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Research Article

Depression Levels and CD4 Counts in HIV Patients at Dr. Saiful Anwar General Hospital Malang

Hubungan Tingkat Depresi terhadap Kadar CD4 pada Pasien HIV di RSUD Dr. Saiful Anwar Malang

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ABSTRACT

Untreated depression in HIV patients is associated with lower CD4 cell counts attributed to the excessive HPA axis activity, which leads to increased cortisol secretion. This can accelerate the progression of HIV through shifting cytokine production from Th1 to Th2, which triggers CD4 cell destruction and stimulates HIV replication. This study aimed to determine the relationship between depression levels and CD4 counts in HIV patients at Dr. Saiful Anwar General Hospital Malang. This study used a quantitative method with an analytical observational study design and a cross-sectional approach. A total of 30 participants were selected through purposive sampling. The Beck Depression Inventory-II (BDI-II) questionnaire was used to evaluate the participants' depression levels. Six participants were identified with moderate depression, while 24 participants exhibited either no depression or minimal depression. The Spearman's Rank Correlation Coefficient test showed p=0.183, p>0.05, with a correlation coefficient of -0.250, indicating no significant relationship between the depression levels and CD4 cell count in HIV patients at Dr. Saiful Anwar General Hospital Malang. Nevertheless, among the study subjects with moderate depression (6 participants), low CD4 counts (≤345cells/mm^3) were observed, suggesting a tendency for depression levels to be associated with CD4 count.

Keywords: *CD4 levels, depression levels, HIV, HIV patients*

ABSTRAK

Depresi yang tidak ditangani pada pasien HIV dikaitkan dengan kadar CD4 yang lebih rendah akibat aktivitas berlebihan dari aksis HPA pada depresi yang menyebabkan peningkatan sekresi kortisol. Hal tersebut dapat mempercepat perkembangan penyakit HIV melalui pergeseran dari sitokin Th1 ke Th2 yang memicu penghancuran sel CD4 dan merangsang replikasi HIV. Tujuan dari penelitian ini adalah untuk mengetahui hubungan antara tingkat depresi dengan kadar CD4 pada pasien HIV di RSUD Dr. Saiful Anwar Malang. Penelitian ini menggunakan metode kuantitatif dengan desain penelitian observasional analitik dan pendekatan *cross sectional*. Subjek penelitian diambil menggunakan teknik purposive sampling berjumlah 30 responden. Kuesioner *Beck Depression Inventory* II (BDI-II) digunakan untuk menilai tingkat depresi responden penelitian. Didapatkan 6 responden dengan depresi sedang dan 24 responden dengan tidak ada depresi atau depresi minimal. Hasil analisis statistik menggunakan Uji Koefisien Korelasi *Spearman's Rank* memperoleh nilai signifikansi p=0,183 (p>0,05) dan nilai koefisien korelasi -0,25 yang menunjukkan tidak terdapat hubungan antara tingkat depresi dengan kadar CD4 pada pasien HIV di RSUD Dr. Saiful Anwar Malang. Meskipun demikian, pada subjek penelitian dengan depresi sedang (6 responden) ditemukan kadar CD4 yang rendah (≤345 sel/mm^3), sehingga hal ini menunjukkan kecenderungan bahwa tingkat depresi berkaitan dengan kadar CD4.

Kata Kunci: HIV, kadar CD4, pasien HIV, tingkat depresi

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INTRODUCTION

The intersection of human immunodeficiency virus (HIV) infection and mental health is a critical public health issue that demands attention. Epidemiological studies indicate that individuals living with HIV experience psychiatric symptoms at rates 1.5 to 8 times higher than those in the general population or among individuals not infected with HIV (1). This heightened vulnerability is compounded by the stigma associated with HIV, which contributes to a greater prevalence of depression among these patients (2).

Depression, a mood disorder characterized by persistent feelings of sadness and loss of interest, poses significant challenges for those affected by HIV. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), classifies depression into several subtypes, each defined by specific diagnostic criteria. Common characteristics include sad, empty, or easily irritated moods, which, when combined with cognitive and somatic symptoms, can lead to considerable distress or impairment (3). Major depressive disorder (MDD) is the most common mental health disorder, particularly prevalent among inpatient and outpatient psychiatric patients, with estimates suggesting a prevalence of 10-25% in females and 5-12% in males (4). This prevalence underscores the need for focused research on MDD in the context of HIV.

