Original Research Report

CD4 COUNT AND CENTRAL NERVOUS SYSTEM INFECTION AMONG HIV/AIDS PATIENTS IN AN INDONESIAN PRESIDENTIAL HOSPITAL FROM 2020 TO 2022

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ABSTRACT

People living with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS), referred to as PLWHA, have a high rate of mortality and morbidity due to opportunistic central nervous system infections. The infections are attributed to the immune deficiency caused by HIV exposure to the immune system's cluster of differentiation 4 (CD4) cells. This allows the central nervous system, the most vital body system, to acquire an opportunistic infection. The purpose of this study was to determine the existence and magnitude of a risk by examining the correlation between CD4 count and the incidence of central nervous system infection among HIV/AIDS patients. This analytical cross-sectional study utilized a simple random sampling technique on the population of HIV/AIDS patients, which consisted of 80 medical records from January 2020 to December 2022. This study was conducted at Gatot Soebroto Presidential Hospital, also known as Gatot Soebroto Central Army Hospital, in Jakarta, Indonesia. The data analysis was performed using Fisher's exact test ($p<0.05$) and the prevalence odds ratio (POR). The results showed that 16.3% of the patients suffered a central nervous system infection, which consisted of cerebral toxoplasmosis (76.9%) and brain abscess (23.1%). The bivariate analysis suggested a significant correlation between CD4 count and the incidence of central nervous system infection, with an 11.5-fold increased risk for HIV/AIDS patients who had a CD4 count of <200 cells/mm^3 ($p=0.000$; OR=11.5; 95% CI=2.9–43.8). This study concludes that CD4 count is correlated with the incidence of central nervous system infection, indicating a higher risk for HIV/AIDS patients with a low CD4 count.

Keywords: Cluster of differentiation 4 (CD4) count; central nervous system infection; opportunistic infection; human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS)

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Highlights:
1. There were insufficient data on the correlation between CD4 count and central nervous system infection as well as the risk magnitude of the infection for HIV/AIDS patients in Indonesia.
2. This study revealed a significant correlation between CD4 count and the incidence of central nervous system infection in HIV/AIDS patients, showing an increased risk with a low CD4 count.
3. The findings suggest that CD4 count is a vital parameter in determining therapy and evaluating the presence of opportunistic infections in HIV/AIDS patients.

INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) is a group of symptoms that represent a decline in the immune system. This happens as a result of a human immunodeficiency virus (HIV) infection (Ministry of Health of the Republic of Indonesia 2020). The viral infection targets the cluster of differentiation 4 (CD4) cells, with the key targets being immune and nervous system cells. This condition leads to a progression of immunodeficiency mechanisms (Kumar et al. 2023). CD4 cells are destroyed to

inject their ribonucleic acid (RNA) as genetic material and convert it into deoxyribonucleic acid (DNA) through reverse transcriptase. HIV has a neuroinvasive nature with a significant potential to affect the nervous system through direct or indirect means, such as opportunistic infections mediated by a decreased immune response (Sheybani et al. 2021, Suleman et al. 2022).

Opportunistic infections arise from microorganisms that can only be pathogenic in individuals with a weakened immune system. These infections manifest in several organs with varying pathologies, such as neurological disorders (Fatimatuzzahra et al. 2022). Anatomically, neurological manifestations due to opportunistic infections in HIV/AIDS patients are classified based on their locations, including the peripheral nervous system and the central nervous system. According to the Ministry of Health of the Republic of Indonesia (2019), the most common neurological manifestations in the country are opportunistic infections of the central nervous system, such as tuberculous meningitis, cerebral toxoplasmosis, and cryptococcal meningitis. During the early stages, HIV/AIDS patients with a central nervous system infection are frequently asymptomatic or exhibit unspecific symptoms such as headaches and fatigue. Central nervous system infections in HIV/AIDS patients often begin at stage 3 with a CD4 count of <200 cells/mm^3 (Cerutti et al. 2020, Meyer et al. 2022).

CD4 is a glycoprotein that functions as a receptor on the surface of immune or nervous cells. Currently, the laboratory examination of CD4 is considered one of the vital parameters in determining therapy and evaluating the presence of opportunistic infections in HIV/AIDS patients (Kumar et al., 2023). Research on HIV/AIDS patients with central nervous system infections in Indonesia, particularly in the Jakarta region, is limited. Meanwhile, Jakarta is the second Indonesian province with the largest number of people living with HIV/AIDS (PLWHA) (Ministry of Health of the Republic of Indonesia 2022). Hence, it is necessary to conduct a study to identify the distribution of sociodemographic and clinical characteristics, the distribution of diagnoses, the correlation between CD4 count and central nervous system infection, as well as the magnitude of risk for HIV/AIDS patients at Gatot Soebroto Presidential Hospital, Jakarta, Indonesia.

