*Magna Neurologica Vol. 2, No. 2, July 2024*

https://journal.uns.ac.id/magna-neurologica
DOI: 10.20961/magnaneurologica.v2i2.1097
**e-ISSN 2985-3729 p-ISSN 2963-6027**

MAGNA NEUROLOGICA

**RESEARCH ARTICLE** **OPEN ACCESS**

# PROFILE OF HIV/AIDS PATIENTS WITH NEUROLOGICAL MANIFESTATIONS IN THE TERTIARY REFERRAL HOSPITAL IN BALI

Anak Agung Ayu Suryapraba[1*], Aurelia Vania[1], Anak Agung Raka Sudewi[1], Ni Made Dewi Dian Sukmawati[2], Ni Made Susilawathi[3]

***Correspondence**: suryaprabaindradewi@unud.ac.id*
*[1]Denpasar Neurology Department, Prof. Dr. I.G.N.G Ngoerah Hospital, Denpasar, Bali, Indonesia*
*[2]Tropical and Infectious Disease Division, Internal Medicine Department, Prof. Dr. I.G.N.G Ngoerah Hospital, Denpasar, Bali, Indonesia*
*[3]Faculty of Medicine, Universitas Udayana, Denpasar, Bali, Indonesia*

***Article History:***
*Received: February 1, 2024*
*Accepted: February 27, 2024*
*Published: July 1, 2024*

***Cite this as:***
*Suryapraba AAA, Vania A, Sudewi AAR, Sukmawati NMDD, Susilawathi NM. Profile of HIV/AIDS Patients with Neurological Manifestations in The Tertiary Referral Hospital in Bali. Magna Neurologica. 2(2) July 2024: 60-64. 10.20961/magnaneurologica.v2i2.1097*

**ABSTRACT**

**Background:** Neurological manifestations in approximately half of Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) patients are related to high morbidity and mortality worldwide. Therefore, there is a need for epidemiological data on HIV/AIDS patients with neurological manifestations in Bali, as an international tourism destination.
**Objective**: This study aimed to describe the clinical profile of neurological manifestations among patients with HIV/AIDS in the tertiary referral hospital for Bali and Nusa Tenggara region.
**Methods:** A descriptive-retrospective study was conducted on HIV/AIDS patients presenting with neurological manifestations hospitalized in the Neurology Department of Prof. Dr. I.G.N.G Ngoerah Hospital Denpasar from January 2018 to December 2021.
**Results**: Among the 227 subjects included in this study, the majority were male (69.9%) and HIV positive newly diagnosed (69.2%). Furthermore, out of 126 subjects who had CD4 data, the majority were with CD4 <200 cells/mm$^3$ (85.7%) and 53.1% were <50 cells/mm$^3$, with ages ranging from 18 to 67 years old, at a median of 36 years old. The most common neurological signs and symptoms found were paresis/paralysis (61.7%), headache (54.6%), decreased consciousness (52.9%), and cranial nerve palsy (52%). Cerebral toxoplasmosis (67.4%) and tuberculous meningoencephalitis (20.3%) were the prevalent opportunistic infections, while the mortality rate was 39.6% with sepsis as the major cause.
**Conclusions:** Neurological manifestations are common initial symptoms in diagnosing HIV infection**.** Therefore, better awareness and earlier detection are required among people with risk factors of HIV transmission, particularly in groups of young and productive age with signs of immunocompromised condition as well as neurological manifestations.

**Keywords:** characteristics; HIV; neurological manifestations; profile



## Introduction

Human Immunodeficiency Virus (HIV) is a retrovirus capable of causing central and peripheral nerve dysfunction. Based on previous estimation, more than 50% of patients with HIV have neurological complications during their lifetime. Groups of nervous system disorders related to HIV infection can be caused by direct primary complications of HIV or secondary due to opportunistic infections (OIs), called Neuro-AIDS. Primary complications of HIV include HIV neuropathy, cognitive dysfunction, and HIV myelopathy. Meanwhile, nervous system OIs commonly found in HIV patients include cerebral toxoplasmosis, tuberculous meningitis, cryptococcal meningitis, cytomegalovirus encephalitis, herpes

zoster encephalitis, neurosyphilis, primary central nervous system lymphoma (PCNSL), and progressive multifocal leukoencephalopathy (PML).[1,2]

