ORIGINAL ARTICLE

The CD4 Count and Viral Load Differences in HIV Patients with and without Infectious Posterior Uveitis at a Tertiary Hospital in Indonesia

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ABSTRACT

Introduction: The human immunodeficiency virus (HIV) compromises the immune system, making the monitoring of cluster of differentiation (CD4) counts and viral loads critical for assessing disease progression and opportunistic infection risks. Eye-related manifestations, such as uveitis, are common among HIV patients. The purpose of this study was to investigate the differences in CD4 count and viral load between HIV patients with infectious posterior uveitis and those without at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.
Methods: A retrospective study with an analytical observational design was conducted using the medical records of 75 HIV patients. The examined variables included CD4 count and viral load as independent variables, alongside the incidence and absence of infectious posterior uveitis as dependent variables. The inclusion criteria were HIV patients with regular follow-ups, thereby excluding those with irregular follow-ups. The analysis used the Mann-Whitney test, with $p<0.05$ indicating a statistically significant difference.
Results: All 75 samples met the inclusion criteria for analysis. The majority of the patients were male (64%) and within the age range of 31 to 40 years (44%). Patients with infectious posterior uveitis had significantly lower CD4 counts ($p<0.05$) compared to those without the disease. However, no significant differences in viral loads ($p>0.05$) were observed between patients with posterior uveitis and those without.
Conclusion: CD4 counts differ significantly between patients with infectious posterior uveitis and those without, while viral loads show no considerable differences.

Keywords: Human immunodeficiency virus (HIV); posterior uveitis; cluster of differentiation (CD4) lymphocytes; viral load

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Highlights:
1. This study highlights the differences in cluster of differentiation (CD4) lymphocyte count and viral load between HIV patients with infectious posterior uveitis and those without.
2. The findings may provide new insights into the immunological mechanisms underlying infectious posterior uveitis in persons living with HIV.
3. This work contributes to determining the factors that affect the development of infectious posterior uveitis and explores the potential use of CD4 lymphocyte count and viral load as biomarkers for the diagnosis and management of the disease.

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INTRODUCTION

The human immunodeficiency virus (HIV) attacks white blood cells, especially lymphocytes, thereby reducing the body's ability to fight disease. The main impact of HIV infection is the

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deterioration of the immune system. Monitoring cluster of differentiation (CD4) counts is an effective method for assessing HIV progression and the risk of opportunistic infections (Aurelina, 2020). CD4, a receptor found on the cell surface, serves as the target of HIV (Wande et al., 2019).

Opportunistic infections arise from microorganisms that exploit certain conditions in the body. In patients with acquired immune deficiency syndrome (AIDS), symptoms are often caused by opportunistic infections, such as cytomegalovirus, *Candida albicans*, herpes simplex virus, as well as mycobacterial, fungal, or parasitic infections (Swinkels et al., 2024). Patients with HIV/AIDS may experience several opportunistic infections, including those caused by cytomegalovirus, *Toxoplasma gondii*, and *Mycobacterium tuberculosis*. HIV infection is also associated with various eye-related manifestations, among which uveitis is a notable ocular condition affecting the posterior segment of the eye. The common causes of posterior uveitis in individuals with HIV include cytomegalovirus, *Toxoplasma gondii*, *Mycobacterium tuberculosis*, and HIV itself (Syadzali et al., 2019). Uveitis is one of the most prevalent ocular complications in people living with HIV. It can be classified into HIV-induced uveitis, coinfection-related uveitis, immune recovery uveitis, and drug-induced uveitis (Yang et al., 2023).

Intraocular inflammation in patients with HIV infection is commonly due to infectious uveitis, as noted by Sudharshan et al. (2020). Opportunistic infections in HIV patients can cause conditions, such as cytomegalovirus chorioretinitis and ocular tuberculosis, which can lead to decreased vision or blindness (Gogri et al., 2014). Kurniawati et al. (2022) demonstrated that most mortality rates in HIV patients are associated with complications from opportunistic infections. Uveitis ranks as the fourth leading cause of blindness among people of productive age in developing countries. Zhang et al. (2020) found that in the United States, infectious etiologies constituted less than 20% of uveitis/scleritis cases, with mean incidence and prevalence rates of 18.9 and 60.6 per 100,000 persons, respectively.

Infectious posterior uveitis is common in HIV patients due to weakened immune systems, which increases susceptibility to opportunistic pathogens. Viral load, a key marker for the severity and speed of disease progression, reflects the amount of circulating virus present in the blood. A higher quantity of viral particles in the blood leads to several effects, including an increased risk of virus transmission and complications related to HIV, such as cytomegalovirus infections and tuberculosis (Dewanti & Handayani, 2021). In resource-limited settings such as Indonesia, where treatment may be delayed, monitoring biomarkers could facilitate early intervention for ocular manifestations.

