ORIGINAL PAPER

Factors affecting hematological abnormality in HIV-infected patients at Dr. Wahidin Sudirohusodo Hospital Makassar, Indonesia

I. Nyoman Yogi Wiraguna[1,2], Andi Fachruddin Benyamin[1,2], Risna Halim[1,2], Syakib Bakri[1,2], Sahyuddin Saleh[1,2], Hasyim Kasim[1,2], Andi Alfian Zainuddin[3]

[1]Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia
[2]Dr. Wahidin Sudirohusodo Hospital, Makassar, Indonesia
[3]Public Health and Community Medicine Department, Hasanuddin University, Makassar, Indonesia

Abstract

Introduction: Human immunodeficiency virus (HIV) is characterized by a progressive damage of immune system, resulting in a number of opportunistic infections and hematological abnormalities, and become more severe in late stages. Hematological abnormalities are common manifestations, with factors including CD4+ count, opportunistic infection, and HIV viral load. The aim of this study was to investigate the correlation between CD4+ count, opportunistic infection, and HIV viral load with hematological abnormality in HIV patients.

Material and methods: An observational study was conducted at tertiary institution, Dr. Wahidin Sudirohusodo Hospital, Makassar, from November 2021 to February 2022. Secondary data from medical records of HIV-infected patients were used. Chi-square test and independent *t*-test were employed to determine the correlation between CD4+ count, opportunistic infection, and HIV viral load with hematological abnormality.

Results: Among 83 HIV subjects, anemia was present in 47% of the cases. Leucopenia, lymphopenia, and thrombocytopenia were observed in 10.8%, 28.9%, and 9.6%, respectively. Anemia and lymphopenia significantly correlated with CD4+ count ($p < 0.001$) and also, anemia correlated with sexually transmitted infection as co-infection ($p = 0.044$). No significant correlation was found between leucopenia and thrombocytopenia with CD4+ count ($p > 0.05$), between anemia and lymphopenia with opportunistic infection and co-infection ($p > 0.05$), and between anemia, leucopenia, lymphopenia, and thrombocytopenia with viral load ($p > 0.05$).

Conclusions: Anemia and lymphopenia significantly correlated with CD4+ count. CD4+ count monitoring is needed for early detection of hematological abnormalities in order to lower morbidity and increase quality of life.

HIV AIDS Rev 2024; 23, 3: 217-225
DOI: https://doi.org/10.5114/hivar/156690

Key words: HIV infection, hematological abnormality, CD4+ count, opportunistic infection, viral load.

Address for correspondence: Dr. I. Nyoman Yogi Wiraguna, Department of Internal Medicine, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia, e-mail: Inyomanyogi_wiraguna@yahoo.co.id

Article history:
Received: 17.05.2022
Revised: 18.11.2022
Accepted: 18.11.2022
Available online: 20.09.2024

International Journal of HIV-Related Problems
HIV & AIDS Review

Introduction

In 2020, there were 37.7 million people living with human immunodeficiency virus (HIV) globally, and 1.5 million people became newly infected. As of 30 June, 2021, 28.2 million people were accessing antiretroviral therapy (ARVs) [1]. The number of HIV/acquired immunodeficiency syndrome (AIDS) cases in Indonesia continues to increase. In 2019, the number of HIV cases in Indonesia was 50,282, and mostly prevalent in males (64.5%) [2].

HIV is characterized by a progressive damage of immune system, resulting in a number of opportunistic infections and hematological manifestations [3]. Hematological abnormalities, including anemia, leucopenia, and thrombocytopenia are common manifestations of HIV infection, especially in advanced stages [4], with anemia being the most commonly encountered hematologic abnormality and significant predictor of progression to AIDS and death [5].

The aim of this study was to assess factors associated with hematological abnormalities, such as anemia, leukopenia, lymphopenia, and thrombocytopenia in HIV-infected patients.

Material and methods

The present cross-sectional study was done on outpatient department at Dr. Wahidin Sudirohusodo Hospital, Makassar. Retrospective data of three years from 2019 to 2021 were retrieved from medical records. Subjects of this study were HIV-infected patients who met the following inclusion criteria: males and females ≥ 18 years old, diagnosed with HIV at Dr. Wahidin Sudirohusodo Hospital, Makassar, with complete medical record data. Exclusion criteria were pregnancy or any previously known underlying disease, such as liver, kidney, and blood disorders, autoimmune diseases, and malignancies. Secondary data from medical records of HIV patients were obtained, and hematologic profile (hemoglobin, leukocytes, lymphocytes, and platelets) was collected as well as CD4+ count, toxoplasmosis, other agents, rubella, cytomegalovirus, and herpes simplex (TORCH) infection status, HIV viral load, and diagnosis of candidiasis, tuberculosis, and sexually transmitted infections (STIs). The research was conducted after ethical approval from the Ethics Committee of Dr. Wahidin Sudirohusodo Hospital, Makassar (approval No.: 535/UN4.6.4.5.31/PP36/2021).

