

COGNITIVE FUNCTION DISORDER AS A REFLECTION OF IMMUNITY STATUS IN PEOPLE LIVING WITH HIV/AIDS

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ABSTRACT

Comorbidity of psychiatric disorder has been linked with HIV (human immunodeficiency virus) since the early epidemics of AIDS (acquired immunodeficiency syndrome), and until recently there have been many literatures focusing on psychiatric problems in relations with HIV seropositive patients (Morrison 2002). Among these patients, 72.3% have psychiatric problems (Cohen et al. 2002). The existing psychiatric problems may exist as dementia, delirium, anxiety, adaptation disorder, depression, substance abuse, and even suicide (Saddock 2003). Data from AIDS treatment house in the United States showed that 65% of the patients had psychiatric disorder other than substance dependency and neurocognitive disorders. If the last two diagnoses are included, the prevalence rate becomes 99.8% (Cohen 1998). In addition, regardless of its correlation with disease progressiveness, the presence of psychiatric disorder may influence life quality, social function, and general health condition of the patients with HIV seropositive (Sherbourne et al 2000). The identification of psychiatric disorders, particularly the disturbance of cognitive function in HIV seropositive patients, becomes important since it has correlation with HIV seropositive progressiveness to become AIDS and to maintain the patients' quality of life. This study examined cognitive function of 34 patients with HIV seropositive in Dr Soetomo Hospital, Surabaya, and correlated it with their immunological status. We found 22 samples in MMSE test who had cognitive disorder (64.7%), and the remaining 12 samples were in normal condition (35.3%). Short memory disorder was found in 19 samples (55.9%) and the other 15 samples were normal (44.1%). The reduction of CD4 immunological status to less than 200 was found 23 respondents (67.6%) and the others had CD4 of more than 200. Significant correlation was found between cognitive function disorder and immunological status of individuals with HIV seropositive ($p = 0.021$). The cognitive function disorder may reflect immunological status of HIV patients. Therefore, regular testing of cognitive function may be a practical and cost-saving marker of CD4 reduction. Studies using longitudinal design are suggested to find correlation between cognitive function disorder and immunological status with period of cognitive function restoration after receiving ARV. Case-control studies should also be performed to find causal correlation and correlation of each MMSE test items with the decrease of immunity to create a more sensitive measuring tool and to identify early symptoms of cognitive disorder.

Keywords: cognitive function, immunity status, HIV/AIDS

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INTRODUCTION

Comorbidity of psychiatric disorder has been linked with HIV (human immunodeficiency virus) since the early epidemics of AIDS (acquired immunodeficiency syndrome), and until recently there have been many literatures focusing on psychiatric problems in relations with HIV seropositive patients (Morrison 2002). The existing psychiatric problems may exist as dementia, delirium, anxiety, adaptation disorder, depression, substance abuse, and even suicide (Saddock 2003). Recently, due to the advance in medical management and antiretroviral drug therapy, patients with HIV may have a longer age. As a consequence, the patient may have longer time for having misery from the symptoms

of pain, malaise, insomnia, anxiety, depression, as well as other psychiatric disorders (Cohen et al. 2002). In the autopsy of AIDS patients, 75-90% were found with brain damage. At least 50% had neuropsychiatric complication, such as HIV encephalopathy and almost 10% had early sign of neuropsychiatric disorder (Kaplan & Saddock 2003).

The identification of psychiatric disorders, particularly the disturbance of cognitive function in HIV seropositive patients, becomes important since it has correlation with HIV seropositive progressiveness to become AIDS. The presence of stress may enhance the course of the disease, and depressed HIV seropositive patients may also enhance the course of the disease to

become AIDS, from averagely 7.6 years to 6.2 years (Laserman 1999). In addition, regardless of its correlation with disease progress, psychiatric disorder may have effect on the quality of life, social function, general health condition of HIV seropositive patients (Sherbourne et al. 2000).

ARV treatment may provide a longer life expectancy, enabling the patients to perform their functions in longer time. However, the virus itself may pass the blood brain barrier. Possibly, the virus enters brain at the early time of systemic infection (McGuire 2003) and it induces brain damage. Neuropsychiatric complications are affected by CD4 and by the number of viruses in the body. The number of virus leads to the emergence of reactions from various inflammatory components, either cellular or non-cellular. This immunological reaction may enter the brain and induce damages in nervous cells as well as the connective tissues (Treisman and Kaplina 2002), resulting in cognitive function disorder.