Despite the well-documented association between HIV and ocular complications, no studies in Indonesia have specifically investigated the relationship between CD4 count, viral load, and infectious posterior uveitis in HIV patients. Therefore, this study aimed to compare CD4 counts and viral loads in HIV-positive patients with and without posterior uveitis at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. By analyzing these variables, this study sought to elucidate potential relationships that could inform clinical management and screening protocols.

METHODS

This retrospective study employed an analytical observational design (Ranganathan & Aggarwal, 2019). The study population consisted of 75 patients diagnosed with HIV and/or infectious posterior uveitis at Dr. Soetomo General Academic Hospital, a tertiary healthcare facility in Surabaya, Indonesia. The period of this study spanned from January 2018 until December 2023. The data analysis was performed using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, N.Y., USA, 2020).

The examined variables were CD4 count and viral load as independent variables, with the incidence and absence of infectious posterior uveitis serving as dependent variables. The samples in this study must meet the inclusion criteria and avoid the exclusion criteria (Patino & Ferreira, 2018). The inclusion criteria encompassed HIV patients who attended routine follow-ups, while the exclusion criteria were those who failed to consistently attend follow-ups. Secondary data were sourced from medical records in the Communication and Information Technology Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia. The obtained data were compiled and underwent statistical analyses.

The CD4 counts were measured in the laboratory through flow cytometry and reported as percentages of total lymphocytes. To determine the absolute CD4 counts (cells/µL), the CD4 percentage was multiplied by the total white blood cell count. Generally, the CD4 percentages corresponded to the established absolute count ranges: values exceeding 29% signified >500 cells/µL, values between 14% and 28% indicated 200–500 cells/µL, and values below 14% suggested <200 cells/µL. It should be noted, however, that the absolute CD4 counts could rise in response to elevated white blood cell counts, while the CD4 percentages remained unchanged. Additionally, the CD4 measurements might exhibit inter-assay or inter-laboratory variability (Salisu et al., 2018).

The categorization of viral loads followed the criteria defined by Thamrin et al. (2023) in a study conducted on HIV patient cohorts. The patients

were classified into two groups based on their viral load measurements: those with a detectable viral load (>50 copies/mL) and those with an undetectable viral load (≤50 copies/mL). Medical records with unavailable viral load data were excluded from the analysis.

This study used the Mann-Whitney test for analysis because the research variables were not normally distributed, as determined by the Kolmogorov-Smirnov test. The Mann-Whitney test, a nonparametric technique, was employed to determine the differences between two paired datasets that lacked normal distribution (Normelia et al., 2022). Specifically, this test was conducted in this study to assess whether there were significant differences in CD4 counts and viral loads between two groups: HIV patients with infectious posterior uveitis and those without such disease. Results with a p-value below 0.05 indicated a significant difference in CD4 counts and viral loads between HIV-positive sufferers with infectious posterior uveitis and those without.

The research protocol received ethical approval from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, certified under number 8047/KEPK/XII/2023, on December 5, 2023. This study was conducted in four sequential phases. Firstly, a preparation that included the identification of eligible HIV patients through medical records from the Communication and Information Technology Unit of the hospital. Secondly, the screening of the medical records to identify cases with documented infectious posterior uveitis. Thirdly, further refining of the cohort to acquire data on infectious posterior uveitis patients with confirmed etiologies (toxoplasmosis, cytomegalovirus infection, tuberculosis, or syphilis) who had undergone CD4 lymphocyte and viral load examinations. Finally, statistical analysis on the extracted data to assess any differences in CD4 counts and viral loads between HIV patients with infectious posterior uveitis and those without (Normelia et al., 2022).

RESULTS

Between 2018 and 2023, 75 patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, were diagnosed with HIV and/or infectious posterior uveitis. All 75 patients met the inclusion criteria for analysis in this research. The patients were categorized based on characteristics, including sex and age groups. The variables examined in this study were CD4 lymphocyte count, viral load, and the presence and absence of infectious posterior uveitis.

The distribution of patients according to age, sex, CD4 lymphocyte counts, and viral loads was presented in frequencies and percentages. Table 1 shows that there were 48 male participants, accounting for 64% of the total samples. Patients under 20 represented the smallest percentage of samples, while those aged 31 to 40 years accounted for the highest proportion (44%).

Table 1. Characteristic of the HIV patients

Characteristics	Infectious posterior uveitis		n (%)
	Present	Absent	
Sex			
Male	18	30	48 (64)
Female	7	20	27 (36)
Age (years)			
≤20	2	4	6 (8)
21–30	3	14	17 (23)
31–40	12	21	33 (44)
41–50	4	6	10 (13)
>50	4	5	9 (12)

Note: HIV=human immunodeficiency virus.