HIV patients are individuals infected with HIV virus, confirmed by HIV-positive antibody through enzyme-linked immunosorbent assay (ELISA). Hematological abnormality was considered a manifestation of atypical complete blood tests measured with hematology analyzer (Sysmex Corporation), and grouped into anemia, leucopenia, lymphopenia, and thrombocytopenia. Anemia is a hemoglobin deficiency, with level falling below normal value (hemoglobin < 13 mg/dl in males, and < 12 mg/dl in females). Leucopenia is a leukocyte count that is below normal value (< 4,000/µl); lymphopenia is a lymphocyte percentage that falls below normal value (< 20%), and thrombocytopenia is a platelet count below normal value (< 150,000 mg/dl). Age was calculated based on date of birth and divided into three groups, such as < 30 years, 30-45 years, and > 45 years. Gender was grouped into male and female. CD4+ count obtained during laboratory examination by using a flow cytometer (CyFlow) device was grouped into < 200 cells/mm^3 and ≥ 200 cells/mm^3. Opportunistic infections are infections caused by organisms that normally do not cause clinical manifestations; they occur in patients with immune system deficiency, and were grouped into candidiasis, tuberculosis (TB), and TORCH. Co-infections are caused by different organisms, occurring simultaneously in patients, such as STIs, hepatitis B, and hepatitis C. Candidiasis was diagnosed if oral thrush was found on a physical examination, or as a result of a supporting examination that indicated *Candida* infection. Tuberculosis was deemed if clinical manifestations were found with the results of supporting examinations showing the presence of *Mycobacterium tuberculosis*. TORCH infection was diagnosed if laboratory examinations' results showed the presence of antibodies of organisms that cause the infection. STIs were considered if risk factors were found accompanied by laboratory examinations' results showing the presence of antibodies of organisms that cause the infection. Hepatitis B or hepatitis C were deemed if laboratory examinations' results showed the presence of viral antigens in the blood. HIV viral load was considered as the number of HIV viruses in the blood calculated through a viral load with HIV-1 monitor test, divided into < 100,000 copies/ml and ≥ 100,000 copies/ml.

All data from the samples were transferred to electronic storage media. Analysis was conducted using SPSS program version 25.0. Independent *t*-test and χ^2 test were employed for statistics, with *p*-value < 0.05 considered statistically significant.

Results

In this study, the study cohort consisted of 71 (85.5%) males and 12 (14.5%) females, with age ranging between 19 and 60 years, and mean age of 33.22 ± 8.62 years. Based on age, most of the patients were in the 30-45 years (50.6%) age group. Based on CD4+ count, 51 (61.4%) subjects had CD4+ < 200 cells/mm^3. Anemia was found in 47% cases, and based on the type of anemia, 17.9% subjects had microcytic hypochromic anemia, and 82.1% subjects had normocytic normochromic anemia. Leucopenia, lymphopenia, and thrombocytopenia were observed in 10.8%, 28.9%, and 9.6% of the participants, respectively. In terms of opportunistic infections, candidiasis was found in 34.9%, tuberculosis in 14.5%, and TORCH in 56.6% of the patients. In addition, STIs were observed in 7.2%, hepatitis B infection in 9.6%, and hepatitis C infection in 2.4% of the cases (Table 1).

Significant correlation was noted between CD4+ count and leukocyte count, lymphocytes, hemoglobin levels, and hematocrit, with $p = 0.041$, $p < 0.001$, $p < 0.001$, and $p < 0.001$, respectively. There was no significant association between CD4+ count and platelet count, neutrophils

count, monocytes count, and eosinophils count, $p = 0.869$, $p = 0.796$, $p = 0.739$, and $p = 0.917$, respectively (Table 2).

There was a significant association between CD4+ count with anemia ($p < 0.001$), where HIV patients with CD4+ < 200 cells/mm^3 had a 90.61 times higher risk of anemia compared with CD4+ ≥ 200 cells/mm^3 (95% CI: 11.22-731.54%). Otherwise, no significant association was found between CD4+ count with leucopenia ($p = 0.286$). There was a significant correlation between CD4+ count and lymphopenia ($p < 0.001$), where HIV patients with CD4+ < 200 cells/mm^3 had a 25.46 times higher risk of lymphopenia than CD4+ ≥ 200 cells/mm^3 (95% CI: 3.22-201.05%). There was no significant association between CD4+ count with thrombocytopenia ($p > 0.949$) (Tables 3-6).