The implications of depression for individuals living with HIV are profound. Depressive symptoms can lead to viral non-suppression by decreasing self-efficacy and adherence to antiretroviral therapy (ART), which results in increased morbidity and mortality associated with HIV (5). Furthermore, stress and depression are linked to lower CD4 counts and higher viral loads (6).

Research has shown that depression can double the rate of CD4 count decline and negatively impact baseline CD4 counts (7). Psychosocial factors, such as elevated scores on the Beck Depression Inventory (BDI), along with neurohormonal factors like cortisol and norepinephrine, significantly influence the progression of HIV to AIDS by causing decreases in CD4 counts and increases in viral load (8). Elevated cortisol levels can accelerate disease progression by altering T lymphocyte cytokine production, shifting from Th1 to Th2 cytokines, which triggers CD4 cell destruction and stimulates HIV replication. Additionally, psychological stress and depression increase plasma catecholamine levels, particularly norepinephrine, which can enhance HIV replication (9).

Despite these concerning trends, research on the relationship between depression levels and CD4 counts in HIV patients remains limited, particularly in Indonesia. Therefore, this study aims to determine the relationship between depression levels and CD4 counts in HIV patients, providing valuable insights for holistic patient care.

METHOD

This study used a quantitative method with an analytical observational research design and a cross-sectional approach. Ethical clearance was obtained from the Research Ethics Commission of Dr. Saiful Anwar General Hospital Malang (Number 400/002/K.3/102.7/2023), and research participants have been provided with informed consent.

The population of this study consisted of HIV patients visiting the Tropical Disease and Infection Subdivision of the Internal Medicine Clinic at Dr. Saiful Anwar General Hospital Malang between May and August 2023. A total sample size of 30 was selected from a population of 118 HIV patients using purposive sampling based on specific inclusion and exclusion criteria. The inclusion criteria included individuals aged 18-50 years who are currently on first-line ART and have undergone at least one CD4 count test apart from the initial diagnostic test. Exclusion criteria encompassed ART-naive patients, those with only one CD4 count test, patients with a history of drug use, those with other illnesses such as cough, cold, diarrhea, or opportunistic infections like candidiasis, tuberculosis, and toxoplasmosis either during the study or within the prior week. Additionally, HIV patients with a prior mental health diagnosis, those currently being treated with antidepressants or anxiolytics, individuals with a history of alcohol consumption or substance use, and those withdrawing from the study were excluded to minimize potential confounding factors.

The dependent variable in this study was the cluster of differentiation 4 (CD4) count, categorized into an ordinal scale based on thresholds established by Dr. Saiful Anwar General Hospital Malang: Low (<637cells/mm^3), Normal (637-1485cells/mm^3), and High (>1485cells/mm^3). The independent variable was depression levels, also measured on an ordinal scale based on the Beck Depression Inventory-II (BDI-II): No or Minimal Depression (score <14), Mild Depression (score 14-19), Moderate Depression (score 20-28), and Severe Depression (score 29-63). The CD4 count used in this research was obtained from the participant's most recent CD4 count processed by the central laboratory of Dr. Saiful Anwar General Hospital Malang. The Indonesian version of the BDI-II questionnaire, which has undergone validity testing by Sorayah, was used in this study (10).

Primary data were collected using a paper based questionnaire which was administered to participants at the Tropical Disease and Infection Subdivision of Dr. Saiful Anwar General Hospital Malang. The researcher ensured that each question in the questionnaire was fully completed by the participants before processing the data and drawing conclusions from the research findings.

Univariate analysis using the Shapiro-Wilk test was conducted to assess normality, given the sample size of less than 50. Bivariate analysis using Spearman's Rank Correlation Coefficient test was subsequently performed to evaluate the relationship between CD4 count and depression levels. The test was conducted using IBM SPSS Statistics 23 for Windows.

RESULTS

Characteristics of Study Subjects

Thirty research participants who met the inclusion and exclusion criteria and had accessible CD4 counts through medical records were identified. Table 1 presents the characteristics of the study subjects.

The age group with the highest number of participants is 25-49 years, comprising 26 participants (86.7%). Female participants dominate the gender composition,

accounting for 20 participants (66.7%). Among the study subjects, the majority, totaling 18 participants (60%), are married. The most prevalent educational attainment is high school, accounting for 12 participants (40%). Similarly, the most frequent occupation among the participants is housewife, with 12 individuals (40%). Most study subjects reported a duration of HIV infection ranging from 2 to 4 years, with a total of 13 participants (43.3%). Regarding the HIV clinical stage, the majority were classified as stage I, comprising a total of 25 participants (83.3%).

