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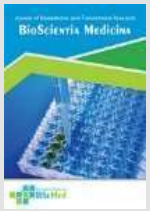

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Ocular Manifestations and Risk Factors of HIV in a Single-Center Observational Study at Dr. M. Djamil General Hospital, Padang, Indonesia

Havilah Zeki Rosa[1*], Havriza Vitresia[1]

[1]Department of Ophthalmology, Universitas Andalas/Dr. M. Djamil General Hospital, Padang, Indonesia

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***Corresponding author:**
Havilah Zeki Rosa

E-mail address:
havilahzeki@gmail.com

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A B S T R A C T

Background: Human immunodeficiency virus (HIV) infection is associated with various ocular manifestations, impacting visual health and quality of life. This study aimed to investigate the spectrum of ocular manifestations and their associated risk factors in HIV-positive individuals at Dr. M. Djamil General Hospital, Padang, Indonesia. **Methods:** This single-center observational study included HIV-positive patients presenting with ocular complaints at Dr. M. Djamil General Hospital between 2019 and 2021. Comprehensive ophthalmic examinations were conducted, and data on demographics, HIV disease stage, CD4+ T-cell count, antiretroviral therapy (ART) status, and ocular findings were collected. Statistical analysis was performed to identify associations between risk factors and specific ocular manifestations. **Results:** A total of 149 HIV-positive patients were included in the study, with 7 (4.7%) presenting with ocular manifestations. The most common ocular manifestation was cytomegalovirus (CMV) retinitis (57.1%), followed by retinal nerve fiber layer (RNFL) thinning (42.9%). Other manifestations included visual field disturbances and herpes zoster ophthalmicus (HZO). Low CD4+ T-cell count (<200 cells/µL) was significantly associated with CMV retinitis ($p < 0.05$). **Conclusion:** CMV retinitis and RNFL thinning were the predominant ocular manifestations in this HIV-positive cohort. Low CD4+ T-cell count emerged as a significant risk factor for CMV retinitis. Early detection and prompt management of ocular manifestations are crucial to prevent visual impairment in HIV-positive individuals.

1. Introduction

The human immunodeficiency virus (HIV) continues to pose a significant global health challenge, affecting millions of individuals worldwide. While advancements in antiretroviral therapy (ART) have transformed HIV into a manageable chronic condition, the virus remains a persistent threat to various organ systems, including the eyes. Ocular manifestations are a common complication of HIV infection, with a wide range of presentations that can significantly impact visual health and quality of life. The eye, with its complex structure and diverse cell types, provides a unique environment for HIV-related pathology. The virus can directly infect ocular tissues, leading to inflammation, tissue damage, and dysfunction. Additionally, HIV-induced immunosuppression predisposes individuals to opportunistic infections and malignancies that can manifest in the eyes. The spectrum of ocular manifestations in HIV is broad and encompasses both the anterior and posterior segments of the eye. Anterior segment manifestations may include dry eye syndrome, keratitis, uveitis, and conjunctival microvasculopathy. Posterior segment complications are often more severe and can involve opportunistic infections such as cytomegalovirus (CMV) retinitis, toxoplasmosis chorioretinitis, and progressive outer retinal necrosis (PORN). Other posterior segment manifestations include HIV

retinopathy, microvasculopathy, and neuro-ophthalmic disorders.[1,2]

CMV retinitis, a sight-threatening opportunistic infection, remains a leading cause of visual impairment in HIV-positive individuals, particularly in those with low $CD4^+$ T-cell counts. The virus can infect retinal cells, leading to necrosis, hemorrhage, and ultimately, retinal detachment. Early detection and prompt treatment with antiviral therapy are crucial to prevent irreversible vision loss. HIV retinopathy, another common ocular manifestation, is characterized by microvascular changes in the retina, including cotton-wool spots, retinal hemorrhages, and microaneurysms. While often asymptomatic in the early stages, HIV retinopathy can progress to more severe forms, leading to visual field defects and decreased visual acuity. Microvasculopathy, a hallmark of HIV infection, can affect the small blood vessels of the eye, leading to impaired blood flow and tissue ischemia. This can manifest as conjunctival microvasculopathy, retinal microvasculopathy, and optic neuropathy. Microvasculopathy can contribute to the development of other ocular complications, such as retinopathy and neuro-ophthalmic disorders. Neuro-ophthalmic manifestations of HIV can involve the optic nerve, visual pathways, and ocular motor system. HIV-associated optic neuropathy, characterized by optic nerve inflammation and demyelination, can lead to progressive vision loss. Other neuro-ophthalmic complications include cranial nerve palsies, visual field defects, and pupillary abnormalities.[3,4]