Currently, coverage of HIV detection in the infected population is still insufficient, due to lack of awareness and absence of regular HIV screening in cases of central nervous system (CNS) infections.[2] Neurological disorders have been found to affect 40% of HIV patients, with neuropathological conditions occurring in 80% of cases, leading to high morbidity and mortality rates.[3] Moreover, neurological manifestations are often presented as the first symptom of newly diagnosed HIV/AIDS.[4]

In Indonesia, Bali is an international tourism destination, posing a high risk of HIV/AIDS transmission due to influences of global culture and lifestyle. These include temporary or multiple sexual partners, unprotected sexual intercourse, homosexuality, or use of intravenous drugs.[5] According to the 2022 report of Basic Health Research Indonesian Ministry of Health, Bali was included in the 10 provinces with the highest prevalence of HIV in the country.[6] Although there are some epidemiological studies of Neuro-AIDS[3,7], epidemiological data of neurological disorders among HIV/AIDS patients in Bali have not been reported comprehensively in a long period. Therefore, this study aimed to show the clinical profile of neurological manifestations among HIV/AIDS patients in a tertiary referral hospital for Bali and Nusa Tenggara region. This clinical profile data is expected to help neurologists facing early HIV cases and OIs diagnosis.

## Methods

A descriptive-retrospective study was conducted on HIV/AIDS patients presenting with neurological manifestations in the Neurology Department of Prof. Dr. I.G.N.G Ngoerah Hospital Denpasar, Bali from January 2018 to December 2021. Data were obtained consecutively from medical records, including demographic data (gender and age), Highly Active Anti-Retroviral Therapy (HAART) status, CD4 level, neurological manifestations, OIs, and outcomes of subjects. Demographic data, HAART status, and CD4 level were obtained from medical record, while neurological manifestations was obtained from history and physical examination. HIV status was taken from existing medical record data and new HIV diagnosis was confirmed by ELISA serology test. Furthermore, diagnosis of OIs was based on liquor cerebrospinal analysis and/or Head computed tomography (CT) scan or Magnetic Resonance Imaging (MRI) results. Outcomes of subjects were determined by the Glasgow Outcome Scale (GOS).

The inclusion criteria were all confirmed HIV adult patients presenting with neurological manifestations who were treated in the neurology department of hospital during study time. Exclusion criteria included patients with other comorbidities that could be the cause of neurological deficits such as vascular events, metabolic disorders, and other complicating conditions in early presentation. Quantitative data were analyzed descriptively using Statistical Package for Social Sciences (SPSS) version 20 for Windows. This study was ethically approved by the Ethics Commission of the Faculty of Medicine at Udayana University.

## Results

### General Characteristics

Among 227 subjects included in this study, 69.6% were males and 69.2% were HIV-positive newly diagnosed when hospitalized or consulted. The ages of subjects ranged from 18-67 years old, with a median of 36 years old, specifically 36.5 for males and 36 for females. The majority of subjects were not on HAART (70.5%), primarily due to being newly diagnosed or dropping out. Data on CD4 level were obtained in 126 subjects, where majority were <200 cells/mm$^3$ (108/126) and 29.5% had CD4 level <50 cells/mm$^3$.

**Table 1.** General Characteristics of Subjects

| Characteristics | N (%) |
|---|---|
| Year of admission | |
| 2018 | 23 (10.1) |
| 2019 | 61 (26.9) |
| 2020 | 76 (33.5) |
| 2021 | 67 (29.5) |
| Gender | |
| Male | 158 (69.6) |
| Female | 69 (30.4) |
| Age | Range 18-67 (median: 36) |
| On HAART | |
| Yes | 67/227 (29.5) |
| No | 160/227 (70.5) |
| CD4 count (cells/mm$^3$) | |
| <50 | 67/126 (53.1) |
| 50-100 | 24/126 (19.0) |
| 100-200 | 17/126 (13.5) |
| >200 | 18/126 (14.3) |
| Deaths | |
| All subjects | 90/227 (39.6) |
| Cerebral toxoplasmosis | 56/153 (36.6) |
| Tuberculous meningitis | 27/46 (58.7) |

CD4: cluster of differentiation 4; HAART: highly active antiretroviral therapy

### Neurological Manifestations

Common neurological signs and symptoms found in this study were paresis/paralysis (61.7%), headache (54.6%), a decrease of consciousness (52.9%), cranial

nerve palsy (52%), and seizure (26.4%) (Table 2). Types of seizure were focal (25%), general (43.3%), and focal to bilateral seizure (31.7%), while fever was found in 32.2% of subjects. All patients had at least one of the immunocompromised risk factors, symptoms, and signs, such as HIV risky behavior, fever, weight loss, diarrhea, or chronic cough.

