

# Screening of Anxiety and Depression Related CD4 Count of People Living with HIV/AIDS with Anti-Retroviral in Medan, Indonesia

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## Abstract

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**BACKGROUND:** HIV, which causes AIDS, infects the immune system cells, by destroying or damaging the function of the CD4. PLWHA will have twice the risk of experiencing mental health disorders such as depression and anxiety compared with the general population, thereby suppressing immune function, decreasing their quality of life, decreasing the level of adherence to treatment, and contributing significantly to the occurrence of premature death.

**AIM:** To determine the correlation Anxiety and Depression symptoms and CD4 levels in PLWHA who are undergoing Anti-Retroviral treatment at the HIV/AIDS

**METHODS:** The study was a cross-sectional study, which assesses the correlation between Hospital Anxiety and Depression Scale scores (HADS) and CD4 levels in PLWHA who are receiving ARV in the HIV/AIDS Special Services Polyclinic Medan Haji general hospital.

**RESULTS:** It was found that the average HADS-A score, PLWHA was 15.286 and the SD  $\pm$  2.244. This shows that PLWHA is in moderate to severe anxiety and moderate to severe depression. The mean CD4 level of people with HIV/AIDS/PLWHA was 288.171 and SD  $\pm$  88.955. According to WHO criteria, regarding the classification of HIV immunodeficiency in adults, are classified as moderate immunodeficiency. There was a significant correlation between the HADS-A score and CD4 level with a correlation value of  $r = -0.592$  indicating a negative correlation with a moderate correlation strength, and the correlation between HADS-D score and CD4 level. The strength of the relationship between HADS-D score and CD4 level is  $r = -0.650$ , shows a negative correlation with strong correlation strength.

**CONCLUSION:** from this study, it was found that there is a relationship between depression and anxiety symptom and CD4 level.

## Introduction

Human Immunodeficiency Virus/HIV, infects the immune system cells, by destroying or damaging the function of the Cluster of Differentiation 4/CD4. This viral infection results in a progressive deterioration of the immune system, which causes immune deficiency. Infections associated with severe immunodeficiency are known as opportunistic infections because this virus utilises a weakened immune system [1]. AIDS is a set of symptoms of a disease caused by decreased immunity which results in a person susceptible to opportunistic infections and

tumours [1]. HIV diagnosis is confirmed by examination laboratory, and always preceded by pre-test counselling or brief information. Laboratory tests carried out by antibody tests using stratification III (examination using 3 types of antibody tests with different sensitivity and specificity) [2], [3].

Mental disorders play several roles in the epidemiology of HIV, both in treatment elements and in comorbidities. Psychiatric conditions are associated with increased risky behaviour for infection, with reduced access to health services, with a decrease in adherence to HIV therapy, and with an increase in medical disorders and comorbidity. Individuals with

various types of mental illness that are not treated are susceptible to an increase in the frequency of unsafe sex and thus increase the risk of HIV infection [4]. PLWHA will have twice the risk of experiencing mental health disorders such as depression and anxiety compared with the general population, thereby suppressing immune function, decreasing their quality of life, decreasing the level of adherence to treatment, and contributing significantly to the occurrence of premature death.

CD4 counts can be used to monitor the progress of severe infections and to see the immune system, determine when to start antiretroviral therapy and to monitor the progress of treatment. The body's initial immune response to HIV, the CD4 count, will return to normal levels, then it will decrease. About 100 CD4 cells per year on average will decrease which is then followed by a decrease in the patient's clinical condition [2], [3].

**Table 1: HIV immunodeficiency classifications in adults using CD4 according to WHO [3]**

Immunodeficiency	CD4 count (cell/mm <sup>3</sup> )
There are no	> 500
Lightweight	350-499
Moderate	200-349
Weight	< 200 or < 15 %

Excerpted from: Ministry of Health of the Republic of Indonesia in 2015. Regulation of the Minister of Health of the Republic of Indonesia Number 87 of 2014 concerning Guidelines for Anti Retro Viral Treatment. 2014:25.

According to Mini ICD-10, depression is a mood that has the main symptoms of a depressive mood, loss of interest and excitement and reduced energy leading to increased fatigue and reduced activity, as well as several other symptoms such as reduced concentration and attention, price self and self-confidence diminish, ideas of guilt and uselessness, gloomy future views, ideas or actions that endanger themselves or suicide, disturbed sleep and reduced appetite [5]. Depression is the most common neuropsychiatric complication in infected patients HIV/AIDS [6], [7]. In the meta-analysis carried out by Cielsa and Robert, PLHIVs had a two-fold increased risk of developing depression compared with the negative control.