The prevalence and severity of ocular manifestations in HIV are influenced by various factors, including $CD4^+$ T-cell count, viral load, ART status, and duration of HIV infection. Individuals with low $CD4^+$ T-cell counts are at higher risk of opportunistic infections, while those with uncontrolled viral load may experience more severe ocular complications. ART has significantly reduced the incidence of ocular manifestations in HIV, but some complications may still occur, particularly in individuals with advanced disease or suboptimal adherence to therapy.

Early detection and prompt management of ocular manifestations are crucial to prevent visual impairment and improve the quality of life for HIV-positive individuals. Regular comprehensive ophthalmic examinations are recommended for all HIV-positive individuals, with increased frequency in those with low $CD4^+$ T-cell counts or other risk factors for ocular complications. In addition to ART, specific treatments for ocular manifestations may include antiviral therapy for CMV retinitis, corticosteroids for uveitis, and laser photocoagulation for retinopathy. Early intervention and multidisciplinary care involving ophthalmologists, infectious disease specialists, and other healthcare providers are essential for optimal management of HIV-related ocular disease.[5,6] This study aimed to investigate the spectrum of ocular manifestations and their associated risk factors in a cohort of HIV-positive patients at Dr. M. Djamil General Hospital, Padang, Indonesia. By characterizing the ocular complications and identifying potential predictors, this research contributes to the growing body of knowledge on HIV-related ocular disease and informs clinical practice in the region.

2. Methods

This single-center observational study was conducted at the Department of Ophthalmology, Universitas Andalas/Dr. M. Djamil General Hospital, a tertiary care referral center in Padang, Indonesia. The study adhered to the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Dr. M. Djamil General Hospital. The study population comprised all HIV-positive patients who attended the ophthalmology, immunology, and infection outpatient clinics at Dr. M. Djamil General Hospital between January 1st, 2019, and December 31st, 2021. Patients were considered eligible for inclusion if they had a confirmed HIV diagnosis based on serological testing and presented with ocular complaints or were referred for ophthalmic evaluation due to their HIV status. Patients were excluded from

the study if they had incomplete medical records, lacked documentation of HIV serological status, or had pre-existing ocular conditions unrelated to HIV infection (e.g., diabetic retinopathy, hypertensive retinopathy, ocular trauma). Additionally, patients with concurrent systemic infections or malignancies that could confound the interpretation of ocular findings were excluded.

Data collection was performed retrospectively through a comprehensive review of electronic medical records (EMRs) and the voluntary counseling and testing (VCT) database at Dr. M. Djamil General Hospital. The following information was extracted from the EMRs: Demographic data: Age, gender, occupation, and educational level; HIV-related data: Date of HIV diagnosis, mode of transmission, duration of HIV infection, current $CD4^+$ T-cell count, nadir $CD4^+$ T-cell count, ART status (on/off ART), type of ART regimen, and duration of ART; Ophthalmic data: Presenting ocular complaints, visual acuity (using Snellen chart or equivalent), anterior segment examination findings (using slit-lamp biomicroscopy), posterior segment examination findings (using indirect ophthalmoscopy or fundus photography), and results of ancillary tests (e.g., optical coherence tomography, visual field testing, fluorescein angiography); Other relevant medical data: History of opportunistic infections, comorbidities (e.g., diabetes mellitus, hypertension), and current medications. The VCT database was used to identify all HIV-positive individuals diagnosed at Dr. M. Djamil General Hospital during the study period. This information was cross-referenced with the ophthalmology clinic records to ensure that all eligible patients were included in the study.