The mean CD4 count among the 30 study subjects is 432.77cells/mm^3, with a standard deviation of 225.357cells/mm^3. Out of the total, 24 participants (80%) exhibit low CD4 counts (<637cells/mm^3), while 6 participants (20%) display normal CD4 counts (637-1485cells/mm^3). Regarding the depression level, the majority of study subjects, comprising 24 participants (80%), report no or minimal depression, whereas moderate depression is observed in 6 participants (20%).

The most common interval between the two activities is >2 weeks to ≤6 months, totaling 17 occurrences (56.7%), while the least common interval between the two activities is >6 months to ≤1 year, totaling 4 occurrences (13.3%).

Table 1. Characteristics of Study Subjects (n=30)

Characteristics		**n**	**%**
Age			
	20-24 years old	3	10.0
	25-49 years old	26	86.7
	≥ 50 years old	1	3.3
Sex			
	Male	10	33.3
	Female	20	66.7
Marital Status			
	Single	8	26.7
	Married	18	60.0
	Divorced	1	3.3
	Widowed	3	10.0
Education Level			
	Elementary school	7	23.3
	Junior high school	5	16.7
	Senior high school/Vocational high school	12	40.0
	Diploma/Undergraduate/Postgraduate degree	6	20.0
Occupation			
	Unemployed	3	10.0
	Student	1	3.3
	Government employee	1	3.3
	Private sector employee	7	23.3
	Housewife	12	40.0
	Merchant	2	6.7
	Craftsman	2	6.7
	Parking attendant	1	3.3
	Farmer	1	3.3
Duration of Infection			
	<2 years	7	23.3
	2-4 years	13	43.3
	5-7 years	3	10.0
	8-10 years	2	6.7
	>10 years	5	16.7
Clinical Stage of HIV			
	I	25	83.3
	II	5	16.7
CD4 Count			Mean (±SD)
	Among 30 study subjects		432.77 (±225.357)
	Low (<637cells/mm^3)	24	80.0
	Normal (637-1485cells/mm^3)	6	20.0
Depression Level			
	No depression or minimal depression	24	80.0
	Moderate depression	6	20.0
Interval between the Date of CD4 Count Collection and the Date of Questionnaire Completion			
≤2 weeks		9	30.0
>2 weeks - ≤6 months		17	56.7
>6 months - ≤1 year		4	13.3

Relationship between Depression Levels and CD4 Counts

Table 2 presents the results of Spearman's Rank Correlation Coefficient test measuring the relationship between depression levels and CD4 counts. The significance value obtained is p=0.183 (p>0.05), indicating no significant relationship between depression levels and CD4 counts.

DISCUSSION

CD4 Count

The mean CD4 count among the 30 study subjects is 432.77cells/mm³. Of these, 24 patients (80%) exhibit low CD4 counts (<637cells/mm³), while 6 patients (20%) have normal CD4 counts (637-1485cells/mm³). According to the

Table 2. Spearman's rank correlation coefficient test

			Depression Level	**CD4 Count (cells/mm³)**
Spearman's rho	Depression Level	Correlation Coefficient	1.000	-.250
		Sig. (2-tailed)	.	.183
		N	30	30
	CD4 Count (cells/mm³)	Correlation Coefficient	-.250	1.000
		Sig. (2-tailed)	.183	.

World Health Organization (WHO), a CD4 count below 200cells/mm³ indicates advanced HIV disease, significantly increasing the risk of opportunistic infections and other complications.

Opportunistic infections occur in HIV patients when the CD4 count is below 200cells/mm³ (11). Additionally, AIDS is diagnosed when the CD4 count falls below this threshold (12). Patients with CD4 counts under 200cells/mm³ face a 6.5 times higher risk of opportunistic infections compared to those with counts of 200cells/mm³ or higher (13).

To minimize bias regarding the rate of CD4 count increase and the level of depression potentially influenced by opportunistic infections, HIV patients experiencing such infections at the time of blood collection for the latest CD4 count examination and questionnaire completion were excluded. Therefore, it is reasonable that the average CD4 count among the 30 study subjects is above 200cells/mm³, specifically 432.77cells/mm³. While this average indicates a level above the critical threshold for opportunistic infections, it remains below the normal range of 637 to 1485cells/mm³. This suggests that although most subjects do not fall into the category of advanced HIV disease, their immune function may still be compromised.

