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Research Article

The Role of Dermatologic Manifestations as a Predictive Value on CD4 Cell Count among HIV/AIDS Patients

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ABSTRACT

Introduction: Dermatologic manifestations can be seen in HIV/AIDS patients, which may worsen following the progression of HIV. This study aims to determine the role of dermatologic manifestations in predicting CD4 cell count among HIV/AIDS patients. Methods: This was a cross-sectional observational analytic study among HIV/AIDS patients who came to Voluntary Counselling Test (VCT) and Dermatology and Venereology (DV) outpatient clinic in Dr. Mohammad Hoesin General Hospital Palembang, South Sumatera, Indonesia, from December 2018 to March 2019. All HIV/AIDS patients' demographic data were recorded, eligible patients were screened for dermatologic manifestations and blood examination was done for CD4 cell count at the appointed laboratory. Data collected was to evaluate the type of dermatologic manifestation association with CD4 cell count and calculate Positive Predictive Value (PPV) using Chi-Square and IBM SPSS Statistics for Windows, Ver.26.

Results: A total of 70 out of 83 HIV/AIDS patients (84.3%) had at least one dermatologic manifestation. The most common dermatologic manifestation is infection (34%), of which 75% had CD4 cell count <200 cells/μL. The non-infection dermatologic manifestations are most commonly found in those with CD4 cell count 200–499 cells/μL (57.9%). Among patients with higher CD4 cell count ≥ 500 cells/μL, there were (53.8%) with no dermatologic manifestation. There was a significant association of low CD4 cell count <200 cells/μL with increasing number and type of dermatologic manifestations with $p \leq 0.001$. This study found HIV/AIDS patients with dermatologic manifestations had a 3.944 times higher chance of having a low CD4 cell count with a Prevalence Ratio (PR) of (95% CI 2.031–7.660, $p \leq 0.001$). Calculation of PPV at 84.3% prevalence with 90% specificity and sensitivity shows that infection and combination dermatologic manifestations had 98.4% of having CD4 cell count <200 cells/μL.

Conclusion: Dermatologic manifestations have a predictive value on CD4 cell count in HIV/AIDS patients.

Keywords: HIV/AIDS, CD4 Cell Count, Dermatologic Manifestations

Abbreviations: ADI: Aids Defining Illness; ARV: Anti-Retroviral Virus; AHR: Aryl Hydrocarbon Receptor; CDC: Centers for Disease Control and Prevention ; CD4: Cluster of Differentiation 4 ; CD8: Cluster of Differentiation 8; DV: Dermatology and Venereology; OHL: Oral Hairy Leukoplakia; HIV/AIDS: Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome; IL-1a: Interleukin–1a; IL-1b: Interleukin–1b; IL-4: Interleukin–4; IL-6: Interleukin–6; IL-12: Interleukin–12; IFN-γ: Interferon Gamma; NPV: Negative Predictive Value; PPE: Papular Pruritic Eruption

INTRODUCTION

Human Immunodeficiency Virus (HIV) is a viral infection that attacks the immune system, particularly those with CD4 receptors such as T helper cells, monocytes, macrophages, and dendritic cells. The CD4 cells are lymphocytes that respond to inflammation and infection as a defense mechanism. Deterioration of CD4 cell count indicates disease progression from HIV to Acquired Immunodeficiency Syndrome (AIDS). Low CD4 cell count reduces the defense mechanism immune

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response, allowing the host to be more susceptible to various opportunistic infections, non-infection dermatologic manifestations, and a combination of both [1].

According to the literature, the prevalence of dermatologic manifestations in patients with HIV/AIDS varied from 90%–95% [2-4]. A study by Reinhardt has shown a progressive deterioration in CD4 cell count will increase the prevalence of dermatology-related AIDS-Defining Illness (ADI), especially among HIV/AIDS patients with CD4 cell count <200 cells/μL ($p<0.005$) [1]. Several International or National studies classify dermatologic manifestations into three groups, namely infection, non-infection and combination (infection and non-infection) [5-7]. Dermatologic manifestations may be the first sign of HIV infections and thus may also predict the patients' immune status. Dermatologic manifestations commonly in HIV patients such as generalized zoster, Kaposi sarcoma, Papular Pruritic Eruption (PPE), extensive fungal infection, and recalcitrant seborrheic dermatitis may vary in appearance from healthy individuals, as they are usually more severe, atypical, widespread and recalcitrant hence making diagnosis and treatment often challenging [3,8].