This far, there have been no data on the correlation between psychiatric disorders, particularly cognitive function disorder in HIV seropositive patients, and their immunity status. Therefore, regular monitoring of the cognitive function may provide immunity status profile of a HIV patient. The earlier the identification of cognitive function in a HIV patient, the earlier the treatment can be provided. Individuals who receive ARV therapy may have a longer life expectancy. However, without taking into account HIV complications in brain function, including their psychological conditions, the individuals' function may be less optimal nad their life quality will be decreasing. This initial study was, therefore, intended to provide data on correlation between cognitive function and HIV seropositive in HIV/AIDS patients with a hope to be able to improve the patients' management. This study revealed correlation of cognitive function disorder and its severity with immunity status in HIV seropositive patients. The results can be used as basic data for optimizing psychiatric management of positive HIV patients in Dr Soetomo Hospital, Surabaya.

MATERIALS AND METHODS

This was an analytic observational study to prove correlation between cognitive function disorder and immunity status in HIV seropositive patients in Infectious Disease Intermediate Treatment clinic, Dr Soetomo Hospital, Surabaya. Sampling was taken for three months using total sampling. The inclusion criteria were as follows: age less than 18 years or more than 55 years, patients diagnosed with HIV seropositive, able to write and read in Bahasa Indonesia, and willing to

participate in this study. The patient was excluded if they had psychosis and/or mental retardation, and had psychosocial stressor score with Holmes and Rahe scale of > 200.

The operational definitions are as follows: HIV seropositive patients were those whose result of blood test was reactive or positive for examination with three methods based on standard procedure in Infectious Disease Intermediate Treatment ward, Dr Soetomo Hospital, Surabaya. HIV stages were referred to WHO standard determined during the patient examination by internist at Infectious Disease Intermediate Treatment ward, Dr Soetomo Hospital, Surabaya. Cognitive function is the function of the cortex in the brain, identified from orientation, attention, memories, calculation, speech, and thinking process, as measured with Folstein's Mini Mental State Examination (MMSE) and short visual memory test. Depression is a depressive condition, not depressive disorder, measured with Beck Depression Inventori (BDI). Anxiety was anxiety condition, not anxiety disorder, measured with Hamilton Anxiety Rating Scale (HARS). Psychosocial stressor was psychosocial condition experienced during the last three months, measured with Rahe & Holmes scale. ARV (Antri Retro Virus) was drugs given with WHO standard for HIV seropositive patients who met the criteria of treatment. Immunity status was immunity system reaction of an individual against the entry of antigen, as measured with cellular immunity, i.e., the CD4 level.

RESULTS

Respondents who met the criteria comprised 34 individuals from 42 samples with positive HIV/AIDS who underwent outpatient treatment at Infectious Disease Clinic, Dr Soetomo Hospital, Surabaya. Based on demographic data, the results were as follows: mean age of the sample was a year with a standard deviation of years distributed with age range. Figure 1 shows that the most common age was 20-29 years, found in 17 individuals (50%).

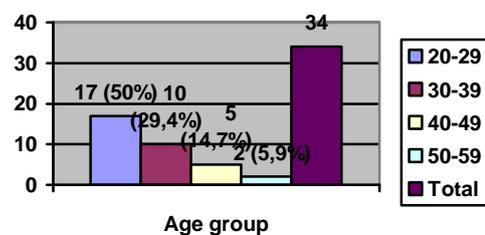


Figure 1. Distribution of age

Distribution according to gender (Figure 2) shows 8.8% were female and 91.2% were male, each comprising 3 and 31 respondents.

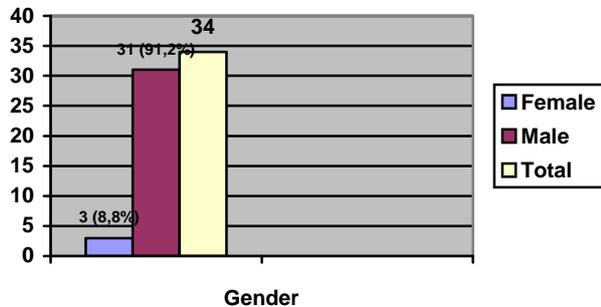


Figure 2. Distribution of gender.

In regard with disease severity, mostly were respondents in stage 3, comprising 21 individuals (61.8%), and the least were those in stage 2 and stage 4, each 1 individual (2.9%) (Figure 3).