Table 2 exhibits the results of the viral load examinations. It was found that 12 (16%) out of the 75 patients had detectable viral loads, while 29 individuals (39%) demonstrated undetectable viral loads. Data were not obtained for the remaining 34 patients (45%) due to incomplete medical records. The results indicated that many patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, had not undergone viral load examinations.

Table 2. Viral loads of the HIV patients

Viral loads (copies/mL)	Infectious posterior uveitis		n (%)	p
	Present	Absent		
Detected (>50)	6	6	12 (16)	0.876
Undetected (≤50)	10	19	29 (39)	
No data	9	25	34 (45)	

Note: HIV=human immunodeficiency virus.

In Table 3, it was displayed that data on CD4 lymphocyte counts were obtained from only 70 HIV patients, either with or without infectious posterior uveitis. The number of samples decreased from 75 to 70 due to incomplete medical record data. Among 70 patients with complete medical records, 38 (54%) had a CD4 lymphocyte count below 200 cells/µL, whereas 23 (33%) demonstrated a count ranging between 200 and 500 cells/µL. The remaining nine patients exhibited a CD4 lymphocyte count over 500 cells/µL.

To assess any differences in CD4 counts and viral loads between HIV patients with infectious posterior uveitis and those without, the Mann-Whitney test was employed. The test was chosen because the research variables were not normally

distributed, as determined by the Kolmogorov-Smirnov test. The results of the Mann-Whitney test indicated a significant difference in CD4 counts between patients with infectious posterior uveitis and those without, noted by a p-value below 0.05. However, the results suggested that no significant differences were detected in viral loads between the two groups, as indicated by a p-value above 0.05.

Table 3. CD4 lymphocyte counts of the HIV patients

CD4 counts (cells/mm^3)	Infectious posterior uveitis		n (%)	p
	Present	Absent		
<200	16	22	38 (54)	0.032
200–500	4	19	23 (33)	
>500	0	9	9 (13)	
No data	5	0	5 (6)	

Notes: CD4=cluster of differentiation; HIV=human immunodeficiency virus.

DISCUSSION

This study presented the distribution of HIV patients according to various characteristics, including the presence and absence of infectious posterior uveitis. The findings of this study revealed that 33% of the HIV patients were diagnosed with infectious posterior uveitis, while 67% did not receive the same diagnosis. Similar results were observed in a survey conducted by Saadouli et al. (2021) in Tunisia. Among 98 HIV-positive individuals who underwent eye examinations, 36.7% exhibited manifestations of posterior uveitis. Ophthalmic manifestations in people living with HIV/AIDS in Tunisia varied, with retinopathy being the most common lesion. However, ocular involvement in this population can be severe, leading to poor visual prognosis, especially in developing countries. Although the introduction of antiretroviral therapy has reduced the incidence and severity of opportunistic eye infections, new manifestations, such as drug-induced uveitis and immune recovery uveitis, have emerged as causes of vision loss. Therefore, collaboration between ophthalmologists and infectious disease specialists is strongly recommended for diagnosing and managing these patients.

This study revealed that HIV patients aged 31–40 years, regardless of the presence of posterior uveitis, had the highest prevalence, accounting for 44% of the total samples. The findings are consistent with those of a study by Sari et al. (2019), which reported an average age of 43.8 years for uveitis patients. The majority of HIV patients in this study, regardless of the presence of infectious posterior uveitis, were male, constituting 64% of the total samples. Meanwhile, female patients made up 36% of the overall samples. These findings align with earlier research reported by Saadouli et al. (2021), which noted a male-to-female ratio of 2:1, comprising 24 male and 12 female patients, hence indicating a higher prevalence in males. HIV can infect individuals of any age, sex, race, or social class. However, the disease can be managed due to the effectiveness of antiretroviral therapy (Kemnic & Gulick, 2022; Huynh et al., 2024).

The categories of viral loads in the HIV patients were divided into two: detectable (>50 copies/mL) and undetectable (≤50 copies/mL). This study found that 20% of the HIV patients exhibited detectable viral loads, 37% had undetectable viral loads, and 43% lacked available data. These findings align with those of Thamrin et al. (2023), who reported that 18.8% of HIV patients at Kendari City Regional General Hospital, Kendari, Indonesia, had detectable viral loads, while 81.2% demonstrated undetectable levels. The study further revealed the following prevalence rates among 25 HIV patients diagnosed with infectious posterior uveitis: 24% were infected with *Toxoplasma gondii*, 36% with cytomegalovirus, 8% with *Mycobacterium tuberculosis*, and 4% with *Treponema pallidum*. Moreover, the study conducted by Saadouli et al. (2021) reported ocular manifestations that affected the posterior segment in 58% of cases, with retinal microvasculopathy being the most common manifestation (36%). Other findings included the prevalence of cotton-wool spots (20%), intraretinal hemorrhages (16%), toxoplasmosis (4%), tubercular retinochoroiditis (9%), syphilitic chorioretinitis (2%), and cytomegalovirus retinitis (9%).