Moreover, no significant correlation was found between opportunistic infection groups of candidiasis, tuberculosis, and TORCH ($p = 0.698$, $p = 0.378$, and $p = 0.484$, respectively) as well as hepatitis B and hepatitis C co-infections with anemia ($p = 0.572$ and $p = 0.931$, respectively). However, there was a significant correlation between co-infection of STIs and anemia ($p = 0.044$) (Table 7).

Also, no significant association was observed between opportunistic infection of candidiasis, tuberculosis, and TORCH with lymphopenia ($p = 0.066$, $p = 0.292$, and $p = 0.206$, respectively) as well as co-infection with STIs, hepatitis B, and hepatitis C ($p = 0.105$, $p = 0.573$, and $p = 0.506$, respectively) and lymphopenia (Table 8).

Additionally, there was no significant association between viral load with anemia, leukopenia, lymphopenia, and thrombocytopenia ($p = 0.630$, $p = 0.803$, $p = 0.137$, and $p = 0.720$, respectively) (Tables 9-12).

Table 1. Characteristics of subjects ($N = 83$)

Variable	*n* (%)
Gender	
Male	71 (85.5)
Female	12 (14.5)
Age	
< 30 years	35 (42.2)
30-45 years	42 (50.6)
> 45 years	6 (7.2)
CD4+ count	
< 200	51 (61.4)
≥ 200	32 (38.6)
Leucopenia	
Yes	9 (10.8)
No	74 (89.2)
Lymphopenia	
Yes	24 (28.9)
No	59 (71.1)
Anemia	
Yes	39 (47.0)
No	44 (53.0)
Types of anemia	
Microcytic hypochromic	7 (17.9)
Normocytic normochromic	32 (82.1)
Thrombocytopenia	
Yes	8 (9.6)
No	75 (90.4)
Opportunistic infections	
Candidiasis	29 (34.9)
Tuberculosis	12 (14.5)
TORCH	47 (56.6)
Co-infection	
Sexually transmitted infections	6 (7.2)
Hepatitis B	8 (9.6)
Hepatitis C	2 (2.4)

Discussion

The current study included 83 study subjects, with predominance of males (85.5%). This finding is in line with a study by Kumar *et al.* [6] who showed male predominance of 78%. A study by Parinitha and Kulkarni *et al.* [7] also showed male predominance in 68% of cases, and Bhardwaj *et al.* [3] from India reported 57.5% of male subjects.

In this study, the age range of the subjects was between 19 and 60 years, with mean age of 33.22 ± 8.62 years. Based on age, it was found that the majority of patients were in the age group of 30-45 years (50.6%). These findings agree with studies done by Wande *et al.* [8] who showed mean age of 34 years. A study by Damtie *et al.* [9] in Ethiopia demonstrated age range of 20-67 years, with mean age of 38.8 ± 9.9 years and median age of 37 years, with majority (35%) of the cases being in the 40-49 age group. Another study by Katemba *et al.* [10] from Uganda showed that the majority of patients were 34 years old.

The present study showed that 39 (47.0%) subjects had anemia, out of which 7 (17.9%) had microcytic hypochromic anemia and 32 (82.1%) subjects had normocytic normochromic anemia. These findings are in line with a research done by Akinbami *et al.* [11] who showed the prevalence of anemia of 24.2%. Other research by Bhardwaj *et al.* [3] reported even higher prevalence of anemia of 72.5%. Katemba *et al.* [10] from Uganda demonstrated anemia in 67.38% of cases, with majority having normocytic normochromic anemia (89.47%), followed by microcytic hypochromic anemia (8.42%) and macrocytic hypochromic anemia (2.11%). In yet another study by Wisaksana *et al.* [12], the most common anemia was normocytic normochromic anemia, with characteristics of normal or low reticulocyte index indicating that chronic disease anemia was the main cause. Other research conducted around the world showed that the prevalence of anemia in HIV patients was ranging from 63% to 95%, and anemia was

