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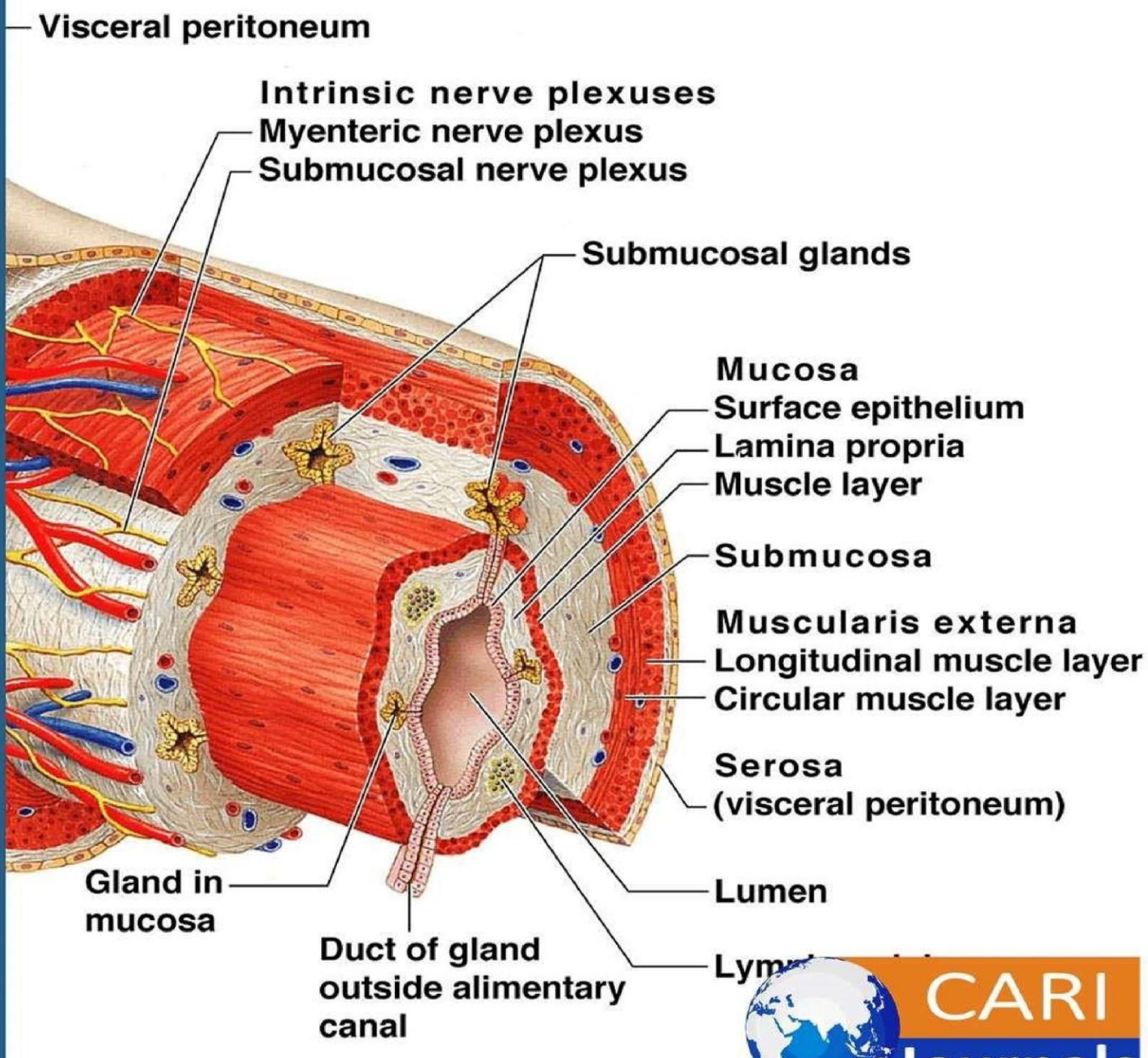

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A STUDY ON TOTAL LYMPHOCYTE COUNT AND CD4 COUNT IN HIV AFFECTED PATIENTS

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ABSTRACT

Purpose: The study aimed to assess the total lymphocyte count and CD4 count in HIV affected patients.

Methodology: The approach we used in this study was to gather and analyze a wide range of research articles.

