fungal therapy.[40] The low number of PLHIV getting ART in our study was caused by the previous guidelines for HIV treatment in Indonesia. The guidelines only recommended administering ART to PLHIV with a CD4 level <200 cells/mm^3 or clinical stage 2, 3 and 4.[41] While the previous guideline in 2011 limited the administration of ART in PLHIV, the newer guideline in 2019 recommends providing ART to all PLHIV regardless of their CD4 level.[42] In addition, some subjects had comorbidities, such as tuberculosis, so ART was delayed in order to prevent IRIS.

One limitation of this study is that the data were acquired retrospectively from medical records, so some data might be lost or not documented since some cases, such as fungal infections of the genital area, were treated in STI clinics and not all diagnoses were established by direct microscopic examination or culture. This study also did not compare the characteristics of PLHIV to subjects without HIV. Future studies with larger samples and a prospective design are needed to establish the correlation between mucocutaneous mycoses and HIV infection, as well as the risk factors for developing mucocutaneous mycoses in PLHIV.

This study reports on the incidence of mucocutaneous mycoses in PLHIV. Candidiasis is the most common fungal infection in PLHIV. This study addressed important aspect of mucocutaneous mycoses in PLHIV, including sociodemographic factors and clinical characteristics. Improving education in each population group and understanding the comorbidities in HIV infection are important measures to prevent the incidence of mucocutaneous mycoses in PLHIV.

ACKNOWLEDGEMENT

None.

CONFLICT OF INTERESTS

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTION

Sandra Widaty: Conceptualization (lead); Data curation (lead); Formal analysis (lead); Funding acquisition (lead); Investigation (lead); Methodology (lead); Project administration (lead); Resources (lead); Software (lead); Supervision (lead); Validation (lead); Visualization (lead); Writing – original draft (lead); Writing – review & editing (lead). **Caroline Oktarina:** Conceptualization (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Writing – original draft (equal); Writing – review & editing (equal). **Pieter Levinus Suling:** Conceptualization (equal); Data curation (equal); Resources (equal); Supervision (equal); Validation (equal); Writing – review & editing (equal). **Nurdjannah Jane Niode:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Supervision (equal); Writing – review & editing (equal). **Eliza Miranda:** Conceptualization (equal); Data curation (equal); Formal analysis (equal); Investigation (equal); Methodology (equal); Resources (equal); Supervision (equal); Visualization (equal); Writing – review & editing (equal). **Anni Andriani:** Conceptualization (equal); Data curation (equal); Investigation (equal); Methodology (equal); Supervision (equal); Writing – review & editing (equal). **Safruddin Amin:** Conceptualization (equal); Data curation (equal); Investigation (equal); Resources (equal); Supervision (equal); Writing – review & editing (equal). **Satya Widya Yenny:** Conceptualization (equal); Data curation (equal); Investigation (equal); Supervision (equal); Writing – review & editing (equal). **Kusmarinah Bramono:** Conceptualization (equal); Formal analysis (equal); Methodology (equal); Supervision (equal); Validation (equal); Writing – review & editing (equal).

ETHICAL STATEMENT

This study was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia.

DATA AVAILABILITY STATEMENT

Data sharing not applicable – no new data generated

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How to cite this article: Widaty S, Oktarina C, Suling PL, et al. Mucocutaneous mycoses in people living with human immunodeficiency virus in Indonesia. *Mycoses*. 2021;00:1–8. doi:10.1111/myc.13414

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