All patients underwent a standardized ophthalmic examination protocol, which included the following components: Visual Acuity Assessment: Best-corrected visual acuity was measured for each eye using a Snellen chart at a distance of 6 meters. For patients unable to read the Snellen chart, alternative methods such as counting fingers, hand motion, or light perception were used; Slit-lamp Biomicroscopy: Detailed examination of the anterior segment structures, including the eyelids, conjunctiva, cornea, anterior chamber, iris, and lens, was performed using a slit-lamp biomicroscope; Fundus Examination: The posterior segment of the eye, including the retina, optic nerve head, and retinal vasculature, was examined using indirect ophthalmoscopy or fundus photography. In cases where media opacity (e.g., cataract) precluded adequate visualization of the fundus, B-scan ultrasonography was performed; Optical Coherence Tomography (OCT): OCT imaging was performed to assess the retinal nerve fiber layer (RNFL) thickness, macular thickness, and other relevant retinal parameters. This was done using spectral-domain OCT (SD-OCT) or swept-source OCT (SS-OCT) devices; Visual Field Testing: Automated perimetry (e.g., Humphrey Field Analyzer) was performed to assess the visual field in patients with suspected or confirmed optic neuropathy or other visual pathway abnormalities; Fluorescein Angiography (FA): FA was performed in selected cases to evaluate retinal vascular abnormalities, such as microaneurysms, capillary non-perfusion, and neovascularization.

Ocular manifestations were classified according to the Standardized Uveitis Nomenclature (SUN) working group criteria. This classification system provides a standardized framework for describing and categorizing various forms of uveitis and other ocular inflammatory conditions. The SUN classification considers the anatomical location of inflammation, clinical features, and associated systemic conditions. In this study, ocular manifestations were broadly categorized as follows: Anterior segment manifestations: Conjunctivitis, keratitis, iritis, and other anterior uveitis; Posterior segment manifestations: Retinitis, choroiditis, vitritis, optic neuropathy, and other posterior uveitis; Other manifestations: Dry eye syndrome, neuro-ophthalmic disorders, and orbital manifestations.

Statistical analysis was performed using SPSS software (version 25.0). Descriptive statistics were used to summarize demographic and clinical

characteristics of the study population. Categorical variables were presented as frequencies and percentages, while continuous variables were presented as means and standard deviations (SD) or medians and interquartile ranges (IQR), as appropriate. The chi-square test or Fisher's exact test was used to assess associations between categorical variables. For continuous variables, the independent t-test or Mann-Whitney U test was used, depending on the normality of the data distribution. Logistic regression analysis was performed to identify independent risk factors for specific ocular manifestations. Variables with a p-value < 0.20 in univariate analysis were included in the multivariate model. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to estimate the strength of associations. The sample size for this study was determined based on the estimated prevalence of ocular manifestations in HIV-positive individuals. A previous study from India reported a prevalence of 37.7%. Assuming a similar prevalence in our population, a sample size of 149 HIV-positive patients was calculated to provide a 95% confidence interval with a margin of error of 5%.

3. Results

Table 1 provides a detailed overview of the demographic, clinical, and ophthalmologic characteristics of the 7 HIV-positive patients with ocular manifestations. Ocular manifestations were found in 4.7% of the HIV-positive patient population at the hospital. The patients were all male, with a mean age of 32.5 years. Most patients (71.4%) had completed high school education. All patients acquired HIV through homosexual transmission. The average duration of HIV infection was 3.2 years. The majority of patients (85.7%) were on ART, primarily with Tenofovir/Emtricitabine/Efavirenz. The mean and nadir CD4+ T-cell counts were 125 cells/μL and 75 cells/μL, respectively, indicating moderate immunosuppression. The most common presenting complaints were blurred vision (71.4%) and floaters (42.9%). Visual acuity ranged from 20/20 to counting fingers, with most patients having mild to moderate visual impairment. Anterior segment findings were mostly normal, with a few cases of mild conjunctivitis and keratic precipitates. Posterior segment findings were dominated by CMV retinitis (57.1%) and RNFL thinning (42.9%). Additional findings included cotton wool spots and retinal hemorrhages. Ancillary tests revealed abnormal visual fields in 28.6% and reduced RNFL thickness on OCT in 42.9%. A history of opportunistic infections, such as oral candidiasis and pneumocystis pneumonia, was present in some patients. No comorbidities like diabetes or hypertension were reported. Most patients were on ART, and some were also taking antibiotics or pain medication. Table 1 paints a picture of a relatively young, predominantly male population with HIV who are experiencing ocular complications. The data highlights the importance of regular ophthalmologic evaluation and monitoring in HIV-positive individuals, especially those with lower $CD4^+$ T-cell counts, to detect and manage these potentially sight-threatening conditions.