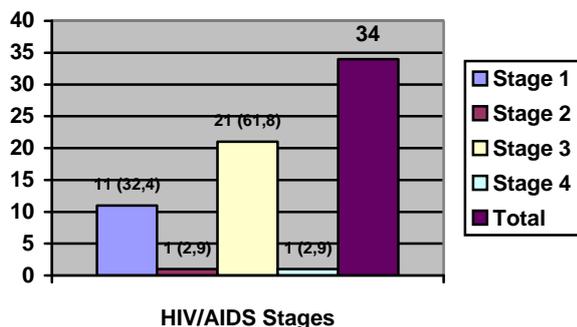


Figure 3. Distribution according to HIV stages

In regard with the time taken to know the presence of HIV (Figure 4), 26 respondents (76.5%) had realized for more than 6 months, while 8 respondents (23.5%) had realized less than 6 months.

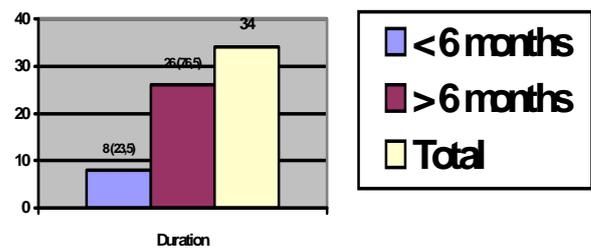


Figure 4. Distribution according to time to know the presence of HIV

As many as 17 respondents (50%) regularly used ARV, and 3 respondents (8.8%) used ARV irregularly. The remaining 14 respondents (41.2%) were without ARV therapy (Figure 5).

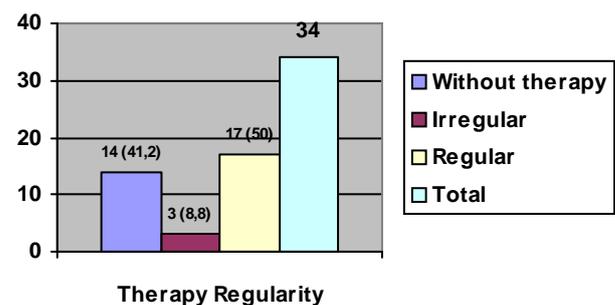


Figure 5. Distribution according to ARV therapy regularity

Depression distribution in HIV patients were mostly mild depression, which was found in 11 respondents (32.4%), while those with normal depression were 12 respondents (35.3%) (Figure 6).

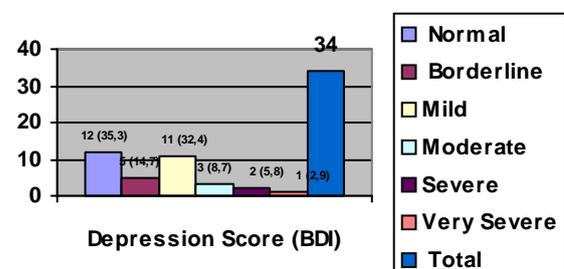


Figure 6. Distribution according to depression score (BDI)

Measurement of the level of anxiety revealed that 11 respondents (32.4%) were not anxious, while the remaining (67.6%) were anxious in a variety of levels: mild (32.4%), moderate (17.6%), severe (14.7%) and very severe (2.9%) (Figure 7).

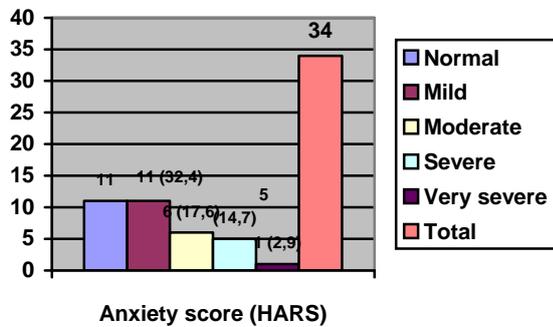


Figure 7. Distribution according to level of anxiety (HARS).

Cognitive function examination revealed that the gradation of cognitive function according to MMSE was normally distributed. Twelve respondents (35.3%) had no mild cognitive deficit, moderate cognitive deficit was found in 21 respondents (61.8%), and severe deficit was found in 1 respondent (2.9%) (Figure 8).

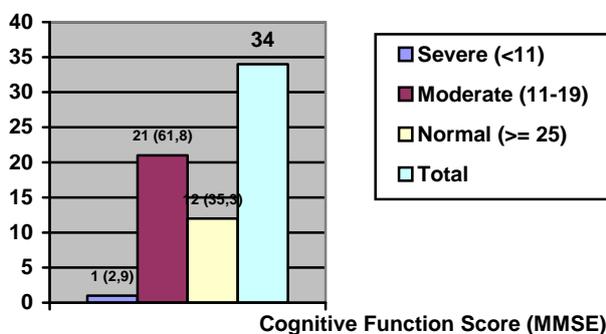


Figure 8. Distribution according to MMSE score.