This section provides descriptive information about the study subjects' CD4 counts, characterizing the population included in this research. It is not intended to compare these findings with previous studies or draw conclusions beyond describing the baseline characteristics of the participants. Understanding these baseline characteristics is crucial for interpreting the relationship between CD4 counts and depression levels in this population.

Depression Level

The majority of study participants exhibit minimal or no signs of depression, as many as 24 patients (80%), whereas 6 patients (20%) demonstrate moderate depression. This finding aligns with the research results of Hapsari *et al.,* at Dr. Kariadi Hospital and Elisha *et al.,* (2022) at the Peer Support Group (*Kelompok Dukungan Sebaya*) Solo Plus in Surakarta City (14,15).

Family support is a significant factor contributing to the low levels of depression observed among the study subjects. A study by Handayani *et al.,* (2022) across healthcare facilities in Jambi City with HIV/AIDS counseling services and ARV therapy reported a significant relationship between family support and the mental health status of HIV/AIDS patients, with a significance value of p=0.001 (p<0.05) using the chi-square test. The study also reported a 1.345 times increased risk of mental health disorders in HIV patients who receive low family support compared to those who receive moderate/high family support (16).

Social support received from the HIV patient community might also contribute to the low levels of depression observed among the study subjects. In Malang, two community support groups, Neolath Community (*Komunitas Neolath*) and Jati Community (*Komunitas Jati*) share similar goals, which aim to reduce negative stigma and discrimination against HIV/AIDS patients in society. These communities provide information, emotional support, and meaningful education to improve the quality of life for HIV/AIDS patients and their families.

Another factor that could explain the low depression levels among the study subjects is the use of the BDI-II questionnaire. Essentially, the BDI-II questionnaire is designed to measure the severity of depressive symptoms occurring within the past 2 weeks. However, due to limitations in the study subjects, this research used the BDI-II questionnaire to assess the severity of depressive symptoms among the study subjects that occurred more than two weeks prior to the date of CD4 count collection (17). This deviation from the recommended use of the BDI-II by Beck *et al.,* might have impacted the accuracy of depression assessment.

However, according to the framework depicted in Figure 1, the outcomes derived from the BDI-II questionnaires administered to all 30 study subjects remain applicable, although with a reduced level of accuracy in the questionnaire. The use of the BDI-II questionnaire to assess the severity of depressive symptoms occurring more than 2 weeks prior to the date of CD4 count collection may explain the observed low level of depression among the study subjects.

Interval between CD4 Count Collection and Questionnaire Completion

The intervals for categorizing the time between CD4 count collection and questionnaire completion are ≤2 weeks, >2 weeks ≤6 months, and >6 months ≤1 year. This categorization is based on the effectiveness of the BDI-II questionnaire in assessing depression levels over the preceding 2 weeks. The reference to ≤6 months aligns with the practical observation that CD4 counts are typically measured every 6 months, although this frequency may not apply uniformly to HIV patients who do not utilize NHI as their financing mechanism.

Studies on the sensitivity of the BDI-II questionnaire for screening depression levels over periods longer than the past 2 weeks are not widely available. However, this issue is addressed by Beck *et al.,* (18), Ahava *et al.,* (19), and Basker *et al.,* (20).

Considering the time span of the findings from these three previous studies, the researcher formulated a framework according to Figure 1.

The BDI-II questionnaire is most accurate in assessing depression levels within the 0-2-week timeframe. Within a 2-4-week timeframe, the BDI-II questionnaire remains accurate in assessing depression levels. In the 4-8-week timeframe, the BDI-II questionnaire is still accurate in assessing depression levels. However, the accuracy of the BDI-II questionnaire decreases when assessing depression levels longer than 8 weeks.

Although this framework has not yet been validated through additional research, it provides useful insight into the relationship between the interval of CD4 count collection and the completion date of the BDI-II questionnaire in this study.

Referring to Figure 1, the BDI-II questionnaire is most accurate in assessing the depression levels in 9 patients (30%), remains accurate in 3 patients (10%), and experiences a decrease in accuracy but remains suitable for 18 patients (60%). Nevertheless, it should be noted that untreated major depressive disorder episodes typically last an average of 10.7 months (21).