Cerebral toxoplasmosis (67.4%) and tuberculous meningoencephalitis (20.3%) were the most prevalent OIs among subjects. This was followed by other forms of CNS tuberculosis, tuberculoma (5.7%), where subjects with more than 1 OIs were 24 (10.6%) (Table 2).

**Table 2.** Neurological Signs and Symptoms

| Overall signs and symptoms | N (%) |
|---|---|
| Headache | 124 (54.6) |
| Decrease of consciousness | 120 (52.9) |
| Mental deterioration | 48 (21.1) |
| Visual loss | 9 (4) |
| Double vision | 8 (3.5) |
| Paresis/paralysis | 140 (61.7) |
| Seizure | 60 (26.4) |
| Balance disorder | 9 (4) |
| Involuntary movement | 2 (0.9) |
| Sensory disorder | 9 (4) |
| Neuropathic pain | 5 (2.2) |
| Cranial nerve palsy | 118 (52) |
| Fever | 73 (32.2) |
| **Diagnosis** | |
| Cerebral toxoplasmosis | 153 (67.4) |
| CNS TB (meningitis, tuberculoma) | 59 (26.0) |
| Bacterial meningitis | 10 (4.4) |
| Cryptococcal meningitis | 2 (0.9) |
| Viral encephalitis | 1 (0.4) |
| PML | 3 (1.3) |
| Neurosyphilis | 3 (1.3) |
| HIV Associated Neurocognitive Disorders (HANDS) | 3 (1.3) |

### Outcomes

The mortality rate in this study was 39.6%, with sepsis as the most common cause of death. Furthermore, the highest case fatality rate was found in tuberculous meningoencephalitis (57.8%) and cerebral toxoplasmosis (36.6%). Subjects with a mild disability were 7.5%, moderate disability was 23.3%, and severe disability was found to be 29.5%, according to the GOS.

## Discussion

The majority of subjects in this study were male (69.6%) at a productive young age, with a median age of 36 years old (Table 1). Males were more prone to HIV/AIDS transmission due to engaging in risky sexual behaviors. These include multi-partner sexual relationships, anal sexual intercourse, homosexual, or intravenous substance/drug abuse, which are more prevalent in males than females.[9] Moreover, awareness regarding HIV screening was higher in males compared to females due to occupation or company requirements.

The age of subjects ranged from 18 to 67 years old, with a median age of 36 years old. This result was relevant to the survey from the Indonesian Ministry of Health, where most HIV/AIDS populations in Indonesia were aged 25-49 years old.[10] This suggested that the majority of subjects were exposed to HIV at a younger age when engaged in active sexual behavior. Neurological OIs were observed in the late-stage of HIV infection when CD4 level decreased below 200 cells/mm3, between 2-10 years without anti-retroviral treatment.[11]

The majority of subjects with CD4 data had CD4 level of <200 cells/mm3 (85.7%) and approximately one-third had a very low CD4 level (<50 cells/mm3). Low CD4 level in HIV/AIDS patients led to a decrease in both cellular and humoral immunity, increasing susceptibility to OIs. Since the introduction of HAART, the incidence of OIs has significantly decreased but remained a burden in caring for HIV/AIDS patients with high morbidity and mortality. However, low CD4 level was specifically observed in pre-HAART patients or those with inadequate treatment compliance.[12]