Short memory test showed 19 respondents (55.9%) had memory deficit, while 15 respondents were normal, no deficit (44.1%) (Figure 9).

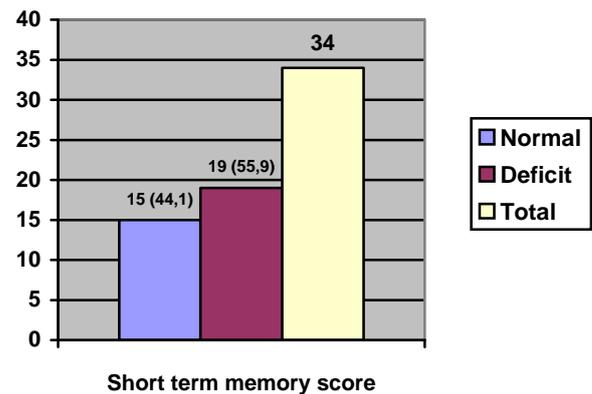


Figure 9. Distribution according to short memory score

Examination of lymphocyte (CD4) count using cut-off 200 showed that 23 respondents (67.6%) had less than 200, while 11 respondents (32.4%) had more than 200 (Figure 10).

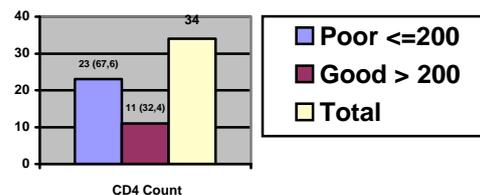


Figure 10. Distribution according to CD4 count

The result of statistical analysis on the correlation between MMSE score and short memory score with CD4 count was as follows: MMSE score had correlation with immunity status (CD4) with significance level of $p = 0.021$ (Table 1). However, the score of memory had no correlation with immunity status (CD4), with significance level of $p = 0.398$ (Table 2).

Table 1. Correlation MMSE score and the number of CD4.

		MMSE			Total
		Normal (> 24)	Moderate (11-19)	Severe (<11)	
CD4	Poor ≤ 200	1	11	11	23
	Good > 200	0	10	1	11
Total		1	21	12	34

$p = 0021$

Table 2. Correlation between memory score and CD4 count

		Memory		Total
		Deficit (<7)	Normal (>=7)	
CD4	Poor ≤ 200	14	9	23
	Rich > 200	5	6	11
Total		19	15	34

p = 0.398

DISCUSSION

This study provides a profile of HIV seropositive patients with cognitive disorder at Infectious Disease Intermediate Treatment Unit, Dr Soetomo Hospital, Surabaya. It was also aimed to prove correlation between cognitive status of HIV patients with their immunity status. The general profiles on the severity of cognitive disorder were that 22 samples had cognitive disorder (64.7%), while the remaining 12 samples were normal (35.3%) in their MMSE score. This study found a higher score than that found by Blanchard who studied 432 respondents, from which 55.1% had cognitive disorder, while the remaining 44.9% had no disorder. Different from this study, Blanchard performed his study to all respondents receiving antiretroviral therapy (Blanchard 2004). This difference may be present because respondents in this study were those who had not received ARV therapy and those who had received ARV therapy, so that cognitive function disorder was more apparent than in those receiving ARV therapy in Blanchard's study (2004). Tresimana (2002) suggested that the use of ARV was able to repair cognitive function. Another possibility is that half of the respondents who had not received ARV therapy had just known their HIV seropositive status, meaning that they were still at the time of adaptation to psychological stressor that emerged due to their suffering from HIV. Adaptation that provides psychological effects of depression and/or anxiety may disturb cognitive function.

Correlation analysis revealed significant correlation between cognitive function disorder (MMSE) and immunity system, the CD4 (p = 0.021). Such condition indicates that cognitive function disorder has correlation with decreasing CD4. The decreased CD4 may reflect disordered SSP immune system and causes brain function disorder in its various manifestations, such as cognitive function. Therefore, regular test of cognitive function can be used as a practical and cost-saving early marker to identify brain function resulting from CD4 reduction.

In addition to immune component that enters the brain, the virus itself is able to pass the blood brain barrier. It was suspected that the virus entered the brain at the initial stage of systemic infection (McGuire 2003). It was possible that gp120 glycoprotein envelope played a role in the passing of the virus through the blood brain barrier, although the real event remains unclear (Banks 2001). HIV is a neurovirulent virus, but it is not neurotropic. The virus induces central nerve system without infecting neuron. The virus is able to rapidly infect macrophage and microglia. The entry of macrophage into brain depends largely on the presence of inflammation. In advanced stage, more predominantly infected sites are perivascular macrophage and microglia, while meningeal macrophage is infected in acute seroconversion reaction. Ten percent of central nervous system comprised of microglia. Branched microglia are resting cells by reducing the activity of secretion and phagocyte, forming cellular tissues in whole central nervous system. In contrast, macrophage perivascular is a weak antigen presenter (Diesing et al. 2002).

