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The Association between CD-4 Level, Stress and Depression Symptoms among People Living with HIV/AIDS

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Abstract

BACKGROUND: The lives of individuals diagnosed with HIV and the subsequent illness, AIDS, were often chaotic because these individuals deal with the physical, emotional, and interpersonal sequelae of this illness. Depressive symptoms and stress were common and impact on functioning, quality of life, and health status, highlighting the importance of diagnosis and treatment of patients with HIV infection. Psychiatric clinical practice and rating scales have come to play an ever-increasing role both in determining specific symptoms and diagnosing an individual condition. Descriptive reports of psychiatric morbidity among those with HIV infection, that relied primarily on self-report rating scales, described high rates of symptomatic depression and stress.

AIM: This study aimed to determine the proportion of depression among people living with HIV/AIDS using the BDI-II and PSS to determine a relationship between symptoms of depression and stress with CD4 counts.

METHODS: This study was a numerical correlative analytic study with a cross-sectional study approach that assessed the correlation between stress, depression and CD4 level in people with HIV/AIDS that were receiving ARV therapy in the Voluntary Counselling Test (VCT) Polyclinic of General Hospital Haji Medan by recruiting 46 subjects. CD4 level was examined in the Pramita Medan laboratory.

RESULTS: When analysis of BDI-II level and CD4 scores were done, a significant correlation was found (P < 0.05). The strength of the relationship between the BDI score and the CD4 score was 0.548 revealing a positive correlation with moderate correlation strength

CONCLUSION: We have shown a significant relationship between depression, stress and CD4 level among people with HIV/AIDS in Medan, Indonesia. Psychological distress may affect the immunity in infected people, leading to the disease progressivity.

Introduction

HIV/AIDS was first launched in 1981 in California [1]. According to the United Nations Program on HIV/AIDS (UNAIDS) data, it is estimated that in 2016 the total number of people living with HIV was around 36.7 million people with new HIV infection rates reaching 1.8 million. The report on the highest number of HIV prevalence in the world comes from Africa, with an estimated 5.1 million people. UNAIDS data in 2016 also showed the prevalence of people living with this infection in Indonesia reaching 620,000 with a new infection rate of 48,000 [2].

Based on data in 2014, HIV infections people were most prevalent in the heterosexual group (61.5%), followed by Injection Drug Users (IDU, 15.2%) and homosexuals (2.4%), and unknown risk factors (17.1%) [3].

While report on the situation of the development of HIV/AIDS and Sexually Transmitted Infectious Diseases (STID) in Indonesia between January-March 2017, the highest number of HIV infections according to the risk factors was in men like men (MLM) (28%, *n* = 2,867), followed by heterosexual risk factors (24%, *n* = 2,448) [4].

HIV is a cytopathic virus classified in the Retroviridae family, subfamily Lentiviridae, Lentivirus genus. Based on its structure HIV belongs to the family of retroviruses, including the RNA virus with a molecular weight of 9.7 kb (kilobases) [5]. Human Immunodeficiency Virus (HIV) is a retrovirus that infects cells and the immune system [6].

Acquired Immune Deficiency Syndrome (AIDS) is a collection of symptoms or diseases caused by decreased immunity due to infection with HIV which belongs to the retroviridae family. AIDS is

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the final stage of HIV infection. People with HIV and AIDS abbreviated as ODHA in Bahasa (Indonesian Language) are people who have been infected with HIV [7]. The course of HIV infection, CD4 T-lymphocyte count, number of viruses and clinical symptoms are classified into 3 phases: acute infection phase, latent phase of infection, chronic infection phase [5].

Psychosocial factors can influence the disease process with various biological parameters that reflect the progression of HIV infection, triggering a biological response through the limbic axis of the hypothalamic-pituitary-adrenal and sympathetic nervous system. Psychosocial factors with a high BDI-II score, high neurohormone factors such as cortisol and norepinephrine (NE) will significantly affect the progression of HIV infection to AIDS, resulting in CD level and an increase in the number of viruses [8], [9].

The Beck Depression Inventory is a self-assessment questionnaire for depression. BDI-II was developed as a concomitant level of validity and discriminant is acceptable among patients with HIV with an acceptable level of internal consistency. Analysis of the Main Components of BDI-II found three components with moderate correlation, one that assessed cognitive dimensions, the second assessed affective dimensions and the third with automatic dimensions of depression. While HIV and depression both have an automatic component, depression has affective, cognitive and automatic manifestations, with affective symptoms emerging as a disease while cognitive symptoms appear later, right for the assessment of the initial presentation of depression. Because of the symptoms of HIV infection and depression, it may be a symptom that is caused solely by depression [10].