Table 2 bivariate analysis presents the association between various risk factors and the presence of CMV retinitis in HIV-positive patients. There was a statistically significant association between low $CD4^+$ T-cell count (<200 cells/μL) and the development of CMV retinitis (p=0.04). This suggests that patients with lower $CD4^+$ T-cell counts are at higher risk of developing this ocular complication. No significant associations were found between CMV retinitis and age, ART status, occupation, educational level, duration of HIV infection, nadir $CD4^+$ T-cell count, or history of opportunistic infections.

Table 1. Demographic and clinical characteristics of HIV-positive patients with ocular manifestations.

Characteristic	Frequency (n)	Percentage (%)
Prevalence of HIV with ocular manifestations	7	4.7
Age (years)		
Mean (SD)	32.5 (5.2)	
Range	21-40	
Gender		
Male	7	100
Female	0	0
Occupation		
Unemployed	3	42.9
Self-employed	2	28.6
Private employee	2	28.6
Educational level		
High school	5	71.4
College	2	28.6
Mode of transmission		
Homosexual	7	100
Duration of HIV infection (years)		
Mean (SD)	3.2 (1.8)	
Range	1-6	
ART status		
On ART	6	85.7
Off ART	1	14.3
Type of ART regimen		
Tenofovir/Emtricitabine/Efavirenz	4	57.1
Zidovudine/Lamivudine/Nevirapine	2	28.6
Other	1	14.3
Duration of ART (years)		
Mean (SD)	2.1 (1.5)	
Range	0.5-5	
$CD4^+$ T-cell count (cells/uL)		
Mean (SD)	125 (85)	
Range	30-250	
Nadir $CD4^+$ T-cell count (cells/uL)		
Mean (SD)	75 (45)	
Range	20-150	
Presenting ocular complaints		
Blurred vision	5	71.4
Floaters	3	42.9
Eye pain	1	14.3
Visual acuity (Snellen equivalent)		
20/20 - 20/40	3	42.9
20/50 - 20/80	1	14.3
20/200 - 20/400	2	28.6
Count fingers	1	14.3
Anterior segment examination findings		
Normal	4	57.1
Mild Conjunctivitis	2	28.6
Keratic Precipitates	1	14.3
Posterior segment examination findings		
CMV retinitis	4	57.1
RNFL thinning	3	42.9
Cotton wool spots	1	14.3
Retinal hemorrhages	1	14.3
Ancillary test results		
Abnormal visual field	2	28.6
Reduced RNFL thickness on OCT	3	42.9
History of opportunistic infections		
Oral candidiasis	3	42.9
Pneumocystis pneumonia	1	14.3
Comorbidities		
None	7	100
Current medications		
ART	6	85.7
Antibiotics	2	28.6
Pain medication	1	14.3

SD = Standard Deviation, ART = Antiretroviral Therapy, CMV = Cytomegalovirus, RNFL = Retinal Nerve Fiber Layer, OCT = Optical Coherence Tomography.

Table 2. Association between risk factors and ocular manifestations in HIV-positive patients.

Risk factor	CMV retinitis (n=4)	No CMV retinitis (n=3)	p-value
Age (years)			
Mean (SD)	30 (6.8)	35 (4.0)	0.31
CD4⁺ T-cell count (cells/uL)			
Mean (SD)	87.5 (58.9)	183.3 (88.2)	0.04*
ART status			
On ART	3 (75)	3 (100)	0.56
Off ART	1 (25)	0 (0)	
Occupation			
Unemployed	2 (50)	1 (33.3)	0.57
Self-employed	1 (25)	1 (33.3)	
Private employee	1 (25)	1 (33.3)	
Educational level			
High school	3 (75)	2 (66.7)	0.32
College	1 (25)	1 (33.3)	
Duration of HIV infection (years)			
Mean (SD)	2.5 (1.3)	4 (1.7)	0.21
Nadir CD4⁺ T-cell count (cells/uL)			
Mean (SD)	50 (35.4)	100 (60.3)	0.12
History of opportunistic infections			
Yes	3 (75)	1 (33.3)	0.33
No	1 (25)	2 (66.7)	

SD = Standard Deviation, ART = Antiretroviral Therapy, CMV = Cytomegalovirus
*Statistically significant ($p < 0.05$).