Many studies to determine the association of Dermatologic manifestations in patients with HIV/AIDS were done in India, South Africa, Korea, China, Iran, Nigeria, and Mauritania. Studies in Indonesia have only been done in major cities e.g., Yogyakarta, Manado, Surabaya and Medan. This study was conducted in Palembang since this smaller city in Indonesia represents a more conservative population with low awareness, high stigmatization, and skepticism towards HIV/AIDS. This study aimed to determine the role of dermatologic manifestations as a predictive value on CD4 cell count among HIV/AIDS patients.

MATERIALS AND METHODS

This is a cross-sectional observational analytic study among patients with HIV/AIDS who came to Voluntary Counseling Test (VCT) and Dermatology and Venereology (DV) outpatient clinic in Dr. Mohammad Hoesin General Hospital from December 2018 to March 2019. This study was approved by the Ethics Committee/Review Board of Sriwijaya University prior to data collection. The inclusion criteria for this study are patients with age ≥ 18 who were tested positive for HIV, willing to cooperate for the study, with or without ARV medications. Patients with negative HIVtest, age<18, failing to return with CD4 result, and refusing to join the study will be excluded. All eligible HIV/AIDS patients who come to seek a consult with VCT or DV outpatient clinic will sign a written consent to be interviewed and be examined by the author to evaluate for the presence of any dermatologic manifestations.

Demographic data were collected according to diagnostic criteria for this study, including age, gender, sexual preferences, intercourse behavior, height, weight, and Body Mass Index (BMI) (Table 1). We also performed essential dermatologic examinations such as gram stain, dermoscopy, potassium hydroxide (KOH) or Tzank smear to aid diagnosis if needed. Dermatologic manifestations are recorded and classified into three categories, i.e., infection, non-infection, and combination [5-7]. Blood examination was done for CD4 cell count at the appointed laboratory in Dr. Mohammad Hoesin General Hospital, Palembang. Results of CD4 cell count are recorded and classified in accordance with Centers for Disease Control and Prevention (CDC) 2004 into CD4 cell count<200 cells/μL, 200–499 cells/μL, and ≥ 500 cells/μL [9]. The study's primary outcome was to determine the role of dermatologic manifestations in predicting CD4 cell count among HIV/AIDS patients. We seek to achieve this by determining the Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of dermatologic manifestations in relation to CD4 cell count <200 cells/μL and ≥ 200 cells/μL, respectively. The study's secondary outcome was to determine the prevalence and variety of dermatologic manifestations among HIV/AIDS patients.

RESULTS

A total of 83 patients were eligible and included in the study. Based on the results of this study, the mean age of the patient with HIV/AIDS was 34 years, with the most common age group 30–39 years of 53 people (64%). The majority of the research patients were male (82%), with a male to female ratio of 4,5:1. Transmission factor in the patient with HIV/AIDS in this study was all due to sexual contact with an unmarried partner, multi-partner and without protection. The most common sexual behavior reported was bisexual (52%). Most of the patients with HIV/AIDS were underweight BMI (76%), with CD4 cell count<200 cells/μL (54.2%). Our result showed that (78.3%) had 1–2 Dermatologic manifestations in each patient. Dermatologic manifestations occurrence as high as 84.3% classified into three groups: (1) infection (34%); (2) non-infection (23%); (3) combination (28%) (Table 2).

Table 1: Diagnostic criteria.

No.	Variable	Definition	Measurement	Predictors	Outcome	Scale
1	Gender	Gender	National identity card	National identity card	Male	Nominal
					Female	
2	Age	Eligible age ≥ 18 years old	National Identity Card	Age category according to Department of Health Republic of Indonesia	<18 years old	Ordinal
					20-29 years old	
					30-39 years old	
					40-49 years old	
					50-59 years old	
					>60 years old	
3	HIV/AIDS	Two out of three Rapid test results reactive will be diagnosed as HIV/AIDS.	Blood examination with three different brands Rapid Test for HIV as assigned according Ministry of Health of Indonesia.	Patient will be check at the laboratory in Dr.	Reactive	Nominal
					Non-reactive	