In HIV infection, fatigue is formulated with the emergence of pathological, diffuse and extensive cell apoptosis which mainly attacks T lymphocytes so that the total and CD4 lymphocyte counts will gradually decrease. Psychological stress also triggers an increase in cortisol and catecholamine, which results in a decrease in the secretion of IL-1 and IL-2 by macrophages and a decrease in antibody formation/decrease in body resistance. The low IL-1 results in a decrease in T-helper monocytes and lymphocytes resulting in a decrease in antibody formation, and a decrease in phagocytic activity of inflammatory cells against germs that cause infection, thus individuals become susceptible to infection. While the increase in catecholamine results in suppression of T-helper cell activity and function. So, with the decrease in immunoglobulins, lymphocyte activity, and NK cells can be used as an indicator of psychological stress followed by suppressing the activity of the ability of macrophages and killer cells in the lysis of the virus [11].

Life stress can dramatically disturb people and their ability to function. Many studies have shown that the onset of episodes of depression is etiologically related to stressful life events. Stress can occur which causes induction of depressive symptoms in HIV-positive people. Roberts et al. conducted a cross-sectional study exploring the impact of stressful life events on emotional stress and life-threatening HIV-positive people. The relationship between acute life events and perceived stress affects the psychological state of dysfunctional attitudes, self-esteem, and neuroticism [12].

Based on the background mentioned above, the present study aimed to evaluate the relationship between CD4, stress, and depression in HIV/AIDS.

Material and Methods

Participants and Procedure

This study was a numerical correlative analytic study with a cross-sectional study approach that assessed the correlation between stress, depression and CD4 level in people with HIV/AIDS that were receiving ARV therapy in the Voluntary Counselling Test (VCT) Polyclinic of General Hospital Haji Medan by recruiting 46 subjects. CD4 level was examined in the Pramita Medan laboratory. The study period was from January to February 2019. Patients were recruited consecutively. Inclusion criteria included people with HIV/AIDS based on the WHO criteria, aged 20-50 years, had been diagnosed less than four years, received ARV therapy > 6 months, agreed to participate and could be interviewed, with last education at least Elementary School or equivalent. Exclusion criteria were people who had a history of mental disorders.

Beck's Depression Inventory-II

BDI-II is a 21-item scale measuring depression manifestations carried out by participants, with high internal consistency. It took about 10 minutes to complete. Each item consists of four statements (rated 0-3). Describes increasing the severity of the disorder in question. The interpretation of the results is as follows: a score of 5-9 shows normal ups and downs, 10-18 mild to moderate depression; 19-29 moderate to severe depression and 30-63 major depression [13].

Perceived Stress Scale

The Perceived Stress Scale (PSS) is used to measure psychological pressure. This instrument is a questionnaire consisting of 14 items that assess thoughts and feelings related to distress. Participants are asked on a 5-point scale to show how often they

have the same thoughts or feelings (0 never, 4 very often) [12].

CD4 T-lymphocytes

CD4 T lymphocytes are the main target for HIV infection due to viral affinity for CD4 surface markers. CD4 T-lymphocytes coordinate important immunological functions; loss of these functions shows a progressive decrease in the immune response. The results of CD4+ T-lymphocyte examination are used as the basis for clinical management and therapy of HIV-infected people. There are three categories of CD4 T-lymphocytes as follows: category 1 (500 cells/µl), category 2 (200-499 cells/µL), and category 3 (< 200 cells/µl) [13].

Infecting HIV T helper lymphocytes or via CD4 antigens. These infected lymphocytes then lysis when the new virion is released or removed by the cellular system immune. In progressive HIV infection, the T-lymphocyte CD4 is in number downhill. The absolute number of CD4 is an important measurement for predict, determine degrees, and monitor progression as well as response to treatment in HIV infection. Check the number of viruses' complete laboratory inspection for disease monitoring. The size inversely proportional to CD4, so the number of CD4 and the number of viruses immediately shows the patient's immune status. This is useful for determining a diagnosis, prognosis, and management of medication in patients who are infected with HIV [14].

Data Analysis

Subjects who fulfilled the criteria were asked for consent to take part in the study. They completed the demographic data and filled in the BDI-II and PSS questionnaires. Blood samples were taken to determine the CD4 level of the subjects.

Measurement of CD4 level was carried out in a private laboratory in Medan using flow cytometric.

Flow cytometry is a method that can be used for identifying the surface characteristics of each cell with ability separating cells that are in a suspension according to the characteristics each automatically through a gap penetrated by a beam of laser light. The method of flow cytometry continues to grow in line with electrical development of computers and reagents, including their use of a monoclonal antibody. Until now, measurements with flow cytometry use fluorescence labels, in addition to measuring cell size, too can detect cell wall markers, intracellular granules, infra-structure cytoplasm, and the cell nucleus.

All data were processed with SPSS. Before data analysis, normality test using the Shapiro-Wilk test was carried out because numbers of samples were less than 50. Then data were analysed to obtain a correlation value (r). If data were normally distributed, data was going to be analysed using the Pearson Correlation test. If data was not normally distributed, data analysis was performed using the Spearman correlation test. A value of $p < 0.05$ was considered significant.