Subjects included in this study were HIV-positive and newly diagnosed (HAART-naïve). After admission or consultation with the department due to their neurological symptoms, 69.2% of subjects were newly diagnosed with HIV infection and did not receive HAART. This was consistent with previous studies where 40-70% of HIV patients had neurological manifestations, which were commonly associated with late-stage disease or low CD4 levels. Meanwhile, in acute HIV infection, neurological manifestations were mild, serving as the initial finding in diagnosing HIV/AIDS.[13,14] Lack of HIV screening in health facilities despite signs and symptoms of immunocompromised became a significant factor contributing to delayed diagnosis.[15]

More than half of the subjects had not received HAART, a condition correlated with low CD4 level and a risk factor for neurological manifestations due to OIs. HAART initiation resulted in suppressed viral load and improved immunity, characterized by the increased level of CD4 and low OIs. Despite HAART initiation, the presence of OIs was related to unmasking immune reconstitution inflammatory syndrome (IRIS), incomplete immune recovery, or HAART failure.[16] Furthermore, neurological

manifestations in HIV/AIDS patients could occur through other mechanisms, such as the direct viral effect of HIV and chronic inflammation due to infection, IRIS, or adverse impact of antiretroviral. These clinical manifestations vary depending on the underlying etiology and area of the affected nervous system.

Cerebral toxoplasmosis and tuberculous meningitis were the most common OIs found as reported by Rahmayanti *et al.* (2019) and Fatimatuzzahra *et al.* (2022)[17,18] Moreover, cerebral toxoplasmosis is also known as the most common neurological OI after the introduction of the antiretroviral era. Some risk factors of cerebral toxoplasmosis in HIV/AIDS patients are a degree of immunosuppression and inadequate cotrimoxazole treatment as prophylaxis for *Pneumocystis jirovecii* pneumonia.[19,20]

Some subjects had more than one diagnosis of neurological OIs due to the poor immune system. Since one OIs could weaken immunity to another, the majority of subjects were at risk of developing multiple OIs at one moment.[21] Mortality rate in this study was significantly high (39.6%), where the highest was found in tuberculous meningitis cases (57.8%), followed by cerebral toxoplasmosis (36.6%). Similarly, Lestari *et al*. (2016) found that case fatality of neurological OIs was 37.7% with the highest occurrence observed in tuberculoma, cryptococcal meningitis, tuberculous meningitis, and cerebral toxoplasmosis. Subjects without HAART had a 2.9-fold higher risk of mortality compared to those on HAART.[22] Another study in China found that there was a significant decline in mortality among HIV/AIDS patients from 5.4% to 2.7%, showing a strong relationship with an increase in HAART coverage.[23] A study in Tanzania by Gunda *et al.* (2017) showed that the highest mortality rate of patients with HAART was 11.6%.[24] Based on these situations, the high fatality rate found in this study was related to the high proportion of subjects who had not received HAART. The results also showed that neurologic OIs were more common compared to other primary complications in HIV. These included neurocognitive disorders, neuropathy, or myelopathy since all subjects were hospitalized with severe neurologic manifestations and mostly had low CD4 level < 200 cells/mm$^3$.

This study is the first to report descriptive data on HIV/AIDS patients with neurological manifestations in Bali. However, some limitations were observed, which included the use single-centre retrospective design, leading to unrecoverable missing data. A small number of patients was included and not all participants had the CD4 level data documented. Our subjects included HIV patients without other comorbidities that could be the cause or risk factors for neurological manifestations. Therefore, the results emphasized suspecting HIV infections in young and productive adults presented with neurological manifestations without significant vascular risk factors. To address these limitations, detailed history taking and physical examination are essential to HIV systemic symptoms and signs. These patients also required further laboratory or neuroimaging studies to diagnose OIs.

## Conclusion

In conclusion, this study successfully described the clinical profile of neurological manifestations among HIV/AIDS patients in Bali. The results showed that the majority of subjects were male HIV/AIDS patients at young and productive ages. Furthermore, most of patients had not received HAART and had low CD4 levels. Paresis/paralysis, headache, decrease of consciousness, and cranial nerve palsy were the most common symptoms frequently complained about among subjects. Approximately, more than half of the subjects were newly diagnosed as HIV positive, showing that neurological manifestations were essential initial points in diagnosing HIV infection. Therefore, HIV infection should be excluded in patients with these characteristics and other signs of immunocompromised conditions.