Depression in people infected with HIV may be related to neurobiological changes caused by the invasion of HIV in the central nervous system. Guerra et al., Provide an understanding of the comprehensive relationship between the role of neuroendocrine, immune-inflammatory and monoaminergic mechanisms for the occurrence of depression in HIV. These interrelated mechanisms are caused directly by the virus and indirectly by psychological stress associated with the psychosocial impact of HIV diagnosis, can induce the activity of the hypothalamus Pituitary Adrenal (HPA) axis and the sympathetic autonomic nervous system which activates immune cells both peripherally and in the central nervous system. From this mechanism there is the release of tumor necrosis factors alpha (TNF- $\alpha$ ), s interferon-gamma (INF- $\gamma$ ), interleukin-1 (IL-1) and interleukin-6

(IL-6), which ultimately causes PLWHA to occur "behaviour a state of chronic illness", characterized by weakness, reduced appetite, lethargy, psychomotor retardation, anhedonia, and changes in mood and cognitive moods.

Glycoprotein 120 and Tat protein can activate brain glial cells. Proinflammatory cytokines can actively become tryptophan degrading enzymes that will reduce the bioavailability of tryptophan, affect the brain serotonergic neurotransmission and lead to symptoms of depression [8].

Comprehensive anxiety disorder is defined as excessive anxiety and worries about several events or activities throughout the day for at least one 6-month period. Worrying is difficult to control and is associated with somatic symptoms, such as muscle tension, irritability, difficulty sleeping, and anxiety. Anxiety is difficult to control, subjectively troublesome and results in a decrease in an important area of one's life [9].

The results of existing studies indicate that genetics may play a role in anxiety disorders. Single nucleotide polymorphism (SNP) in brain-derived neurotrophic factor (BDNF) plays a role in fear response as in animal studies. Individuals who have a history of first-degree families who suffer from anxiety disorders are more at risk of suffering from anxiety disorders than the general population. Individuals born with lower transporters have a higher risk of anxiety disorders [10]. Neurotransmitters that play a role in anxiety disorders are norepinephrine, serotonin, and gamma-aminobutyric acid [11], [12]. Depression and anxiety are very important psychopathological comorbidities in patients with HIV/AIDS [13].

## Methods

### Subjects and Procedure

This is a cross-sectional study approach that is describing and analysing a situation in a given moment, which assesses the correlation between HADS and CD4 levels in PLWHA who are currently receiving ARV therapy at the HIV/AIDS Special Services Polyclinic Medan Haji general hospital. Inclusion criteria, namely participants are people with stage II and III HIV/AIDS based on WHO criteria, aged 25-49 years, long diagnosed < 4 years, had received line I ARV therapy > 6 months, are willing as respondents and could be interviewed, last education was minimal graduated from junior high school or equivalent. Exclusion criteria are suffering from other psychiatric diseases before being diagnosed with HIV/AIDS, a history of the use of alcohol and prohibited substances.

## Measurements

Before further analysis of the demographic characteristics of age, education, marital status, duration of diagnosis, occupational status must be tested for normality. Variables with a numerical scale are expressed in mean and standard deviations. HADS consists of 14 questions consisting of two subscales, namely anxiety (7 questions) and depression (7 questions). Each question is measured by 4 scale value, from a value of 0 (not at all) to a value of 3 (very often) [11], [12], [13]. Higher values indicate the existence of a problem. Answers are summed separately, i.e. assessments for anxiety and assessment for depression, with minimum and maximum amounts of 0 and 21 for each scale [11], [12], [15]. Recommended values are: 16-21 severe state cases, 11-15 values are cases moderate, grades 8-10 state mild cases, and less than 7 are not cases of anxiety or depression [1], [12], [14], [15].