4	Body Mass Index (BMI)	BMI is a person's weight in kilograms divided by the square of height in meters.	Patient weight in kilograms divided by the square of height in meters.	According to CDC [9].	Underweight <18.5 kg/m^2 Normal 18.5- <25 kg/m^2 Overweight 25.0- <30 kg/m^2 Obesity ≥ 30 kg/m	Ordinal
5	CD4 cell count	CD4 cell count in blood to determine the current stage of HIV/AIDS.	Flow cytometry blood examination in laboratory assigned in Dr. Mohammad Hoesin General Hospital	According to CDC. [9]	CD4 cell count <200 cell/µL CD4 cell count 200- 499 cell/µL CD4 cell count ≥ 500-499 cell/µL	Ordinal
6	Dermatologic manifestations	Dermatologic manifestations group	History taking, physical examination, biopsy, stain and coloring, dermoscopy.	Previous study by Tzung et.al.[19] Rane et.al. [20] Malkud et.al. [21] Premanadham et.al.[11]	Infection Non-infection Combination	Nominal
7	Total number of dermatologic manifestations	Divided according to the type of dermatologic manifestations	History taking, physical examination, biopsy, stain and coloring, dermoscopy.	According to previous study by Premanadham et al.[11]	1-2 dermatologic manifestations 3-4 dermatologic manifestations >5 dermatologic manifestations	Ordinal
8	Transmission factor	Factor that determine HIV was transmitted to the patient.	History taking	According to CDC [9].	Sexual contact (heterosexual, homosexual, bisexual) Blood transfusion Tattoo Needle pricked	Nominal
9	Infection Dermatologic manifestations	All Dermatologic manifestations due to infection from bactery, fungal or viral	History taking, physical examination, biopsy, stain and coloring, dermoscopy	According to previous study by Chawhan et al.[15] Pudjiati et.al.[16]	Oropharyngeal Candidiasis dermatophytes (,tinea korporis et kruris), herpes zoster, herpes simplex, varicella, leprosy, impetigo, furunkulosis, abscess, folliculitis,etc.	Nominal
10	Non-infection Dermatologic manifestation	All Dermatologic manifestations due to allergic reaction or inflammation or autoimmune	History taking, physical examination, biopsy, stain and coloring, dermoscopy	According to previous study by Chawhan et al.[15] Pudjiati et.al.[16]	Seborrheic dermatitis, Papular Pruritic Eruption (PPE), prurigo nodularis, etc.	Nominal
11	Combination (infection and non-infection) Dermatologic manifestations	Having >1 disease in one patient with different pada 1 pasien, kasus infeksi dan non infeksi	History taking, physical examination, biopsy, stain and coloring, dermoscopy	According to previous study by Chawhan et al.[15] Pudjiati et.al.[16]	Oropharyngeal Candidiasis and seborrheic dermatitis; Oropharyngeal, Candidiasis and PPE; etc.	Nominal

Table 2: Characteristics of HIV/AIDS patients.

Characteristic	Total (n)	Percentage (%)
Age		
20–29 years	18	22
30–39 years	53	64
40–49 years	9	11
50–59 years	3	3

Gender		
Male	68	82
Female	15	18
Behavior		
Bisexual	43	52
Heterosexual	26	31
Homosexual	14	17
Body Mass Index (BMI)		
Underweight	63	76
Normal	12	14
Overweight	8	10
Obesity (≥ 30 kg/m^2)	0	0
CD4 cell count		
<200 cell/μL	45	54.2
200–499 cell/μL	24	28.9
≥ 500 cell/μL	14	16.9
Dermatologic manifestation		
Infection	28	34
Non–infection	19	23
Combination (Infection and Non-infection)	23	28
Number of dermatologic manifestations in 1 patient		
No manifestation	13	15.7
1–2 Manifestations	65	78.3
3–4 Manifestations	5	6
>5 Manifestations	0	0