Findings: Worldwide estimates of people living with Human Immunodeficiency Virus was approximately 32 million in 2007 with thousands of people getting infected every day. Most people living with HIV are from developing countries with less than 5% receiving antiretroviral therapy. In 2009, an estimated 2.6 million people became infected out of which approximately 1.8 million were from sub-Saharan Africa. The initiation of antiretroviral therapy is based on CD4 counts of less than 350 cells/mm^3 according to the World Health Organization (WHO) and Centre for Disease Control (CDC). The determination of CD4 count however in resource-limited localities is difficult. A total lymphocyte count (TLC) of <1200 cells/mm^3 has been recommended in addition to WHO staging (stage II) of the disease, for the initiation of antiretroviral therapy in such localities.

Unique contribution to theory, practice and policy: The use of absolute lymphocyte count as a marker for HIV progression has been argued in many quarters over the years. Studies have suggested that when the absolute lymphocyte count is used in conjunction with blood hemoglobin, it gives a more sensitive marker for HIV progression with other studies discrediting the use of TLC in such settings.

Key words: *lymphocyte count, CD4, RBC*

INTRODUCTION

HIV is a virus that attacks the human body's immune system, causing AIDS. HIV is a retrovirus that uses RNA. HIV attacks a type of white blood cell called a T lymphocyte, which serves to ward off infections. These specific T lymphocytes are white blood cells that have CD4 as a marker on their surface. HIV infection will damage the T lymphocytes, especially CD4+ cells, which can cause immunodeficiency (Nnoruka, et.al, 2007). Over time, HIV will become AIDS when the CD4+ T lymphocyte levels drop below 200 cells/µL. The reduced CD4 value in the

human body shows that reduced white blood cells or lymphocytes were supposed to play a role in overcoming infections that enter the human body. In people with a good immune system, CD4 levels range from 1400 to 1500 cells/µL, whereas in people with an immune system impaired by HIV, CD4 levels have decreased, even to zero.

HIV is a virus that attacks and destroys the body's immune system. When the immune system is damaged or weak, the body is susceptible to various diseases that exist around us, such as tuberculosis, diarrhea, skin diseases, etc. HIV transmission can occur through the sharing of bodily fluids, including sex with someone who has HIV/AIDS, blood or wound contact and blood transfusions, sharing needles, and from an infected mother to her unborn child (Miller, et.al, 1999). This literature aims to determine the effect of depression on the decline of CD4 cells in HIV patients.

The Total lymphocyte count and CD4 count is the determination of the concentration of CD4 and Total lymphocyte in the blood. The associated immune deficiency in human immunodeficiency virus (HIV) patients leading to infection by opportunistic pathogen is ascribed to depletion of CD4 T-cells (Lepri, et.al, 1998). CD4 count can therefore be regarded as the accurate measurement of the robustness and functionality of the immune capability to protect the body against general infection. CD4 and T lymphocyte cell depletion is one of the hallmarks of progression of HIV infection and a major indicator of the stage of the disease in HIV infected individuals (WHO, 2002). World Health Organization recommended that most treatment initiation decisions be guided by CD4 measurement and clinical staging (Rodríguez, et.al, 2013). Previous study has shown good correlation between CD4 count and development of various complications in HIV/AIDS (Tinarwo, et.al, 2019). Patients with low CD4 and T lymphocyte cell count have been reported as long-time infected patients than those with higher CD4 count (Agrawal, et.al, 2016).

Retroviral disease has become a matter of relative chronicity in patients that have access to antiretroviral therapy and have benefitted greatly in marked reductions in morbidity and mortality. General treatment guidelines for the treatment of HIV-infected patients in many countries have adopted three approaches for the initiation of antiretroviral therapy. Early intervention in asymptomatic patients involves the commencement of antiretroviral therapy once the CD4 count is less than < 500 cells/µl. A less intensive approach is to recommend antiretroviral therapy when the CD4 count falls to 350 cells/µl (Akinola et.al, 2004).