Table 2. Blood component levels with CD4+ count

Variable (unit)	CD4+ < 200 (*n* = 51)	CD4+ ≥ 200 (*n* = 32)	*p*-value
WBC (/µl)	6262.75 ± 3090.82	7595.63 ± 2380.85	0.041*
Neutrophil (/µl)	4077.88 ± 2871.07	4223.49 ± 1687.87	0.796*
Lymphocyte (%)	21.62 ± 9.58	32.67 ± 9.59	< 0.001*
Monocyte (/µl)	535.50 (282.10-2201.80)	528.15 (297.60-1367.40)	0.978**
Eosinophil (/µl)	181.50 (0.00-2263.00)	216.70 (22.80-1287.50)	0.340**
Basophil (/µl)	21.60 (0.00-116.00)	48.20 (2.28-407.00)	0.027**
Hemoglobin (gr/dl)	11.38 ± 1.97	14.92 ± 1.32	< 0.001*
RBC (10^6/µl)	3.99 ± 0.72	5.05 ± 0.52	< 0.001*
HCT (%)	33.33 ± 6.95	44.07 ± 3.66	< 0.001*
MCV (fl)	87.00 (64.00-97.00)	86.50 (79.00-98.00)	0.388**
MCV (pg)	29.00 (19.00-35.00)	29.00 (26.00-45.00)	0.134**
MCHC (gr/dl)	33.00 (30.00-38.00)	34.00 (32.00-35.00)	0.026**
Platelet (/µl)	277431.37 ± 103419.77	281187.50 ± 95149.94	0.869*
PCT (%)	0.13 ± 0.12	0.16 ± 0.10	0.385*

**Independent t-test. **Mann-Whitney test.*

Table 3. Relationship of CD4+ count with anemia

CD4+ count	Anemia		Total	*p*-value*
	Yes	No		
< 200				
n	38	13	51	< 0.001
%	97.4	29.5	61.4	
≥ 200				
n	1	31	32	OR**: 90.61
%	2.6	70.5	38.6	(95% CI: 11.22-731.54%)
Total				
n	39	44	83	
%	100.0	100.0	100.0	

**χ^2 test*

Table 4. Relationship of CD4+ count with leucopenia

CD4+ count	Leucopenia		Total	*p*-value*
	Yes	No		
< 200				0.286
n	7	44	51	
%	77.8	59.5	61.4	
≥ 200				
n	2	30	32	
%	22.2	40.5	38.6	
Total				
n	9	74	83	
%	100.0	100.0	100.0	

**χ^2 test*

Table 5. Relationship of CD4+ count with lymphopenia

CD4+ count	Lymphopenia		Total	*p*-value*
	Yes	No		
< 200				
n	23	28	51	< 0.001
%	95.8	47.5	61.4	
≥ 200				
n	1	31	32	OR: 25.46
%	4.2	52.5	38.6	95% CI: 3.22-201.05%
Total				
n	24	59	83	
%	100.0	100.0	100.0	

**χ^2 test*

Table 6. Relationship of CD4+ count with thrombocytopenia

CD4+ count	Thrombocytopenia		Total	*p*-value*
	Yes	No		
< 200				0.949
n	5	46	51	
%	62.5	61.3	61.4	
≥ 200				
n	3	29	32	
%	37.5	38.7	38.6	
Total				
n	8	75	83	
%	100.0	100.0	100.0	

**χ^2 test*

Table 7. Relationship of opportunistic infection and co-infection with anemia

	Anemia		Total	*p*-value*
	Yes	No		
Candidiasis				
Yes				0.698
n	12	17	29	
%	37.5	33.3	34.9	
No				
n	20	34	54	
%	62.5	66.7	65.1	
Tuberculosis				
Yes				0.378
n	6	6	12	
%	18.8	11.8	14.5	
No				
n	26	45	71	
%	81.3	88.2	85.5	
TORCH				
Yes				0.684
n	23	24	47	
%	59.0	54.5	56.6	
No				
n	16	20	36	
%	41.0	45.5	43.4	
IMS				
Yes				0.044
n	0	6	6	
%	0.0	11.8	7.2	
No				
n	32	45	77	
%	100.0	88.2	92.8	
Hepatitis B				
Yes				0.572
n	3	5	8	
%	7.7	11.4	9.6	
No				
n	36	39	75	
%	92.3	88.6	90.4	
Hepatitis C				
Yes				0.931
n	1	1	2	
%	2.6	2.3	2.4	
No				
n	38	43	81	
%	97.4	97.7	97.6	

χ^2 test

Table 8. Relationship of opportunistic and co-infective infection with lymphopenia

	Lymphopenia		Total	*p*-value*
	Yes	No		
Candidiasis				
Yes				0.066
n	12	17	29	
%	50.0	28.8	34.9	
No				
n	12	42	54	
%	50.0	71.2	65.1	
Tuberculosis				
Yes				0.292
n	5	7	12	
%	20.8	11.9	14.5	
No				
n	19	52	71	
%	79.2	88.1	85.5	
TORCH				
Yes				0.206
n	11	36	47	
%	45.8	61.0	56.6	
No				
n	13	23	36	
%	54.2	34.0	43.4	
IMS				
Yes				0.105
n	0	6	6	
%	0.0	10.2	7.2	
No				
n	24	53	77	
%	100.0	89.8	92.8	
Hepatitis B				
Yes				0.573
n	3	5	8	
%	12.5	8.5	9.6	
No				
n	21	54	75	
%	87.5	91.5	90.4	
Hepatitis C				
Yes				0.506
n	1	1	2	
%	4.2	1.7	2.4	
No				
n	23	58	81	
%	95.8	98.3	97.6	