## Data Analysis

Data was analysed by using SPSS ver. 22, the correlation was analyzed by using Pearson Correlation. For determining the level of relations between variables, based on the correlation coefficient value which is the output of SPSS as below [14]: coefficient correlation 0.00 –< 0.2 = very weak relationship; coefficient correlation 0.2 –< 0.4 = weak relationship; coefficient correlation 0.4 –< 0.6 = enough relationship; coefficient correlation 0.6 – 0.8 = strong relationship; coefficient correlation 0.81 – 1.00 = very strong relationship

## Results

The sample of the experiments of this study included 35 peoples diagnosed with HIV. Based on Table 2 shows that the sex proportion of PLWHA is 19 men,  $n = 54.3\%$ , and women as many as 16 people,  $n = 45.7\%$ . The proportion of education status for PLWHA 7 people (20%) is junior high school, 14 people (40%) high school, and 14 people (40%) Strata 1. The proportion of the marriage status of PLWHA is 16 people (45.7%) married, and 19 people (54.3%) are unmarried. The mean age of PLWHA is 34.914 with a standard of  $\pm 6.391$ . From the results of the normality test data using Shapiro-Wilk, the value of  $p = 0.133$  ( $p > 0.05$ ). The mean length of diagnosed PLWHA is 26.543 with an SD  $\pm 10.531$ . From the results of the normality test data using Shapiro-Wilk  $p$ -value = 0.333 ( $p > 0.05$ ). The mean length of getting ARV therapy for PLWHA is 25.143 with a standard of  $\pm 10.201$ . From the results of the normality test data using Shapiro-Wilk the value of  $p = 0.203$  ( $p > 0.05$ ). The mean CD4 level of PLWHA is 288.171 with the

SD  $\pm 88.955$ . From the results of the normality test of data using Shapiro-Wilk the value of  $p = 0.153$  ( $p > 0.05$ ).

**Table 2: Socio-demographic Characteristics**

Characteristics	mean $\pm$ SD n (%) p	N (%)	P
Age (years)	34.914 $\pm$ 6.391		0.133
Duration of arv treatment (months)	25.143 $\pm$ 10.201		0.203
Gender			
Man		19 (54.3%)	
Women		16 (45.7%)	
HIV clinical stadium			
Stage ii		18 (51.4 %)	
Stage iii		17 (54.3 %)	
Job-status			
Work		16 (45.7 %)	
Does not work		19 (54.3 %)	
Level of education			
Junior high school		7 (20 %)	
High school		14 (40 %)	
Pt		14 (40 %)	
Long diagnosed (months)	26.543 $\pm$ 10.531		0.333
Marital status			
Married		16 (45.7 %)	
Not married		19 (54.3 %)	

\*Shapiro-Wilk Test.

Based on Table 3, the average HADS-A score of PLWHA is 15.286, and the standard deviation is 2.244. From the results of the data normality test using Shapiro-Wilk, the  $p$ -value = 0.221 ( $p > 0.05$ ).

**Table 3: Average levels of HADS-A PLWHA**

Variable	Average	SD	P
Skor HADS-A PLWHA	15.286	$\pm 2.244$	0.221

\*Shapiro-Wilk Test.

Based on Table 4, the average HADS-D score of PLWHA is 15.286, and the standard deviation is 2.244. From the results of normality test data using Shapiro-Wilk, the value of  $p = 0.072$  ( $p > 0.05$ ).

**Table 4: Average levels of HADS-D PLWHA**

Variable	Average	SD	P
Skor HADS-D PLWHA	15.286	$\pm 2.244$	0.072

\*Shapiro-Wilk Test.

Table 5 shows that CD4 levels of PLWHA are with an average of 288.171 and the standard deviation is 88.955. From the results of the normality test of data using Shapiro-Wilk the value of  $p = 0.153$  ( $p > 0.05$ ).

**Table 5: Average CD4 Levels of PLWHA**

Variable	Average	SB	P
CD4 PLWHA Level	288.171	$\pm 88.955$	0.153

\*Shapiro-Wilk Test.

## Correlation Analysis

The results of the Pearson Correlation test of HADS-A and CD4 levels obtained  $p < 0.001$  ( $p < 0.05$ ) and it was concluded that there was a correlation between HADS-A scores and CD4 levels. The strength of the relationship between HADS-A scores and CD4 levels was  $r = -0.592$ , indicating a negative correlation with the strength of moderate correlation ( $r = 0.4 < 0.6$ ) (Table 6).

**Table 6: Correlation of HADS-A Scores and CD4 Levels of PLWHA**

	Level of CD4
Score HADS-A	r = -0.592 p < 0.001 n = 35

\*Pearson Correlation Test.