The most common dermatologic manifestation in the infection group was oropharyngeal candidiasis (42.8%) followed by herpes zoster reactivation (14.3%) and dermatophytes (10.7%). Other dermatologic manifestation in the infection group were giant condyloma acuminatum (7.1%), scrofuloderma (3.6%), oral hairy leukoplakia (3.6%), herpes simplex (3.6%), molluscum contagiosum (3.6%), Lepromatous Leprosy (LL) (3.6%), rubella (3.6%), and secondary syphilis (3.6%) (Table 3). The most common dermatologic manifestation in the non-infection group was seborrheic dermatitis (47.3%), followed by xerosis (21%). Other non-infection manifestation were PPE (15.8%), eosinophilic folliculitis (5.3%), erythema multiforme (5.3%) and prurigo nodularis (5.3%) (Table 4). The most common dermatologic manifestation in the combination group was a combination of oropharyngeal Candidiasis with seborrheic dermatitis (34.8%), followed by a combination of oropharyngeal Candidiasis, seborrheic dermatitis and PPE (21.7%). Other combination dermatologic manifestations were oropharyngeal Candidiasis with PPE (13%), oropharyngeal Candidiasis with eosinophilic folliculitis (13%), seborrheic dermatitis with head lice (4.3%), pityrosporum folliculitis with seborrheic dermatitis (4.3%), oropharyngeal Candidiasis with drug reaction (4.3%), and dermatophytes with seborrheic dermatitis (4.3%) (Table 5).

Majority of HIV/AIDS patients with infection dermatologic manifestations (75%) had CD4 cell count<200 cells/μL and (25%) had CD4 cell count 200-499 cells/μL. All HIV/AIDS patients with combination dermatologic manifestations had CD4 cell count <200 cells/μL. While HIV/AIDS patients with non-infection dermatologic manifestations (57.9%) had CD4 cell count 200-499 cells/μL, only one patient (5.3%) had CD4 cell count <200 cells/μL, and others (36.8%) had CD4 cell count ≥ 500 cells/μL. There are 13 HIV/AIDS patients that present with no dermatologic manifestation; among them (46.2%) had CD4 cell count 200-499 cells/μL and (53.8%) had CD4 cell count ≥ 500 cells/μL. Statistical analysis using chi-square showed This study shows there was a significant association between dermatologic manifestations with CD4 cell count <200 cells/μL among HIV/AIDS patients ($p \leq 0.001$) (Table 6). The presence of significant association in this study had a prevalence ratio of 3.944 (95% CI 2.031–7.660, $p \leq 0.001$), which means HIV/AIDS patients having an infection or combination type of dermatologic manifestations had an increased risk of 3.944 times having low CD4 cell count <200 cell/μL (Table 7).

The number of dermatologic manifestations in one patient varies. Majority (78.5%) had 1–2 dermatologic manifestations, only (6%) had 3–4 dermatologic manifestations. All HIV/AIDS patients having more than one dermatologic manifestation had CD4 cell count<200 cells/μL. There was a significant association between the number of dermatologic manifestations with CD4 cell count <200 cells/μL among HIV/AIDS patients ($p \leq 0.001$) (Table 8).

Infection and combination dermatologic manifestations had 97.8% Positive Predictive Value (PPV) of having CD4 cell count <200 cells/μL. Non-infection or no dermatologic manifestation had 31.6% Negative Predictive Value (NPV) of having CD4 cell count ≥ 200 cells/μL (Table 9).

Another calculation of PPV and NPV based on this population at 84.3% prevalence with 90% specificity and sensitivity shows that infection and combination dermatologic manifestations had 98.4% PPV of having CD4 cell count <200 cells/μL. Non-infection or no dermatologic manifestation had 63.1% Negative Predictive Value (NPV) of having CD4 cell count ≥ 200 cells/μL (Table 10).

Table 3: Infection dermatologic manifestations among HIV/AIDS patients.

Infection dermatologic manifestations	Total (n)	Percentage (%)
Oropharyngeal Candidiasis	12	42.8
Herpes zoster reactivation	4	14.2
Dermatophytes	3	10.7
Giant condyloma acuminatum	2	7.1
Scrofuloderma	1	3.6
Oral hairy leukoplakia	1	3.6
Herpes simplex	1	3.6
Molluscum contagiosum	1	3.6
Lepromatous Leprosy (LL)	1	3.6
Rubella	1	3.6
Secondary Syphilis	1	3.6
Total	28	100

Table 4: Non-infection dermatologic manifestations among HIV/AIDS patients.

Non-infection dermatologic manifestations	Total (n)	Percentage (%)
Seborrheic dermatitis	9	47.3
Xerosis	4	21
Papular Pruritic Eruption (PPE)	3	15.8
Eosinophilic folliculitis	1	5.3
Erythema multiforme	1	5.3
Prurigo nodularis	1	5.3
Total	19	100

Table 5: Combination dermatologic manifestations among HIV/AIDS patients.