MATERIALS AND METHODS

This analytical cross-sectional study was conducted at Gatot Soebroto Presidential Hospital, also known as Gatot Soebroto Central Army Hospital, Jakarta, Indonesia, from October to November 2023. Patients diagnosed positive for HIV/AIDS from January 2020 to December 2022 were selected using simple random sampling (Setia 2016). Ethical approval for this study was granted by the Research Ethics Committee of Universitas Pembangunan Nasional "Veteran" Jakarta, Jakarta, Indonesia (No. 370/X/2023/KEP dated 13/10/2023). In addition, this research secured authorization from the hospital before data collection.

The sampling calculation account a potential 10% dropout rate, resulting in 80 samples. The inclusion criteria for this study were HIV/AIDS patients with a minimum age of 15 years, currently in clinical stage 3 or 4 according to the World Health Organization (WHO) clinical staging, and having complete medical records. Patients with HIV/AIDS with primary or secondary immunodeficiency not related to HIV/AIDS, undergoing immune-suppression therapy, and having congenital or acquired neurological and/or brain abnormalities were excluded from this study (Gumarianto et al. 2022).

The research results were analyzed through univariate and bivariate analyses using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA). Fisher's exact test was used in lieu of the Chi-square test with a 95% confidence interval for the bivariate statistical analysis to determine the correlation between variables. Additionally, the prevalence odds ratio (POR) was employed to assess the magnitude of the risk (Jung 2014).

RESULTS

This study collected samples from the population confirmed positive for HIV/AIDS over the years 2020–2022. A total of 80 medical records were selected through simple random sampling for the purpose of conducting data analysis.

The data presented in Table 1 indicate that the HIV/AIDS patients in this study were predominantly male, accounting for 80% of the total cases. The majority of the patients were between the ages of 25 and 49 (80%), suggesting they were in their most productive years. Regarding their educational backgroung, 58.8% of the patients had graduated from high school, whereas 41.3% were working in the private sector or as entrepreneurs.

Table 1. Distribution of HIV/AIDS patients according to sociodemographic characteristics.

Characteristics	n	%
Sex		
Male	64	80
Female	16	20
Age		
20–24 y.o.	2	2.5
25–49 y.o.	64	80
≥50 y.o.	14	17.5
Education		
Primary school	1	1.3
JHS	3	3.8
SHS	47	58.8
College/university	15	18.8
Others	14	17.5
Occupation		
Civil servant/military personnel/police	28	35
Entrepreneur/private-sector employee	33	41.3
Teacher	2	2.5
Farmer	1	1.3
Housewife	7	8.8
Unemployed	3	3.8
Others	6	7.5

Legends: JHS=junior high school; SHS=senior high school.

Table 2 displays the distribution of HIV/AIDS patients according to their clinical characteristics. Most of the research subjects were HIV/AIDS patients in stage 3 (61.3%) based on the WHO clinical staging. Furthermore, 75% of the patients exhibited a CD4 count of ≥200 cells/mm^3.

Table 2. Distribution of HIV/AIDS patients according to clinical characteristics.

Characteristics	N	%
Clinical stage		
Stage 3	49	61.3
Stage 4	31	38.8
CD4 count		
<200 cell/mm^3	20	25
≥200 cell/mm^3	60	75

Legend: CD4=cluster of differentiation 4

The diagnoses confirmed among the HIV/AIDS patients in this study are presented in Table 3. As many as 16.25% of the 80 HIV/AIDS patients suffered from central nervous system infections. Among these diagnosis, cerebral toxoplasmosis accounted for 76.9%, while brain abscess made up 23.1%. The results also showed that the HIV/AIDS patients without central nervous system infection did not exhibit any opportunistic infection (60%). Meanwhile, among HIV/AIDS patients who had a central nervous system infection, cerebral toxoplasmosis was the most common diagnosis (12.5%).

Table 3. Distribution of diagnoses among the HIV/AIDS patients.

Diagnoses	n	%	
Without CNS infection	67	83.75	
Without opportunistic infection	48	60	
Pulmonary TB	8	10	
Extrapulmonary TB	2	2.5	
Pulmonary and extrapulmonary TB	2	2.5	
CMV retinitis	1	1.3	
Secondary syphilis	1	1.3	
Hepatitis C	1	1.3	
Tinea cruris	1	1.3	
Oral candidiasis	2	2.5	
Multiorgan infection	1	1.3	
With CNS infection	13	16.25	100
Cerebral toxoplasmosis	10	12.5	76.9
Brain abcess	3	3.8	23.1

Legends: CNS=central nervous system; TB=tuberculosis; CMV=cytomegalovirus.