The results of the Pearson Correlation test of HADS-D score and CD4 levels obtained p values < 0, 001 (p < 0.05) and it was concluded that there was a correlation between HADS-D scores and CD4 levels. The strength of the relationship between the HADS-A score and CD4 level was -0.650, indicating a negative correlation with a strong correlation strength (r = 0.6 < 0.8) (Table 7).

**Table 7: Correlation of HADS-D Scores and CD4 Levels of PLWHA**

	Level of CD4
Score HADS-D	r = -0.650 p < 0.001 n = 35

\*Pearson Correlation Test.

## Discussion

On the demographic characteristics of the research, subjects showed that the average age of PLWHA was 34.914 years, with the standard deviation being 6.391. This result is in line with data from the Indonesian Ministry of Health Data and Information Center which reported the number of HIV infections according to age groups from 2010 to September 2014 in the age range of 25-49 years [17]. Report on the progress of HIV/AIDS & quarterly infectious social in 2017, reported the highest percentage of infections occurred in the age group 25-49 years [18]. A study conducted by Getachew T et al., in 2015 found that the highest age range for PLWHA was in the age of 30-39 years [19]. The study conducted by Saragih J in 2008 at H. Adam Malik General Hospital Medan also found that the highest ODHA age range was at the age of 30-39 years [20].

The proportion of sex of PLWHA was 19 people (54.3%) for men, and 16 people (45.7%) for women. Data from the Indonesian Ministry of Health's Data and Information Center, which reported the number of AIDS cases in Indonesia by sex from 1987 to September 2014, was more prevalent in the male group (54%) or almost twice compared to the female group (29%) [17]. The proportion of education levels for PLWHA is 7 people (20%), Senior high school as many as 14 people (40%) and S1 as many as 14 people (40%). The proportion of occupational status of PLWHA is 19 people (54.3%) working and 16 people (45.7%) not working. The proportion of the marriage status of PLWHA is 16 people (45.7%) with marital status and 19 people (54.3%) with unmarried status. A

study conducted by Saragih J in 2008 at H. Adam Malik General Hospital in Medan found slightly different results, namely the most educated PLWHA were high school (73%), followed by junior high school (14%), S1 (8%) and elementary school (5%), for the marriage status of PLWHA, the majority are married (51%), not married is (49%), the highest employment status is not working (62%), not working as much (36%) [20].

The proportion of HIV/AIDS clinical stadiums of PLWHA were 18 people (51.4%) in stage II, and 17 people (48.6%) were in stage III. HIV/AIDS Stadium is determined based on WHO criteria by looking at the clinical condition of PLWHA [2], [3]. The average length of diagnosed PLWHA is 26.543 months with a standard of 10.531. The length of time diagnosed with HIV/AIDS affects the mental condition and CD4 levels of PLWHA. From a study conducted by Rachel Ramovha in 2012 it was said that the initial response from someone who just found out that he was suffering from HIV/AIDS will occur in various responses, such as feeling not believe in diagnosis, denial, anger, anxiety, feelings of depression, to the worst is the thought of suicide [21]. The average length of ARV treatment for PLWHA is 25.143 months with standards deviation 10.201. From a study conducted by Saurez N, and colleagues in 2017 in Mexico, said that anxiety symptoms and depression symptoms were associated with poor rates of ARV treatment in PLWHA, and also associated with poor virology control and lower CD4 cell counts [22].

The mean HADS-A score of PLWHA is 15.286 and SD ± 2.244. This shows that PLWHA is in a moderate to severe anxiety condition, as indicated by the HADS-A score of 11-15 is moderate anxiety, and the HADS-A score is 16-21 is severe anxiety [15]. A study conducted by Monica N et al. in 2017 in Brazil anxiety symptoms were found as measured by the BAI measuring scale, getting results that were as much as 31.9% with mild anxiety, based on the BAI score of 11-19 [23].

The mean HADS-D score of PLWHA is 15,286 and the sd ± 2,244. This shows that PLWHA is in moderate to severe depression, indicated by the value of the HADS-D score is 11-15 is moderate anxiety, and the HADS-D score is 16-21 is severe anxiety.

In conclusion, from this study, it was found that there is a relationship between depression and anxiety symptom and CD4 level. There is a significant correlation between the HADS-A score and CD4 level with a correlation value of r = -0.592 indicating a negative correlation with a moderate correlation strength. There is a correlation between HADS-D scores and CD4 levels. The strength of the relationship between HADS-D scores and CD4 levels was r = -0.650 indicating a negative correlation with strong correlation strength.

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