The researcher can ensure that the six study subjects with moderate depression had not taken any medications related

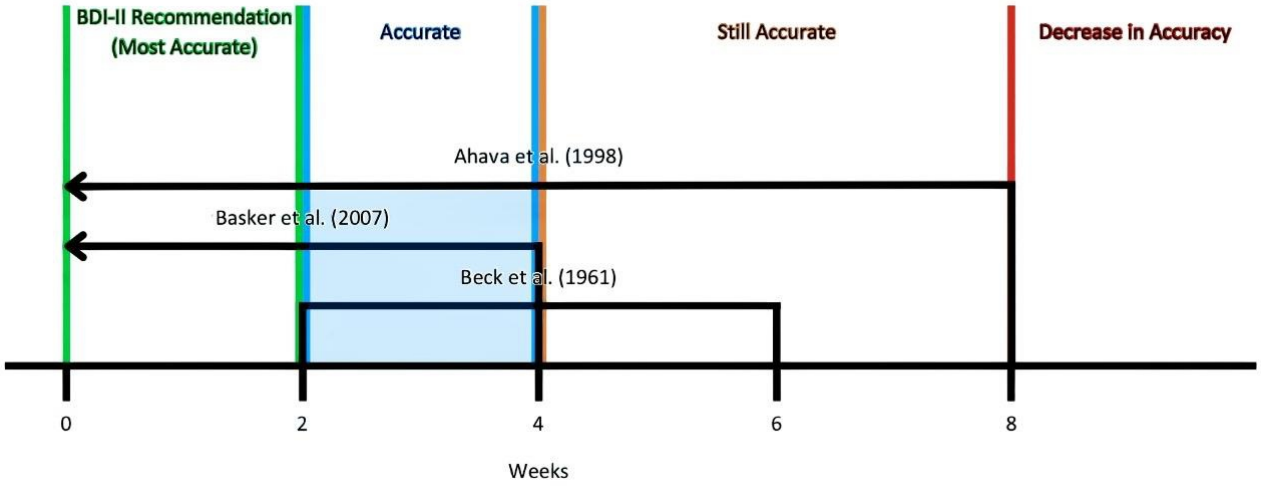

Figure 1. The Accuracy of the BDI-II questionnaire based on previous studies

Note: The time range is solely for internal use and cannot yet be applied to other research as it has not undergone the research phase.

to mental health, as this was included in the exclusion criteria of this study. Additionally, the interval between the date of CD4 count collection and the date of questionnaire completion for these six study subjects with moderate depression did not exceed the 10.7-month timeframe. None of the study subjects in this research exceeded this timeframe. Thus, it can be accepted that the results of the BDI-II questionnaire in this study are valid for use.

Relationship between Depression Levels and CD4 Counts

Despite no statistically significant relationship between the level of depression and CD4 count, the study found that all 6 patients with moderate depression had low CD4 counts (≤345cells/mm^3).

The findings are consistent with the study by Amoko *et al.,* conducted at HIV clinics based in family medicine at the University of Ilorin Teaching Hospital in Nigeria, that respondents with low CD4 counts (≤349cells/mm^3) had the highest prevalence of depression (37%), while respondents with high CD4 counts (≥500cells/mm^3) had the lowest prevalence of depression (28.3%). However, this relationship was not statistically significant (p=0.302), as the study used the chi-square test, which considers data statistically significant if p<0.05 (22).

This study has several limitations. First, the time gap between the date of CD4 count measurement and the date of questionnaire completion for some subjects exceeded 2 weeks. Second, the small sample size may have limited the ability to detect statistically significant relationships between variables. Third, the use of a cross-sectional approach, where data for each subject were collected only once, made it difficult to infer temporal relationships between variables. A longitudinal approach, with repeated data collection over time, would have been more effective in estimating these relationships (23,24). Fourth, the reliance on self-assessment questionnaires to evaluate depression could have been improved by using structured interviews, which are more objective.

Acknowledging the study's limitations particularly in terms of sample size and methodology our findings still provide valuable insights. Specifically, we conclude that there is no significant relationship between depression levels and CD4 counts in HIV patients at Dr. Saiful Anwar General Hospital Malang. These results underscore the need for further research using more robust methodologies, such as longitudinal studies and structured interviews, to enhance objectivity. Ultimately, gaining a deeper understanding of these dynamics will be crucial for developing tailored therapeutic approaches that aim to improve both mental health and immune resilience in this vulnerable patient group.

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