Combination dermatologic manifestations	Total (n)	Percentage (%)
Oropharyngeal Candidiasis+Seborrheic dermatitis	8	34.8
Oropharyngeal Candidiasis+Seborrheic dermatitis+PPE	5	21.7
Oropharyngeal Candidiasis+PPE	3	13
Oropharyngeal Candidiasis+eosinophilic folliculitis	3	13
Seborrheic dermatitis+Head lice (Pediculosis capitis)	1	4.3
Pityrosporum folliculitis+seborrheic dermatitis	1	4.3
Oropharyngeal Candidiasis+Drug reaction	1	4.3
Dermatophytes+Seborrheic dermatitis	1	4.3
Total	23	100

Table 6: Association of CD4 cell count with dermatologic manifestations among HIV/AIDS patients.

CD4 cell count (cell/µL)	Dermatologic manifestations					p-value
	Infectionc	Non-infection	Combination	None	Total	
	n (%)	n (%)	n (%)	n (%)	n (%)	
<200	21 (75)	1 (5.3)	23(100)	0 (0)	45 (54.2)	≤ 0.001
200-499	7 (25)	11 (57.9)	0 (0)	6 (46.2)	24 (28.9)	
≥ 500	0 (0)	7 (36.8)	0 (0)	7 (53.8)	14 (16.9)	
Total	28 (100)	19 (100)	23 (100)	13 (100)	83 (100.0)	

Table 7: Association of CD4 cell count with dermatologic manifestations among HIV/AIDS patients with Prevalence Ratio (PR).

CD4 cell count (cell/µL)	Dermatologic manifestations					p- value	PR (95% CI)
	Infection	Non-infection	Combination	None	Total		
	n (%)	n (%)	n (%)	n (%)	n (%)		
< 200	21 (75)	1 (3.1)	23 (100)	45 (54.2)	45 (54.2)	≤0.001	3.944 (2.031-7.660)
≥ 200	7 (25)	31 (96.9)	0 (0)	38 (45.7)	38 (45.7)		
Total	28(100)	32(100)	23(100)	83(100)	83 (100)		

Table 8: Association of CD4 cell count with number of dermatologic manifestations among HIV/AIDS patients.

	Number of dermatologic manifestations					
CD4 cell count (cell/µL)	None	1-2	3-4	>5	Total	p-value
13 (100)	n (%)	n (%)	n (%)	n (%)	n (%)	
<200	0	40	5	0	45 (54.2)	
200 - 499	6	18	0	0	24 (28.9)	≤ 0.001
≥ 500	7	7	0	0	14 (16.9)	
Total	13 (15.7)	65 (78.3)	5 (6)	0 (0)	83 (100.0)	

Table 9: Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

	Dermatologic manifestations				
CD4 cell count (cell/µL)	Infection and Combination	Non-infection and no manifestation	Total	Positive predictive value (PPV)	Negative predictive value (NPV)
	n	n	n		
<200	45	1	46	97.8%	31.6%
≥ 200	25	12	38		
Total	70	13	83		

Table 10: Positive Predictive Value (PPV) based on prevalence, 90% sensitivity and 90% specificity.

		Dermatologic manifestations				
CD4 cell count (cell/µ)	Disease prevalence in this study	Infection and Combination	Non-infection and no manifestation	Total	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
		n	n	n		
<200	84.3%	63	1	64	98.4%	63.2%
≥ 200		7	12	19		
Total		70	13	83		

DISCUSSION

The majority of the study populations were male, with a male to female ratio of 4.5:1. This ratio was twice higher in compared to other studies or local Government National Health Palembang 2018 [10]. Similar studies by Neeti, et al. also reported that the majority of the study population were male, with male to female ratio was 2:1, likely due to high number of sexual activities [11]. In this study 76% had underweight BMI (<18.5 kg/m^2). This is in concordance with a study by Hu, et al. [12] whom also reported 77.2% of HIV/AIDS patients had low BMI <18,5 kg/m^2. Hu, et al. [12] found inadequate food intake were common in HIV/AIDS patients and malnourished HIV patients were at a higher risk of developing opportunistic infections and AIDS-related illness [12].

Our study showed that a total of 70 out of 83 patients (84.3%) had dermatologic manifestation; among them (64%) had lower CD4 cell count <200 cells/µL. This is also in concordance with a study by Neeti, et al. [11]. on dermatologic manifestations in HIV [11]. Therefore, we seek to show that dermatologic manifestations can serve as a predictive value to indicate HIV progression and underlying immune status.