Fisher's exact test replaced the Chi-square test for cross-tabulation testing in this study, and the results are shown in Table 4. The test was selected because the expected value was <5, which did not meet the requirements of the Chi-square test. After conducting the bivariate analysis, the study continued by calculating the prevalence odds ratio (POR). The results of the analysis revealed a significant correlation between CD4 count and the incidence of central nervous system infection. The results further indicated HIV/AIDS patients with a CD4 count of <200 cells/mm^3 had an 11.5 times higher risk for central nervous system infection (p=0.000; OR=11.5; 95% CI=2.9-43.8).

Table 4. Results of analysis using Fisher's exact test and prevalence odds ratio.

CD4 count (cell/mm^3)	CNS infection		OR	95% CI	p
	Yes	No			
<200	9 (45%)	11 (55%)	11.5	2.9–43.8	0.000
≥200	4 (6.7%)	56 (83.8%)			

Legends: CD4=cluster of differentiation 4; CNS=central nervous system; OR=odds ratio; CI=confidence interval; Significance with p<0.05.

DISCUSSION

This study found that 80% of the HIV/AIDS patients were male. This finding was in line with previous research in multiple hospitals, which showed that male patients represent the highest proportion among those with HIV/AIDS (Apriasari et al. 2021, Tan et al. 2021). The Ministry of Health of the Republic of Indonesia (2023) reported that in July–September 2022, the majority of HIV/AIDS patients in Indonesia were male (71%). The high prevalence of HIV/AIDS in male patients may result from

engaging in risky sexual behaviors and high mobility, particularly within the men who have sex with men (MSM) community. This community has been known to be prone to HIV transmission (Mwaniki et al. 2023). According to a preceding study conducted at Dr. Slamet Regional General Hospital, Garut, Indonesia, the most common risk factors for HIV/AIDS in productive-age men are homosexual behaviors. The infection in this community is mainly transmitted anally. The susceptibility of the rectum to HIV is attributed to the thin wall of the simple columnar epithelium, making it prone to lacerations (Kusumah et al. 2023, Moyo et al. 2023).

Referring to the classification set by the Ministry of Health of the Republic of Indonesia (2022), the analysis of the HIV-AIDS population was performed according to the patients' age. The findings revealed that individuals most commonly affected by HIV/AIDS were in the age group of 25–49 years, accounting for 80% of cases. The data from this study aligned with prior research showing that HIV/AIDS patients fell within the age group of 30-49 years old (Widayanti 2019). The increased frequency of HIV infection among working-age adults has been linked to financial stability through employment. Individuals with great financial resources can easily facilitate their needs and potentially engage in risky lifestyles (Tan et al. 2021).

The results of this study further showed the educational attainment of the subjects. It was found that patients with confirmed HIV/AIDS diagnoses had mostly completed senior high school or its equivalent (58.8%). Earlier studies have shown that the highest education attainment among HIV/AIDS patients is senior high school (Tan et al. 2021, Kurniawati 2022). This educational level is expected to provide a basic understanding of HIV/AIDS and its modes of transmission. However, limited access to comprehensive sexual education and health information could be a contributing factor to the high prevalence of HIV/AIDS in this group.

The analysis in this study showed that the majority of the HIV/AIDS patients were entrepreneurs or had jobs in the private sector (41.3%). This finding is in line with a previous study in Palembang, Indonesia, which revealed a significant proportion of entrepreneurs or private-sector employees (34.5%) among HIV/AIDS patients (Framasari et al. 2020). According to Pasaribu (2021), employment status can influence people's economic capacity to satisfy their needs by earning wages that allow them to purchase goods or services. Entrepreneurs or private-sector employees tend to have a high and diverse income, which can increase the possibility of fulfilling their lifestyle needs, including engaging in risky behaviors that may result in HIV transmission horizontally or transsexually.

This study analyzed the clinical characteristics of HIV/AIDS patients according to the clinical staging defined by the World Health Organization. During stages 3 and 4, patients may exhibit symptoms associated with the development of an opportunistic infection in the central nervous system (World Health Organization 2021). The data revealed that the prevalence of HIV/AIDS patients at stage 3 was higher (61.3%) compared to those at stage 4. Similarly, prior research conducted by Marshalita (2020) at Dr. H. Abdul Moeloek Regional General Hospital, Lampung, Indonesia, revealed that 40.3% of the patients were in stage 3. The high prevalence rates could be due to a lack of awareness about early detection, resulting in the confirmed diagnosis of HIV/AIDS with symptoms of stage 3 opportunistic infections such as pulmonary tuberculosis. Prompt and thorough control and management offer optimism for preventing progression to stage 4.