χ^2 test

Table 9. Relationship of viral load with anemia

	Anemia		Total	*p*-value*
	Yes	No		
Viral load (copies/ml)				
< 100,000				0.630
n	11	22	33	
%	91.7	95.7	94.3	
≥ 100,000				
n	1	1	2	
%	8.3	4.3	5.7	
Total				
n	12	23	35	
%	100.0	100.0	100.0	

*χ^2 test

Table 10. Relationship of the viral load with leucopenia

	Leucopenia		Total	*p*-value*
	Yes	No		
Viral load (copies/ml)				
< 100,000				0.803
n	1	32	33	
%	100.0	94.1	94.3	
≥ 100,000				
n	0	2	2	
%	0.0	5.9	5.7	
Total				
n	1	34	35	
%	100.0	100.0	100.0	

*χ^2 test

Table 11. Relationship of the viral load with lymphopenia

	Lymphopenia		Total	*p*-value*
	Yes	No		
Viral load (copies/ml)				
< 100,000				0.137
n	4	29	33	
%	80.0	96.7	94.3	
≥ 100,000				
n	1	1	2	
%	20.0	3.3	5.7	
Total				
n	5	30	35	
%	100.0	100.0	100.0	

*χ^2 test

Table 12. Relationship of viral load with thrombocytopenia

	Thrombocytopenia		Total	*p*-value*
	Yes	No		
Viral load (copies/ml)				
< 100,000				0.720
n	2	31	33	
%	100.0	93.9	94.	
≥ 100,000				
n	0	2	2	
%	0.0	6.1	5.7	
Total				
n	2	33	35	
%	100.0	100.0	100.0	

*χ^2 test

more commonly seen than leucopenia and thrombocytopenia [13].

In the current study, the prevalence of leucopenia was reported in 9 (10.8%) subjects. This finding is in agreement with a study by Kotwal *et al.* [14] who showed leucopenia in 12.72% of patients. However, higher results were obtained by Bhardwaj *et al.* [3] who reported leukopenia in 18.33% of participants, and by Ako *et al.* [15] with leucopenia observed in 20% of subjects, whereas Kumar *et al.* [6] form India noted leucopenia in 35% of patients.

In this study, there were 24 (28.9%) lymphopenia subjects. This result is lower than that reported by Parinitha and Kulkarni (65.2%) [7] and Bhardwaj *et al.* (49.17%) [3].

In this study, thrombocytopenia was found in 8 (9.6%) patients. This finding is in line with Wondimeneh *et al.* [16] who showed thrombocytopenia prevalence of 5.9%. However, the result of this study is lower than that in Akinbami *et al.* [11] research, where thrombocytopenia was found in 16.1% of patients as well as meta-analysis by Getawa *et al.* [17] with 17.9% of thrombocytopenia cases and Tamir *et al.* [18] from Ethiopia who showed thrombocytopenia in 18.7% of patients.

Regarding the prevalence of opportunistic infections in the present research, 29 (34.9%) subjects had candidiasis, 12 (14.5%) had tuberculosis, and 47 (56.6%) had TORCH infection. In addition, 6 (7.2%) patients had STI, 8 (9.6%) had hepatitis B infection, and 2 (2.4%) had hepatitis C infection. Other studies demonstrate different results. Fan *et al.* [19] showed that hepatitis B prevalence was 5% and hepatitis C was 19.5%, while Suja *et al.* [13] reported tuberculosis in 25%, candidiasis in 8%, and hepatitis B co-infection in 2% of cases. Moreover, Duguma *et al.* [20] showed candidiasis in 6.2% and tuberculosis in 2.3% of individuals.

In the present study, there was a significant correlation between CD4+ count and the number of leukocytes, lymphocytes, and hemoglobin level ($p < 0.05$). However,

there was no significant correlation between CD4+ count and platelets, neutrophils, monocytes, and eosinophils ($p > 0.05$). These findings are concordant with Aryastuti *et al.* [21] study who reported a significant association between hemoglobin level and CD4+ count ($p = 0.039$), but no significant association between leukocytes and platelets with CD4+ count. Additionally, Dhal *et al.* [22] showed a significant relationship between lymphocytes and CD4+ count ($p = 0.031$), but no significant relationship between neutrophils, monocytes, and platelets with CD4+ count ($p > 0.05$). Study by Olaniyi *et al.* [23] demonstrated a significant correlation between hemoglobin, neutrophils, and lymphocytes with CD4+ count ($p < 0.05$), but no significant correlation between leukocytes, monocytes, and platelets with CD4+ count ($p > 0.05$).