Ethical Consideration

This study was approved by the Ethical Committee of Research, Faculty of Medicine Universitas Sumatera Utara (ID 215/KEPK FK USU-RSUP HAM/2018). Informed verbal consent was ensured before administration of the questionnaire. The beneficiaries were taken into consideration, and subjects were not coerced to participate in the study and confidentiality was maintained.

Results

We enrolled 46 patients in the study. The demographic description of patients was presented in Table 1. Variables with categorical scales were presented in frequency and proportion, and variables with numerical scales are presented in mean and standard deviation.

Table 1: Distribution of Demographic Characteristics of Participants

Variable	n	%
Gender		
Male	28	60.9
Female	18	39.1
Age (year)		
20-30	21	45.7
31-40	20	43.5
41-50	5	10.9
Education		
Junior High School	7	15.2
Senior High School	21	45.7
Undergraduate	18	39.1
Marital Status		
Single	27	58.7
Married	19	41.3
HIV stage		
I	19	41.3
II	22	47.8
III/IV	5	10.9
Transmission		
Sex	21	45.7
Drugs	25	54.3

Table 1 showed that the proportion of the sex of patients was male (60.9%) and female (39.1%). The age distribution was 20-30 years (45.7%), 31-40 years (43.5%), and 41-50 years (10.9%).

The proportion of patients with junior high school education, high school education, and undergraduate education were 15.2%, 45.7%, and 39.1%, respectively. The majority of patients also went into HIV stage I (41.3%) and stage II (47.8%), while the remaining were classified as stage III-IV (10.9%). HIV transmission occurred through sex (45.7%) and drugs (54.3%).

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Table 2: Distribution of stress (PSS scores) and depression (BDI-II Scores) among HIV Patients

Variable	Average	SD	Min	Max
BDI-II	46.35	16.60	24	63
PSS	30.63	8.12	15	40

Table 2 showed that the PSS scores with a mean of 30.63, the standard deviation of 8.12, a minimum value of 15, and a maximum value of 40. The BDI-II score with a mean of 46.35 and a standard deviation of 16.60, a minimum value of 24, and a maximum value of 63.

Table 3: Distribution of CD4 among HIV Patients

Variable	Average	SD	Min	Max
CD4	345,30	104.67	158	564

Table 3 showed that CD4 counts with a mean of 345.00, the standard deviation of 104.46, the minimum value of 158, and the maximum value of 564.

The Shapiro Wilk Test showed that the CD4 score was normally distributed. Therefore a correlative test of baseline data used the Pearson Correlation test. When analysis of BDI-II level and CD4 scores were done, a significant correlation was found ($P < 0.05$). The strength of the relationship between the BDI score and the CD4 score was 0.548 revealing a positive correlation with moderate correlation strength ($r = 0.5 - < 0.6$).

The results of the Pearson Correlation test for PSS level and CD4 scores obtained a P-value of < 0.05, showing a significant correlation between PSS and CD4 score. The strength of the relationship between PSS scores and CD4 was 0.45 meaning a positive correlation with moderate correlation strength ($r = 0.5 - < 0.6$).

Discussion

Depression can affect behaviour and contribute to adherence to therapy so that HIV infection damages immune function. A study by Moosa (2005) recruiting forty-one people aged 18 years or over from an HIV outpatient clinic showed that about 56% of patients in this study had significant depressive symptoms (BDI > 10). However, this study did not find a significant correlation between BDI and CD4 scores ($r = 0.274$, $p > 0.05$) [13].

In this study, we also showed similar findings as described previously by Moosa et al., where BDI-II was an appropriate tool to determine depression in these patients. Nevertheless, our study was able to show a positive correlation between BDI-II scores and CD4 scores. This was in line with a longitudinal study conducted by Ironson et al., (2015) of 177 individuals with HIV/AIDS that underwent ARV treatment. The study showed that psychosocial and neurohormone influences the predictors of the progression of HIV/AIDS infection. Psychosocial factors determined by a high BDI score, high neurohormone factors such as cortisol and norepinephrine significantly affected the progression of HIV infection to AIDS by allowing a significant decrease in CD4 level and an increase in viral load [9].

In 2007, a study by Remor et al., at the Outpatient Clinic at the Madrid Teaching Hospital assessed psychological distress as measured by the PSS was associated with a decrease in CD4 level in 59 men and 41 women living with HIV/AIDS within six months. The study showed that the perceived stress was significantly (p = 0,0001) associated with a decrease in CD4 level in people living with HIV, i.e. every increase in 1 point PSS score (score between 3 and 43), is followed by a decrease in the score of 4.82 of CD4 counts after observation for six months [15]. We did not follow the patients in our study. Nevertheless, we have shown that the PSS score had a moderate correlation with the CD4 level among our patients.

In conclusion, we have shown a significant relationship between depression, stress and CD4 level among people with HIV/AIDS in Medan, Indonesia. Psychological distress may affect the immunity in infected people, leading to the disease progressivity. Routine screening of psychosocial status in these population is important to determine their mental health status and allow early management and prevent disease progression.

Acknowledgements

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