This study found that the most common dermatologic manifestation with CD4 cell count <200 cells/µL is the infection group. Oropharyngeal Candidiasis is the most common infectious case followed by herpes zoster reactivation. This finding was similar to other studies in the countries ranked highest for HIV/AIDS, e.g., South Africa, Nigeria and India. Chandrakala, et al. [13] reported oropharyngeal Candidiasis and dermatophytosis were the most common infection cases among HIV/AIDS patients [13]. Villar, et al. [14] study explained that more extensive distribution of candida infection up to oropharyngeal is due to the decrease in protein moiety annexin A1 to inhibit *Candida* Sp. [14] Epithelial mucosa in a healthy individual may inhibit fungal infection from its acidlabile moiety. However, an altered natural flora in HIV/AIDS patients heightened the risk of opportunistic fungal infections. Fidel, et al. [15] compared biopsied epithelial mucosa of HIV/AIDS patients with CD4 cell count <200 cells/µL with and without oropharyngeal Candidiasis. This study reported dysfunction of CD8 cells with the accumulation of CD8 cells on the epitheliallamina propria interface. The proteolytic capability in *Candida* Sp., causing lower expression of E-cadherin adhesion molecule in HIV/AIDS patients with oropharyngeal Candidiasis [15].

Herpes zoster reactivation is the second most common dermatologic manifestation found in this study. Ku, et al. [16] reported HIV/AIDS patients to have a 3-20 times higher risk of herpes zoster reactivation than non-HIV infected individuals [16]. All four of our patients were male with CD4 cell count <200 cells/µL, this is in concordance with Ku, et al. [16], who reported male with CD4 count <200 cells/µL were significant risk factors for herpes zoster in HIV-infected patients [16]. However, others have found herpes zoster to occur with a wide range of CD4 cell count Davarpanah, et al. [17] reported 15 cases (6.3%) with CD4 cell count 380–450 cells/µL [17]. The most commonly involved dermatome in our patients is cervical (75%). One of them had bilateral lesions on the cervical, and two other patients also had bilateral cervical lesions complicated with disseminated zoster. This is in concordance with Vora, et al.

[18], who had reported cervical dermatome was most commonly involved dermatome in patients of HIV [18]. Akimoto, et al. [19], in Japan explained that there are two possible mechanisms for a bilateral lesion of herpes zoster reactivation in immune compromised patients. The first virus may diffuse and spread from one ganglion to another ganglion or two different ganglia were re-infected simultaneously. He also postulated that the dermatome involved in herpes zoster reactivation followed the ganglion, which had the most virus genome load [19].

The non-infection dermatologic manifestations are most commonly found in those with CD4 cell count 200-499 cells/μL. Seborrheic dermatitis is the most common non-infection case followed by xerosis. This finding is in concordance with Pudjiati, et al. [20] who also reported the most common dermatologic manifestation with CD4 cell count 200–499 cells/μL is the non-infection group [20]. Zaib, et al. [21] reported that seborrheic dermatitis is a dermatological manifestation of HIV, often present early and worsen along with the individual immune status. A healthy individual may carry a 10% risk of having an undetected HIV infection [21]. Malassezia species form part of a normal cutaneous commensal flora of humans. In humans, they are associated with the sebum-rich areas of the body, including the trunk and the head region. Dessinioti, et al. [22] reported that there is an increased susceptibility of a normal Malassezia furfur transform into its pathogenic form among HIV/AIDS patients [22]. The pathogenic form of Malassezia will provide proteolytic enzymes (lipases, phospholipases) and indole intercellular signaling molecules through the Aryl Hydrocarbon Receptor (AhR) ligand that may release free fatty acid metabolites such as arachidonic acid, oleic acid, Malassezia, and indole-3-carbaldehyde. These metabolites may further disrupt the skin barrier and induce proinflammatory cytokines to release IL-1a, IL-1b, IL-12, IL-4, IFN-γ and TNF-a. which explain a more severe and recalcitrant seborrheic dermatitis among HIV/AIDS patients [22].