In the current study, a significant relationship between CD4+ count and anemia ($p < 0.001$) was found, where HIV-infected patients with CD4+ < 200 cells/mm^3 had a 90.61 times higher risk of anemia compared with CD4+ ≥ 200 cells/mm^3 (95% CI: 11.22-731.54%). These findings are in line with Suja *et al.* [13] who observed a significant relationship between anemia with CD4+ count ($p = 0.008$). Furthermore, Deressa *et al.* [24] showed an increased risk of anemia events in subjects with CD4+ < 200 cells/mm^3 (AOR = 2.4; 95% CI: 1.3-4.9%), which can be caused by erythrotropic dysfunction due to an increase in the number of viruses along with a decline of immune system. A study by Wisaksana *et al.* [12] observed that anemia was significantly associated with low CD4+ count ($p < 0.001$).

In this study, there was no significant association between CD4+ count with leucopenia ($p > 0.05$). This finding is not in line with Shen *et al.* [25] who reported that leucopenia is associated with a decrease in CD4+ count ($p < 0.001$). A study by Talargia *et al.* [26] showed a significant association between leucopenia and CD4+ count < 200 cells/mm^3 ($p < 0.05$), while Ciccacci *et al.* [27] observed a significant relationship between leucopenia and low CD4+ count ($p < 0.05$). The results of the current study is possibly due to the low percentage of subjects who experienced leucopenia (10.8%). In the hematological profile, a significant relationship between CD4+ count and leukocyte count was seen, but if there is a hematological manifestation in the form of leucopenia compared with CD4+ count, there is on significant relationship.

In this study, there was a significant association between CD4+ count and lymphopenia ($p < 0.05$), where HIV patients with CD4+ count < 200 cells/mm^3 had a 25.46 times higher risk of lymphopenia than CD4+ count ≥ 200 cells/mm^3 (95% CI: 3.22-201.05%). These findings agree with that in Bhardwaj *et al.* [3] study who showed a significant relationship between lymphopenia and CD4+ count ($p = 0.018$). Also, Talargia *et al.* [26] observed a significant association between lymphopenia and CD4+ count < 200 cells/mm^3 ($p < 0.05$), and Parinitha and Kulkarni *et al.* [7] reported a significant relationship between CD4+ count and lymphopenia ($p < 0.0001$).

In the current study, there was no relationship between CD4+ count with thrombocytopenia ($p > 0.05$). This finding is concordant with Parinitha and Kulkarni *et al.* [7] and Wondimeneh *et al.* [16] who found no significant relationships between CD4+ counts and thrombocytopenia ($p > 0.05$ and $p > 0.05$, respectively). However, these findings are not in line a study done by Bhardwaj *et al.* [3] who showed a significant relationship between thrombocytopenia and CD4+ count ($p = 0.044$) as well as Gebreweld *et al.* [28] who found the same, with $p = 0.001$. A study by Shen *et al.* [25] showed that thrombocytopenia was associated with a decrease in CD4+ count ($p < 0.001$).

In this study, there was no relationship between opportunistic infections, and hepatitis B and hepatitis C co-infections with anemia ($p > 0.05$), and there was a relationship between STI with anemia ($p < 0.05$). These findings are not concordant with Gebreweld *et al.* [28] study who observed a significant association between anemia and opportunistic infections ($p < 0.001$). A research by Fan *et al.* [19] reported that hepatitis B infection was one of the risk factors of cytopenia in HIV patients ($p = 0.01$), while hepatitis C infection was not associated with the incidence of cytopenia ($p = 0.14$). One of the factors, which play a role in the incidence of anemia is opportunistic infection, along with nutritional deficiencies, types of ARV drugs, direct effects of HIV on the bone marrow, and malignancies associated with AIDS [12].

In the present study, there was not significant relationship between opportunistic infections and co-infection with lymphopenia ($p > 0.05$). This findings are not in line with Fan *et al.* [19] who reported that stage IV HIV is one of the risk factors in cytopenia ($p < 0.001$), where the incidence of opportunistic infections is often found at that stage.

In the current study, there was no significant relationship between viral load and anemia, leucopenia. lymphopenia, and thrombocytopenia ($p > 0.05$). These findings are in line with Denue *et al.* [4] study who showed that there was no significant correlation between cytopenia and viral load. A study by Ciccacci *et al.* [27] observed a significant relationship between anemia and viral load ($p < 0.05$), but no significant relationship between leucopenia and thrombocytopenia and viral load ($p > 0.05$). The results of this study are not concordant with Suja *et al.* [13] who reported a relationship between anemia, neutropenia, and thrombocytopenia with a high viral load ($p < 0.001$). Fan *et al.* [19] found that viral load > 100,000 copies/ml is one of risk factors for the occurrence of cytopenia in HIV patients ($p < 0.001$).