Total lymphocyte count (TLC) is a derived immunological marker calculated from white blood cell count and relative lymphocyte count. For instance, if a patient has a total white blood cell count of 6.0×10^9/L and relative lymphocyte count of 40% obtained from differential leukocyte count, total lymphocyte count of such patient would be 2.4×10^9/L. There are series of controversial research outcomes over the use of TLC as a surrogate marker for CD4 count estimation (Wande, et.al, 2019). Decisions became difficult to take as our health care providers

insist on scientific evidence on the use of total lymphocyte count as an inexpensive point-of care alternative for absolute CD4 count.

LITERATURE REVIEW

The HIV epidemic in Indonesia is already a global crisis and one of the most serious threats to development and social progress. This epidemic is expected to increase rapidly. The sharp increase is mostly in adult cases, especially drug users, sex workers, and their customers. Based on the 2016 Ministry of Health report, the progress of HIV in Indonesia in the fourth quarter from October to December 2016 included as many as 13,287 people (Tinarwo, et.al, 2019). The highest percentage of HIV infection was reported in the age group of 25–49 years (68%) followed by the age group of 20–24 years (18.1%) and then the age group of 50 years (6.6%). The ratio of HIV between men and women is 2:1. The percentage of HIV risk factors is the highest in the heterosexual category (53%), followed by the MSM (Men Sex Men) category (35%), then others (11%), and, finally, sterile hypodermic needle use among IDUs (1%)[3] (Agrawal, et.al, 2016).

In other countries where patients have limited financial resources, treatment decisions are typically delayed until the CD4 count becomes less than 200 cells/µl (Lepri, et.al, 1998). Recent study by the French researchers at the 7th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention in Kuala Lumpur, Malaysia (Agrawal, et.al, 2016) showed that people with HIV who start treatment with CD4 counts above 500, after the first phase of primary infection is over, are much more likely to experience substantial reductions in the reservoir of HIV- infected cells in their bodies, making them strong candidates for future research studies that seek to control HIV without medication. The French group found that people with HIV who started treatment with a CD4 cell count above 500 were 56 times more likely to experience a normalization of immune function and a reduction in HIV DNA to low levels when compared to people who started treatment at lower CD4 counts. Although it is well established that people who start HIV treatment with a CD4 count above 500 stand a better chance of achieving a CD4 cell count in the normal range (defined as 900 to 1000 cells/mm3 according to the study), studies of people treated in chronic infection have not found evidence of a substantial reduction in HIV DNA (the reservoir of HIV within cells) over time (Nnoruka, et.al, 2007). This outcome gives strong support to earlier interventions and showed the likely future direction in HIV treatment modalities. It then becomes very vital at every health institution involved in HIV/AIDS testing and treatment to establish the usefulness of total lymphocyte count as an alternative and inexpensive immunological marker for CD4 count where flowcytometric technique is not available. This is imperative not only at CD4 count threshold of < 200 and ≤ 350 cells/µl only but also at < 500 and ≥ 500 cells/µl thresholds (Maini, et.al, 1996).

Monitoring individuals with HIV infection/AIDS involves the use of expensive tools, which are not readily available in resource-limited settings. In April 2002, the World Health Organization

(WHO) recommended that, when a CD4 cell count is not available or is not affordable to obtain for affected individuals, a total lymphocyte count of less than 1000–1200 lymphocytes/mm^3 in individuals with stage II or III disease be used as an indication to initiate antiretroviral therapy (Rodríguez, et.al, 2013). This recommendation was based on rigorous evaluation of data obtained almost exclusively from developed countries. In 1996, Maini et.al reported that total lymphocyte count could not be used as a surrogate for CD4 cell count in monitoring response to antiretroviral therapy. There is limited information on the relationship between CD4 cell counts and total lymphocyte count and other hematological indices in resource-limited settings (Tinarwo, et.al, 2019). This study was initiated to ascertain the reliability of total lymphocyte count as a substitute for CD4 cell count, determine the relationship of other hematological indices with CD4 cell count, and observe the influence of the person's sex, if any, on data collected.

Recently published PEPFAR II goals stated that an estimate of 100,000 children needed to be newly initiated on highly active antiretroviral therapy before 2013 (PEPFAR, 2011). In line with this, new sites have been established throughout Nigerian states including Ekiti. Five new sites are receiving services from our treatment center across Ekiti state as a comprehensive HIV treatment center owing to lack of CD4 cyflow counter. Most of those sites across the country do not have cyflow counter to perform routine CD4 count analysis, and flow cytometry remains the reference method for the performance of CD4 count (Angelo, et.al, 2007). Even in centers where CD4 equipment are available, treatment decisions are sometimes delayed owing to varying factors ranging from proximity of the patients to testing and treatment sites, equipment breakdown, non-availability of reagents on consistent basis to late access to service engineers (Rodríguez, et.al, 2013).