Toxoplasmosis was identified as the most important cause of posterior uveitis in a previous study conducted by Al-Shakarchi (2014). Ocular toxoplasmosis is considered the most frequent form of infectious posterior uveitis, resulting from the protozoan parasite *Toxoplasma gondii* (Maenz et al., 2014). A retrospective analysis of eight eyes from six patients was described in a study by Cabrera et al. (2017) taking place at the ophthalmology service of Hospital Universitario de Canarias in Santa Cruz de Tenerife, Spain. The findings revealed that the patients were diagnosed with atypical chorioretinitis associated with vitritis. The mean age of the patients at presentation with ocular manifestations was 33.37 years. All eight eyes were found to be affected by chorioretinitis caused by *Toxoplasma gondii* (12.5%).

This study demonstrated the distribution of HIV patients, irrespective of the presence of infectious posterior uveitis, according to their CD4 lymphocyte counts. Due to incomplete medical records for five patients, data on CD4 lymphocyte counts were acquired only for 70 samples. The findings revealed that 54% of the total samples had a CD4 count below 200 cells/µL, 24% had a value count ranging from 200 to 500 cells/µL, and 22% had a value

above 500 cells/µL. The lower CD4 counts in HIV patients with infectious posterior uveitis, as compared to those without, might also be attributable to the presence of additional opportunistic infections that attack their immune system alongside HIV infection. One of the opportunistic infections is ocular tuberculosis, a chronic extrapulmonary manifestation of *Mycobacterium tuberculosis* infection, characterized by diverse clinical presentations that can lead to blindness (Supit, 2022). The disease may affect both the anterior and posterior segments of the eye and can occur in immunocompetent and immunocompromised patients (Gupta et al., 2015). Nevertheless, a separate study suggests that in HIV-positive patients, the impaired activity of the immune system exacerbates the clinical symptoms of ocular tuberculosis, creating a mutual relationship between tuberculosis and HIV (Silitonga et al., 2019).

The Mann-Whitney test yielded a p-value of less than 0.05, indicating a significant difference in CD4 counts between patients with infectious posterior uveitis and those without. Conversely, the results of the differential test for viral load data indicated a p-value greater than 0.05, suggesting no significant differences. The findings align with those of research by Kurniawati et al. (2022), which reported a p-value of 0.126 ($p>0.05$) from the Mann-Whitney test for the neutrophil-lymphocyte ratio, suggesting an absence of statistical relationships between the marker and opportunistic infections. No significant relationships were also observed in the analysis of viral load and the occurrence of opportunistic infections. However, the Mann-Whitney test for CD4 counts yielded a p-value of 0.039 ($p<0.05$), indicating an association between the marker and the occurrence of opportunistic infections in HIV patients.

This study provides several contributions to the field of internal medicine and ophthalmology, especially in enhancing clinical knowledge and understanding the relationship between CD4 lymphocyte cell counts and infectious posterior uveitis in HIV patients. As a study conducted at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, this research contributes to region-specific epidemiological data, filling a gap in literature regarding HIV-related ocular infections in this demographic. However, this study is not without limitations. First, there was a risk of selection bias due to its retrospective design, which might have led to incomplete or questionable medical records. Additionally, the study did not track the course of therapy and treatment history, factors that could affect viral load and CD4 lymphocyte examination results. Lastly, the precise timeline for diagnosis was unclear in the patients' medical records, making it difficult to determine the duration of treatment and potentially affecting the results of viral load and CD4 lymphocyte assessments.

CONCLUSION

This study suggests that CD4 counts differ significantly between HIV patients with infectious posterior uveitis and those without. CD4 counts are generally lower in HIV patients with infectious posterior uveitis compared to those without the disease. Conversely, this study indicates that viral loads are not significantly different between the two groups.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICS CONSIDERATION

The Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, granted approval for this study under reference number 8047/KEPK/XII/2023, issued on December 5, 2023.

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This study did not receive any funding.

AUTHOR CONTRIBUTION

All authors made substantial contributions to this research. Specifically, SAH contributed to the conceptualization and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, provision of study materials or patients, statistical expertise, provision of funding as well as administrative, technical, or logistic support, and collection and assembly of the data. IZ participated in the conceptualization and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, provision of study materials or patients, statistical expertise, and provision of technical or logistic support, as well as collection and assembly of the data. MVA was involved in the conceptualization

and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, final approval of the article, provision of study materials or patients, and collection and assembly of the data. RP contributed to the conceptualization and design, analysis and interpretation of the data, drafting of the article, critical revision of the article for important intellectual content, and final approval of the article.

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