According to Treismana and Kaplina (2002), neuropsychiatric complication is affected, in addition to CD4, by the number of viruses in the body. The number of virus caused the emergence of cellular and non-cellular inflammatory components. This immunological reaction may enter the brain and causes damage in nerve cells and its connective tissues (Treismana and Kaplina 2002). Two most possible sources at the initial stage of invasion were infected CD4 and free virion cells. At the advanced stage of AIDS, HIV invasion to central nervous system was thought to passing the BBB (Blood Brain Barrier). Both reach high level before the development of antiretroviral immune response. HIV attacks brain cells, the microglia, that protects other parts of the brain from infection. Microglia is a derivate of white blood cells, which are the target of HIV in whole body. These infection-fighter cells have receptors to enter the surface, which is called as CD4. Through CD4 the virus was placed within the vestibule of the cells. The damage of microglia causes inhibition in the system that protects neuron cells, through the disturbance of immune system, and the production of proinflammatory cytokines like TNF-alpha, IL-1 (interleukin-1) and IL-6. It is possible that IL-6 affects the work of nerve system, resulting in cognitive disorder as can be seen in the presence of IL-6 increase along with the increasing age during which the cognitive process abnormality occurs (Nancy 2002).

Although in 19 (55.9%) of the patients had short visual memory deficit, in the analysis of correlation between memory disorder and immune system of CD4, there was no significant correlation with the same significance

level of $p = 0.398$. This condition is possible since memory is the part of cognitive function. Memory examination itself, however, was not significant yet, although the reduction was found in 55.9% of the patients. Significance was found after undergoing comprehensive cognitive function examination. Another possibility was that visual memory of the patient was still sufficient, not a good marker to reflect the CD4 reduction.

The shortcoming of this study was that it did not divide the use of ARV in more details that should have been enabled the authors to assess the range in which the use of ARV would be significant. This study did not break and count any items of MMSE test to find which item was the most sensitive for early detection of cognitive function disorder since the profile of immunological status reduction according to time was not linear. To determine whether the profile of cognitive function reduction is parallel with immunological status reduction, a longitudinal study by investigating cognitive function and immunological status of HIV seropositive patients should be performed regularly, and comparison between ARV and non-ARV treatment should also be undertaken.

CONCLUSION

This study reveals significant correlation between cognitive function disorder (MMSE) and immunity system CD4 ($p = 0.021$). Such condition indicates that cognitive function disorder has correlation with CD4. It may reflect the immunological status of HIV patient. Therefore, regular testing of cognitive function can be used to obtain practical and cost-saving indication of CD4 reduction.

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Several studies have identified increased age as a risk factor for the development of cognitive impairment in human immunodeficiency virus (HIV)-infected subjects, but few have examined the potential synergistic effect of age and HIV serostatus on cognitive decline. The authors examined the possible combined effect of age and HIV serostatus on cognitive decline in 254 subjects stratified by age group and HIV status. After controlling for the effect of education, there were significant effects for serostatus and age group on overall cognitive impairment and a number of neuropsychological measures. Cognitive function disorder as a reflection of immunity status in people living with HIV/AIDS. NUTRITION FOR PEOPLE LIVING WITH HIV/AIDS: A VITAL AND OFTEN NEGLECTED COMPONENT OF HOME-BASED CARE Malnutrition is a serious danger for people living with HIV/AIDS. Even at the early stages of HIV infection when no symptoms are apparent, HIV makes demands on the body's nutritional status. The risk of malnutrition increases significantly during the course of the infection. Good nutrition cannot cure AIDS or prevent HIV infection, but it can help to maintain and improve the nutritional status of a person with HIV/AIDS and delay the progression from HIV to AIDS-related diseases. It can help for people with HIV/AIDS in hospitals and other institutional settings, including hospices. The People Living with HIV Stigma Index was used to measure stigma and discrimination, and a short version of general health questionnaire (GHQ-12) was used to measure mental disorders. Multivariate logistic regression analysis was conducted. AIDS-related stigma and discrimination impede millions of PLHIV from accessing and benefiting from effective prevention and treatment services [1]. As a result, approximately 50-60% of HIV-infected people are unaware of their sero-status, and many choose to hide it [2]. Furthermore, AIDS-related stigma and discrimination have been found to be associated with delays in seeking care [3] and potential.