In established market economies, the CD4 lymphocyte count is measured in HIV-1 infected people every three months to guide decisions about prognosis, starting and changing prescriptions for highly active antiretroviral therapy (HAART), and opportunistic infection prophylaxis. However, flow cytometry to measure lymphocyte subsets requires trained personnel and perishable reagents, extensive specimen processing and infrastructure. There are data suggesting that in resource poor settings, the cost of monitoring HIV-1 treatment exceeds the cost of HAART (Akinola, et.al, 2004). While new technologies are becoming available for CD4 count testing, they are not readily available and remain expensive.

Measurement of total lymphocyte count (TLC) is straightforward and does not rely on prohibitively complex systems. We therefore assessed the utility of TLC measurement as a predictive marker for the development of AIDS defining opportunistic infections (ADOI) in a large cohort of HIV-1 positive patients (Miller, et.al, 1999).

METHODOLOGY

The approach we used in this study was to gather and analyze a wide range of research articles related to the effect of depression on the deterioration of CD4 cells in HIV patients. Articles were obtained from a variety of electronic journals, including EBSCOhost, NCBI, BioMed Central, Google Scholar, PLOS, and PubMed, using the keywords depression, immunology, CD4, and HIV. The literature review inclusion criteria were articles which can be accessed in full text.

FINDINGS

High HIV prevalence tends to increase from year to year. People with HIV have a reciprocal relationship with psychiatric disorders, such as depression. Most studies on the HIV-positive population have shown a higher level of depression among women than men.

Based on extensive evidence that depression is prevalent in HIV patients, there may be a relationship with neurobiological changes caused by the presence of the virus in the central nervous system (CNS). Several groups of researchers found that the virus could penetrate the central nervous system after systemic infection of peripheral blood mononuclear cells, astrocytes, oligodendrocytes, and neuronal progenitor cells. These mechanisms are interrelated due to direct and indirect effects of psychological stress HIV patients' experience, which can cause the activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, subsequently activating the peripheral immune system and the central nervous system.

The prevalence of mental disorders in HIV patients is reported to be about 5% and 23%. Symptoms of depression are common psychiatric disorders in HIV patients, and the prevalence of depression was 53.9% in HIV-positive patients at the Hospital of Uganda in a recent study. The cause of low compliance with antiretroviral treatment in HIV patients is depression. This is based on the results of the multivariate analysis, which indicated that women with HIV and AIDS coupled with symptoms of chronic depression are at twice the risk of death than women without depression. Low CD4 count and viral growth rate are also associated with increased mortality, clinical depression, dysthymia, suicide, and anxiety. If CD4 levels are associated with inflammatory changes in the central nervous system, this could be a marker for HIV-associated lowered immune system, which can lead to lymphocyte dysfunction, followed by brain damage.

In the developed world, early survival improvements occurred soon after the introduction of highly active antiretroviral therapy (HAART) in the mid-1990s and they have continued to increase. HAART itself is responsible for most of the improvement as before antiretroviral, HIV caused an almost uniformly fatal illness. While fewer than one million people worldwide are currently receiving HAART, the number receiving HAART in developing countries is likely to increase.

We show that in the absence of sophisticated testing for CD4 counts, TLC can be used as a reliable predictor of ADOIs in HIV-1 infected people. As such, TLC can also be used to facilitate decisions about timing of HAART and ADOI prophylaxis. Additional studies are required to determine the utility of TLC as a predictive marker in place of the CD4 count, in different settings.

CONCLUSION

The study of this literature shows that depression greatly affects the immune system, which can lead to a decrease in the CD4 cell count of HIV patients. This can have a negative impact on people living with HIV, potentially leading to more severe symptoms. Depression is a very significant danger to people living with HIV. Based on these data, patients need their families, communities, and health care workers to provide positive support, knowledge, and spiritual development. This support can help people living with HIV to avoid the symptoms of depression.

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