All patients in the combination dermatologic manifestation group had CD4 cell count<200 cells/μL. The most common combination dermatologic manifestation is oropharyngeal Candidiasis with seborrheic dermatitis. This finding is in concordance with Premanadham, et al. [23] who reported that combination infection also had CD4 cell count <200 cells/μL, although they did not report the type of dermatologic manifestation [23]. Our result is slightly different from Dewi, et al. [24] who reported the most common combination dermatologic manifestation is oropharyngeal Candidiasis with PPE [24]. Severe, extensive, recurrent and treatment-resistant seborrheic dermatitis with other opportunistic infection is not only a dermatological marker of disease but an indicator of disease progression. In this study, a higher CD4 cell count ≥ 500 cells/μL is associated with either a non-infection dermatologic manifestation or no dermatologic manifestation. According to Boushab, et al. a decrease in CD4 cell count induced lower immune response hence harboring skin at a condition prone to infection environment especially opportunistic infection with moderate to severe clinical manifestation [25,26]. Dermatologic manifestations may occur in any stage, early or late, with increased risk along with disease progression of the patient with HIV/AIDS regardless of ARV. There is a dysregulation of immune system homeostasis, which explains higher CD4 cell count associated with non-infection or no dermatologic manifestations [3,16].

Results of this study showed a statistically significant association of CD4 cell count with dermatologic manifestations. Lower CD4 cell count <200 cells/μL present with infection and combination dermatologic manifestation, CD4 cell count 200–499 cells/μL present with noninfection dermatologic manifestation, and CD4 cell count ≥ 500 present with non-infection or no dermatologic manifestation. This finding is in concordance with previous studies by Pudjiati, et al. reported that lower CD4 cell count increased the risk of occurrence of Dermatologic manifestation [20,25,27,28].

This study found HIV/AIDS patients with lower CD4 cell count <200 cell/μL had an increased risk by 3.944 times of having dermatologic manifestations with a Prevalence Ratio (PR) of 3.944 (95% CI 2.032-7.660, $p \leq 0.001$). This result was slightly higher than the previous study by Pudjiati et al. [20] with an increased risk by 3.8 times [20]. There was still a lack of conclusive evidence linking HIV-1 associated gene products to the pathogenesis of primary dermatological disorders among HIV/AIDS patients. However, the reduction in the number of antigen-presenting and CD4 T cells causes the skin becomes vulnerable to numerous opportunistic infectious agents and neoplastic disorders [21,29].

This study's Positive Predictive Value (PPV) refers to the likelihood of patients with infection and combination dermatologic manifestations having CD4 cell count <200 cells/μL. Based on the population in this study which includes the prevalence 84.3% at specificity and sensitivity of 90%, infection and combination dermatologic manifestations had 98.4% PPV of having CD4 cell count <200 cells/μL. Our result is higher than the previous study by Levy, et al. [30] who reported HIV related oral lesions had 75% PPV of finding a CD4 cell count <200 cells/μL [30]. Negative Predictive Value (NPV) in this study refers to the likelihood of patients with non-infection or no dermatologic manifestation having CD4 cell count ≥ 200 cells/μL in this study, non-infection or no dermatologic manifestation had 31.6% NPV of having CD4 cell count ≥ 200 cells/μL. These results show that dermatologic manifestations may aid in the assessment of immune status among HIV/AIDS.

The limitation of this study was the small number of patients who come for medication to VCT or DV outpatient clinic in General Hospital Dr. Mohammad Hoesin Palembang. The diagnosis was made majority based on clinical diagnosis with simple dermatologic examinations. Treatment of Anti-Retroviral Virus (ARV) among HIV/AIDS patients was not homogenous. The author is aware that CD4 cell count is not the only variable to determine the sign of deterioration among HIV/AIDS patients. A more extensive population study along with viral load examination may be done for further studies.

CONCLUSION

Dermatologic manifestations play an important role as a valuable indicator for disease diagnosis or progression among HIV/AIDS patients. Especially those with atypical, recurrent, wide distribution, recalcitrant to treatment, unusual predilection and having one or more dermatologic manifestations. In limited health facilities with difficulty of CD4 count measurements, skin examination can be an important tool for assessing the immune

status of HIV/AIDS patients. Dermatologic manifestations have a predictive value on CD4 cell count in HIV/AIDS patients. The author hopes that this study may benefit readers and may act as a cornerstone for further studies in the future with a larger sample population.

CONFLICT OF INTEREST

This study has no conflict of interest.

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