Table 3 presents the results of a multivariate logistic regression analysis examining the independent risk factors for CMV retinitis in HIV-positive patients. The findings indicate: CD4⁺ T-cell Count: For every 10 cells/μL decrease in CD4⁺ T-cell count, the odds of developing CMV retinitis increase by 12% (OR 1.12, 95% CI 1.01-1.24, p=0.03). This confirms the strong association between lower CD4⁺ T-cell counts and increased risk of CMV retinitis, highlighting the importance of immune status in this ocular complication. Duration of HIV Infection: Although not statistically significant (p=0.20), the analysis suggests a trend towards an increased risk of CMV retinitis with a longer duration of HIV infection. For each additional year of infection, the odds of developing CMV retinitis are estimated to increase by 87% (OR 1.87, 95% CI 0.72-4.86). However, this finding should be interpreted cautiously due to the wide confidence interval and lack of statistical significance. Overall, Table 3 emphasizes the critical role of CD4⁺ T-cell count in predicting the risk of CMV retinitis in HIV-positive individuals. The data suggests that while the duration of HIV infection may play a role, its impact is less definitive than that of immune suppression. These findings underscore the importance of early and effective ART to maintain higher CD4⁺ T-cell counts and reduce the risk of CMV retinitis and other opportunistic infections in this population.

Table 3. Multivariate logistic regression analysis for risk factors of CMV retinitis in HIV-positive patients.

Risk factor	Odds ratio (OR)	95% confidence interval (CI)	p-value
$CD4^+$ T-cell Count (per 10 cells/uL decrease)	1.12	1.01-1.24	0.03*
Duration of HIV Infection (per year increase)	1.87	0.72-4.86	0.20

* Statistically significant ($p < 0.05$).

4. Discussion

Cytomegalovirus (CMV) retinitis stands as a well-recognized and potentially devastating ocular manifestation of HIV infection. The intricate pathophysiology of CMV retinitis involves a complex interplay between viral factors, host immune response and the unique microenvironment of the retina. CMV, a ubiquitous herpesvirus belonging to the Betaherpesvirinae subfamily, establishes latency in various tissues throughout the body, including the retina. In individuals with competent immune systems, CMV reactivation is typically suppressed and controlled by robust immune surveillance. However, in the context of HIV infection, where the immune system is progressively compromised, particularly in those with low $CD4^+$ T-cell counts, CMV can reactivate and initiate replication within the retina. This reactivation and uncontrolled viral replication lead to significant tissue damage and a cascade of inflammatory responses. The virus exhibits a predilection for infecting retinal endothelial cells, the cells lining the blood vessels within the retina. This infection triggers vasculitis, an inflammation of the blood vessels, which disrupts blood flow and leads to ischemia, a condition characterized by inadequate oxygen supply to the retinal tissues. The resulting ischemia sets the stage for the characteristic clinical features of CMV retinitis, including areas of retinal necrosis (cell death), hemorrhage (bleeding), and edema (swelling).[6,7]