Most of the HIV/AIDS patients in this study had a CD4 count of ≥200 cells/mm^3 (75%). This is consistent with an earlier study conducted by Apriasari et al. (2021) in Banjarmasin, Indonesia. The study discovered that the majority of patients diagnosed with HIV/AIDS had a CD4 count of ≥200 cells/mm^3 (60%). CD4 is a glycoprotein that becomes the main target of HIV infection. The high prevalence of HIV-infected patients with a CD4 count of ≥200 cells/mm^3 might be influenced by the level of patient compliance with treatment and regular consumption of antiretroviral therapy (ART) (Kumar et al. 2023).

This study investigated the distribution of diagnoses among patients with confirmed HIV/AIDS at Gatot Soebroto Presidential Hospital in Jakarta, Indonesia, from 2020 to 2022. It was found that 16.3% of the patients were additionally diagnosed with central nervous system infections. Cerebral toxoplasmosis (76.9%) was the most common diagnosis of central nervous system infections among the patients. Several prior studies support the results of this study, identifying cerebral toxoplasmosis as the most prevalent diagnosis for neurological manifestations (Rahmayanti et al. 2019, Massi et al. 2022). However, the results of this study differed from the research conducted by Fatimatuzzahra et al. (2022) at Dr. Hasan Sadikin Central General Hospital, Bandung, Indonesia. The research documented cases of tuberculosis meningitis and cryptococcal meningitis in HIV/AIDS patients with central nervous system infections.

The incidence of central nervous system infection is influenced by the low prophylaxis and high seroprevalence of a particular disease etiology, such

as *Toxoplasmosis gondii*. In Jakarta, Indonesia, the seroprevalence rate of *Toxoplasmosis gondii* was found to reach 70% (Riyanda et al. 2019). Cerebral toxoplasmosis is on the rise because the parasite can remain dormant as bradyzoites in the brain. This parasite can become active in individuals with a compromised immune system, such as HIV/AIDS patients (Cerutti et al. 2020). The 2022 Tuberculosis Control Program by the Ministry of Health of the Republic of Indonesia (2023) identified Jakarta as a priority province because of its high tuberculosis prevalence. The low cases of tuberculosis meningitis in this study could result from the patients' enhanced awareness regarding the importance of maintaining regular monitoring and treatment to prevent tuberculosis infection from progressing to advanced stages.

The bivariate analysis using Fisher's exact test revealed a significant correlation between the CD4 count of HIV/AIDS patients and the incidence of central nervous system infection (p=0.000). Moreover, the incidence of central nervous system infection is 11.5 times higher in patients diagnosed with HIV/AIDS who had a CD4 count below 200 cells/mm^3 (OR=11.5; 95% CI=2.9-43.8). According to a study conducted in Brazil, a significant association was also found between a CD4 count of <50 cells/mm^3 and the incidence of central nervous system infection (p=0.016; OR=4.6; 95% CI=1.3-16) (Telles et al. 2021).

The risk of central nervous system infection in HIV/AIDS patients may increase as the CD4 count decreases. This infection mechanism occurs when HIV-infected immune cells enter the blood-brain barrier. In addition, HIV infection can also induce inflammation by damaging the structure and function of the blood-brain barrier and allowing systemic neurotoxins to enter the central nervous system (Kumar et al. 2023). This mechanism leads to an easier way for secondary pathogens to enter the central nervous system.

Strength and limitations

The strength of this study lays in its precise measurement of the researched variables, facilitated by the use of reliable software. However, the data were limited because of incomplete medical records, leading to their exclusion from this study.

CONCLUSION

This study inferred a significant correlation between CD4 count and the incidence of central nervous system infections among HIV/AIDS patients at Gatot Soebroto Presidential Hospital, Jakarta, Indonesia, between 2020 and 2022. HIV/AIDS patients who had a low CD4 count were at a greater risk of developing central nervous opportunistic infections compared to those with a higher CD4 count.

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Conflict of interest

None.

Ethical consideration

This study received ethical approval from the Research Ethics Committee of Universitas Pembangunan Nasional "Veteran" Jakarta (No. 370/X/2023/KEP on 13/10/2023) and authorization from Presidential Hospital Gatot Soebroto, Jakarta, Indonesia.

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Author contribution

AAR contributed to the conception and design, drafting of the article, as well as the collection, analysis, and interpretation of the data. RVA and HY contributed to the critical revision of the article for important intellectual content. AYS provided final approval of the article.

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