The results of this study showed no significant association between viral load and anemia, leucopenia, lymphopenia, and thrombocytopenia due to limited number of samples (only 35 out of 83 subjects): 2 subjects with a viral load > 100,000 copies/ml and 33 patients with a viral load of < 100,000 copies/ml.

The limitation of this study is the small number of samples of viral load (only 35 samples), and the analysis was not optimal for interpretation. In addition, we did not investi-

gate hematological abnormalities in HIV-infected patients after receiving ARV therapy.

From the current study, it can be concluded that there is a significant relationship between CD4+ count and hemoglobin level, leukocytes, and lymphocytes, but there is no significant relationship between CD4+ count and platelet count, neutrophils, monocytes, and eosinophils. There is a significant association between CD4+ counts and anemia and lymphopenia. No significant association was found between CD4+ counts and leucopenia and thrombocytopenia. There is a significant association between STIs with anemia, otherwise no significant association was observed between opportunistic infections and co-infections with anemia and lymphopenia. There was no significant association between viral load and anemia, lymphopenia, leucopenia, and thrombocytopenia.

Recommendations

Anemia and lymphopenia significantly correlated with CD4+ count. CD4+ count monitoring is needed for early detection of hematological abnormalities in order to lower morbidity and increase quality of life.

Disclosures

1. Institutional review board statement: This study was approved by the Ethics Committee of Dr. Wahidin Sudirohusodo Hospital, Makassar, with approval number: 535/UN4.6.4.5.31/PP36/2021.
2. Assistance with the article: We would like to express our appreciation to Prof. Andi Makbul Aman MD, Professor and Head of the Department of Internal Medicine, for his assistance. The authors would like to express their gratitude to Dr. Khalid Saleh, the Hospital's Chief, for providing the necessary information and data for the completion of this original article.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

References

1. UNAIDS. Global HIV statistics [Internet]. 2021. Available from: https://www.usaid.gov/global-health/health-areas/hiv-and-aids/technical-areas/dreams/unaids-fact-sheet-2021 (Accessed: 19.11.2022).
2. Ministry of Health Republic of Indonesia. Data and Information Center of the Ministry of Health of the Republic of Indonesia. 2020.
3. Bhardwaj S, Almaeen A, Wani FA, Thirunavukkarasu A. Hematologic derangements in HIV/AIDS patients and their relationship with the CD4 counts: a cross-sectional study. Int J Clin Exp Pathol 2020; 13: 756-763.
4. Denue BA, Gashau W, Bello HS, Kida IM, Bakki B, Ajayi B. Relation between some haematological abnormalities, degree of immunosuppression and viral load in treatment-naïve HIV-infected patients. East Mediterr Health J 2013; 19: 362-368.
5. Richard A, Olayanju AO, Ntuhun BD, Chollom S, Enitan S. Haematological parameter in human immunodeficiency virus positive individuals on different HAART regimen. World J Pharm Res 2015; 4: 1-9.
6. Kumar MB, Thippeswamy T, Shankar R, Prathima C. Hematological abnormalities in early and advanced HIV infection patients. Int J Sci Study 2016; 3: 1-5.
7. Parinitha SS, Kulkarni H. Haematological changes in HIV infection with correlation to CD4 cell count. Australas Med J 2012; 5: 157-161.
8. Wande IN, Fuadi MR, Hadi S. The correlation between total lymphocyte count, hemoglobin levels, lymphocyte/leukocyte ratio (LLR), and lymphocyte/neutrophil ratio (LNR) to CD4 levels in patients with human immunodeficiency virus infection at Sanglah Hospital. Bali Med J 2019; 8: 337-341.
9. Damtie S, Workineh N, Kiros T, Eyayu T, Tiruneh T. Hematological abnormalities of adult HIV-infected patients before and after initiation of highly active antiretroviral treatment at Debre Tabor Comprehensive Specialized Hospital, Northcentral Ethiopia: a cross-sectional study. HIV AIDS (Auckl) 2021; 13: 477-484.
10. Katemba C, Muzoora C, Muwangu Z, Mwambi B, Atuhairwe C, Taremwa IM. Hematological abnormalities in HIV-antiretroviral therapy naïve clients as seen at an immune suppression syndrome clinic at Mbarara Regional Referral Hospital, southwestern Uganda. J Blood Med 2018; 9: 105-110.
11. Akinbami A, Oshinaike O, Adeyemo T, Adediran A, Dosunmu O, Dada M, et al. Hematologic abnormalities in treatment-naïve HIV patients. Infect Dis Res Treat 2010; 3: 45-49.
12. Wisaksana R, Sumantri R, Indrati AR, Zwitzer A, Jusuf H, de Mast Q, et al. Anemia and Iron homeostasis in a cohort of HIV-Infected patients in Indomesia. BMC Infect Dis 2011; 11: 213. DOI: 10.1186/1471-2334-11-213.
13. Suja S, Saravanan T, Karthikeyan S. Profile of hematological abnormalities and its correlation with absolute CD4 count and human immunodeficiency virus viral load in human immunodeficiency virus-infected patients in a tertiary care hospital. Indian J Sex Transm Dis AIDS 2020; 41: 156-161.
14. Kotwal CJ, Singh MV, Kotwal A, Dutta V, Nair V. A study of haematological and bone marrow changes in symptomatic patients with human immune deficiency virus infection with special mention of functional iron deficiency, anaemia of critically ill and haemophagocytic lymphohistiocytosis. Med J Armed Forces India 2013; 69: 319-325.
15. Ako SE, Njunda LA, Akum EA, Benjamin PT, Eteneneng EJ, Bernard W, et al. Hematological related disorders and transfusion of HIV therapy (HAART) in the South-West Region of Cameroon: hematological monitory parameters for HIV follow-up. J HIV Retrovirus 2018; 4: 5.
16. Wondimeneh Y, Muluye D, Ferede G. Prevalence and associated factors of thrombocytopenia among HAART-naive HIV-positive patients at Gondar University Hospital, northwest Ethiopia. BMC Res Notes 2014; 7: 5.
17. Getawa S, Aynalem M, Bayleyegn B, Adane T. The global prevalence of thrombocytopenia among HIV-infected adults: a systematic review and meta-analysis. Int J Infect Dis 2021; 105: 495-504.
18. Tamir Z, Seid A, Haileslassie H. Magnitude and associated factors of cytopenias among antiretroviral therapy naïve human immunodeficiency virus infected adults in Dessie, Northeast Ethiopia. PLoS One 2019; 14: e0211708. DOI: 10.1371/journal.pone.0211708.
19. Fan L, Li C, Zhao H. Prevalence and risk factors of cytopenia in HIV-infected patients before and after the initiation of HAART. Biomed Res Int 2020; 28: 3132589. DOI: 10.1155/2020/3132589.
20. Duguma N, Kiya GT, Maleko WA, Bimerew LG. Hematological parameters abnormalities and associated factors in HIV-positive adults before and after highly active antiretroviral treatment in Goba Referral Hospital, southeast Ethiopia: a cross-sectional study. SAGE Open Med 2021; 9: 20503121211020175. DOI: 10.1177/20503121211020175.
21. Aryastuti SA, Dewi SR, Masyeni S. High prevalence of anemia among human immunodeficiency virus infected patients: a cross-sectional study in Bali-Indonesia. Biomed Pharmacol J 2021; 14: 329-334.