The inflammatory response elicited by CMV infection further exacerbates retinal damage. The virus induces the production of pro-inflammatory cytokines and chemokines, signaling molecules that attract and activate immune cells. While this immune response is intended to combat the virus, it can also contribute to collateral damage to the retinal tissue. The recruitment of additional immune cells, such as macrophages and neutrophils, amplifies the inflammatory cascade, leading to further tissue destruction and visual impairment. Molecular studies have shed light on the intricate mechanisms underlying the pathogenesis of CMV retinitis. Viral factors, such as the expression of viral immediate-early (IE) genes, play a pivotal role in initiating viral replication. These IE genes encode regulatory proteins that orchestrate the expression of other viral genes necessary for viral replication and assembly. Additionally, CMV produces viral chemokines, which are signaling molecules that can modulate the host's immune response. These viral chemokines can attract specific immune cells to the site of infection, potentially facilitating viral spread and immune evasion. Host factors also contribute significantly to the development and progression of CMV retinitis. The expression of pro-inflammatory cytokines and chemokines by infected retinal cells and infiltrating immune cells amplifies the inflammatory response. These molecules can induce vascular permeability, leading to edema, and can also activate additional immune cells, perpetuating the inflammatory cycle. The balance between pro-inflammatory and anti-inflammatory responses is crucial in determining the extent of retinal damage.[7,8]

The intricate interplay between viral and host factors creates a permissive environment for CMV replication and dissemination within the retina. The virus can spread from cell to cell, leading to the progressive destruction of retinal tissue. This destruction manifests as areas of retinal necrosis, which appear as yellowish-white patches on funduscopic examination. Hemorrhages, resulting from damaged blood vessels, can also occur, further compromising retinal function. The progressive destruction of retinal tissue ultimately leads to visual

field loss. Patients with CMV retinitis may experience blind spots, blurred vision, or floaters. If left untreated, the infection can progress to involve the macula, the central part of the retina responsible for sharp, central vision, resulting in severe visual impairment or even blindness. CMV retinitis is a complex and multifactorial disease process. The interplay between viral factors, host immune response, and retinal microenvironment determines the severity and progression of the disease. Understanding the molecular mechanisms underlying CMV retinitis is crucial for developing effective therapeutic strategies to prevent visual loss in HIV-positive individuals. Early diagnosis, prompt initiation of antiviral therapy, and close monitoring of immune status are essential for managing this sight-threatening complication.[8,9]

Retinal nerve fiber layer (RNFL) thinning, a prevalent ocular manifestation in HIV-positive individuals, is frequently associated with HIV-associated neuroretinal disorder (HAND). This condition signifies a progressive loss of retinal ganglion cells (RGCs), the neurons forming the RNFL, and their axons. The underlying molecular mechanisms driving RNFL thinning in HIV are multifaceted and remain an area of ongoing research. However, a growing body of evidence suggests a complex interplay of direct viral neurotoxicity, immune-mediated damage, and microvasculopathy. HIV, a neurotropic virus, can directly infect RGCs, leading to their dysfunction and eventual demise. Viral proteins, such as Tat and gp120, have been implicated in this process. Tat, a transactivator of transcription protein, is known to disrupt cellular functions, including mitochondrial respiration and calcium homeostasis, ultimately triggering apoptosis in RGCs. Gp120, the envelope glycoprotein of HIV, can bind to various cellular receptors, including chemokine receptors and N-methyl-D-aspartate (NMDA) receptors, leading to excitotoxicity and neuronal damage. Furthermore, HIV infection can induce oxidative stress in RGCs, contributing to their degeneration. The virus can upregulate the production of reactive oxygen species (ROS) and downregulate antioxidant defenses, leading to an imbalance that damages cellular components, including DNA, proteins, and lipids. This oxidative damage can further impair mitochondrial function, exacerbating the neurotoxic effects of HIV.[10,11]

In addition to direct viral neurotoxicity, HIV infection can dysregulate the immune system, leading to chronic inflammation and the activation of autoreactive T cells. These T cells can infiltrate the retina and target retinal antigens, including those expressed on RGCs. This immune-mediated attack can result in RGC damage and subsequent RNFL thinning. The inflammatory response in HIV is characterized by the release of pro-inflammatory cytokines and chemokines, such as tumor necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and monocyte chemoattractant protein-1 (MCP-1). These molecules can further amplify the inflammatory cascade, attracting additional immune cells to the retina and perpetuating the cycle of RGC damage. Moreover, HIV infection can impair the function of regulatory T cells (Tregs), which normally suppress immune responses and maintain self-tolerance. This loss of immune regulation can contribute to the activation of autoreactive T cells and the development of autoimmune-like processes in the retina.[11,12]