22. Dhal N, Panda S, Mohapatra N, Pattanayak NC, Pattanaik R. Study of haematological abnormalities in HIV infected patients and its correlation with CD4 counts. Int J Res Med Sci 2018; 6: 2937-2942.
23. Olaniyi JA, Emeka GJ, Onifade AA, Adeyanju AO, Rahamon SK. Changes in haematological parameters and serum beta-2-microglobulin levels in CD4+ T-cells-stratified Nigerian HIV patient. Eur J Clin Exp Med 2021; 19: 33-39.
24. Deressa T, Damtie D, Workineh M, Genetu M, Melku M. Anemia and thrombocytopenia in the cohort of HIV-infected adults in northwest Ethiopia: a facility-based cross-sectional study. EJIFCC 2018; 29: 36-47.
25. Shen Y, Wang J, Wang Z, Shen J, Qi T, Song W, et al. A cross-sectional study of leukopenia and thrombocytopenia among Chinese adults with newly diagnosed HIV/AIDS. Biosci Trends 2015; 9: 91-96.
26. Talargia F, Teshome Y, Aynalem YA. Prevalence of leucopenia and associated factors before and after initiation of ART among HIV-infected patients, North East Ethiopia: cross-sectional study. J Blood Med 2021: 12: 269-276.
27. Ciccacci F, Lucaroni F, Latagliata R, Morciano L, Mondlane E, Balama M, et al. Hematologic alterations and early mortality in a cohort of HIV positive African patients. PLoS One 2020; 15: e0242068. DOI: 10.1371/journal.pone.0242068.
28. Gebreweld A, Fiseha T, Girma N, Haileslasie H, Gebretsadik D. Prevalence of cytopenia and its associated factors among HIV infected adults on highly active antiretroviral therapy at Mehal Meda Hospital, North Shewa Zone, Ethiopia. PLoS One 2020; 15: e0239215. DOI: 10.1371/journal.pone.0239215.