Microvasculopathy, a hallmark of HIV infection, is characterized by endothelial dysfunction and capillary dropout. In the retina, these microvascular changes can lead to reduced blood flow, ischemia, and subsequent RGC loss. The resulting hypoxia can trigger the release of pro-angiogenic factors, such as vascular endothelial growth factor (VEGF), leading to neovascularization and further disruption of the retinal architecture. Additionally, microvascular damage can compromise the integrity of the blood-retinal barrier (BRB), a selective barrier that regulates the passage of molecules and cells between the circulation and the retina. Disruption of the BRB can allow for the infiltration of inflammatory cells and neurotoxic substances into the retina, exacerbating RGC damage and RNFL thinning. Recent studies have highlighted the role of mitochondrial dysfunction in

the pathogenesis of RNFL thinning in HIV. Mitochondria, the powerhouses of the cell, are essential for energy production and cellular homeostasis. HIV infection can impair mitochondrial function in RGCs through various mechanisms, including direct viral protein interactions, oxidative stress, and inflammation. Impaired mitochondrial function can lead to a decrease in ATP production, disruption of calcium homeostasis, and increased production of ROS. These changes can trigger apoptosis and contribute to the progressive neurodegeneration observed in HAND.[12,13]

Understanding the molecular mechanisms underlying RNFL thinning in HIV is crucial for developing effective therapeutic strategies. Current approaches focus on controlling HIV replication with ART, which can help to reduce viral neurotoxicity and immune-mediated damage. However, ART alone may not be sufficient to prevent or reverse RNFL thinning, particularly in individuals with advanced HIV disease or those who initiate ART late in the course of infection. Emerging therapies targeting specific molecular pathways involved in RNFL thinning are under investigation. These include neuroprotective agents, antioxidants, anti-inflammatory drugs, and therapies aimed at restoring mitochondrial function. Additionally, strategies to enhance immune regulation and prevent autoreactive T-cell activation may hold promise for mitigating immune-mediated damage to the retina. RNFL thinning in HIV is a complex process involving multiple interconnected pathways. Direct viral neurotoxicity, immune-mediated damage, microvasculopathy, and mitochondrial dysfunction all contribute to the loss of RGCs and their axons. Further research is needed to fully elucidate the molecular mechanisms involved and to develop targeted therapies that can prevent or reverse this debilitating complication of HIV infection.[14-17]

The findings of this study have several implications for clinical practice in the management of HIV-positive individuals. First, the high prevalence of CMV retinitis and RNFL thinning underscores the importance of regular ophthalmologic evaluation in this population. Early detection of these complications is crucial for timely intervention and prevention of visual loss. Second, the association between low $CD4^+$ T-cell count and CMV retinitis highlights the need for close monitoring of immune status in HIV-positive individuals. Early initiation of ART and maintenance of optimal $CD4^+$ T-cell counts are essential for reducing the risk of opportunistic ocular infections. Third, the study emphasizes the importance of a multidisciplinary approach to the care of HIV-positive individuals with ocular manifestations. Collaboration between ophthalmologists, infectious disease specialists, and other healthcare providers is essential for comprehensive management and optimal outcomes. Further research is needed to elucidate the complex pathophysiological mechanisms underlying HIV-related ocular complications. Longitudinal studies are required to assess the long-term effects of HIV infection on the visual system and to evaluate the impact of ART on the incidence and progression of ocular manifestations. Additionally, research should focus on identifying novel therapeutic targets for the prevention and treatment of HIV-related ocular disease. The development of new antiviral agents, immunomodulatory therapies, and neuroprotective strategies may offer promising avenues for improving visual outcomes in this population. This study provides valuable insights into the ocular manifestations and associated risk factors in HIV-positive individuals. The findings emphasize the importance of early detection, prompt management, and a multidisciplinary approach to care for preserving vision and improving the quality of life in this population.[18-20]

5. Conclusion

This study demonstrates that CMV retinitis and RNFL thinning are the predominant ocular manifestations in HIV-positive individuals at Dr. M. Djamil General Hospital, Padang, Indonesia. Low $CD4^+$ T-cell count is a significant risk factor for CMV retinitis, emphasizing the importance of early ART initiation and regular monitoring of immune status.

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