The results showed that OIs were more common compared to other primary complications, with cerebral toxoplasmosis being the most prevalent, followed by CNS TB (meningoencephalitis, tuberculoma). The overall case fatality rate was relatively high, with the highest being TB meningitis, which was attributed to OIs and low CD4 levels of subjects. Improving awareness among the population with a high risk of HIV transmission, family, and health professionals, was found to be crucial in achieving earlier detection of HIV infections. Additionally, prevention of neurological complications, morbidity, and mortality of HIV patients could be anticipated through good counseling, information, as well as education to patients and caregivers, with proper supervised medication.

## References


1. Corral I, Quereda J, Garcia Monco J.C. CNS infections. Springer International Publishing Switzerland 2018. https://doi.org/10.1007/978-3-319-70296-4_15.
2. Saylor D. Neurologic Complications of Human Immunodeficiency Virus Infection. Contin Lifelong Learn Neurol. 2018 Oct;24(5):1397–421.

3. Munir B, Candradikusuma D. Manifestations of HIV AIDS in case neurology : epidemiology study at Saiful Anwar Hospital year 2013-2014. MNJ (Malang Neurol Journal). 2015 Jan 1;1(1):7–11.
4. Sharma S, Hussain M, Habung H. Neurologic Manifestations in HIV. Neurol India. 2017;65:64–8.
5. Directorate General of Disease Prevention and Control Ministry of Health Republic Indonesia . 2017. HIV Epidemiology REview Indonesia 2016.
6. P2P D. Laporan Perkembangan HIV-AIDS dan Penyakit Infeksi Menular Seksual _PIMS_ Triwulan 1 -januari-Maret 2022. Kemenkes. 2022.
7. Imran D, Estiasari R, Maharani K, Sucipto, Lestari DC, Yunus RE, et al. Presentation, etiology, and outcome of brain infections in an Indonesian hospital: A cohort study. Neurol Clin Pract. 2018;8(5):379–88.
8. Leunupun S, Kembuan M, Ngantung D. 2014. Insiden Penderita HIV/AIDS dengan komplikasi INtrakranial yang dirawat oleh bagian Neurologi di RSUP Prof. Dr. R.D. Kandou Manado PeriodeJuli 2011-2012. e Journal Unsrat
9. Sajadipour M, Rezaei S, Irandoost SF, Ghaumzadeh M, Salmani nadushan M, Gholami M, et al. What explains gender inequality in HIV infection among high-risk people? A Blinder-Oaxaca decomposition. Arch Public Heal. 2022 Dec 4;80(1):2.
10. Health IM of. Quarterly report on the development of HIV & AIDS in Indonesia up to 31 December 2020. 2021.
11. Punitha S,Kiruthiga N, Kavitha M, DivyaPresenna S. Clinical Stages og HIV. *HIV Nursing* 2021; 21(2): 103-106
12. Achhra A, Petoumenos K, Law M. Relationship between CD4 cell count and serious long-term complications among HIV-positive individuals. Curr Opin HIV AIDS. 2014;9(1):63–71.
13. Hellmuth J, Fletcher JLK, Valcour ., Kroon E, et al. Neurologic signs and symptoms frequently manifest in acute HIV. Neurology® 2016;87:148–154.
14. Modi G, Mochan A, Modi M. Advances in HIV & AIDS control Chapter 7: Neurological manifestations of HIV. 2018 IntechOpen.
15. Xie J, Hsieh E, Sun M, Wang H, Lv W, Fan H, et al. Delays in HIV diagnosis and associated factors among patients presenting with advanced disease at a tertiary care hospital in Beijing, China. Zhang C, editor. PLoS One. 2017 Aug 9;12(8):e0182335.
16. Arefaine ZG, Abebe S, Bekele E, Adem A, Adama Y, H. Brockmeyer N, et al. Incidence and predictors of HIV related opportunistic infections after initiation of highly active antiretroviral therapy at Ayder Referral Hospital, Mekelle, Ethiopia: A retrospective single centered cohort study. Dholakia YN, editor. PLoS One. 2020 Apr 20;15(4):e0229757.
17. Rahmayanti R, Retnaningsih R, Sofro MAAU. HIV-Associated Neurological Disorders Clinical Manifestations. Medica Hosp J Clin Med. 2019 Nov 25;6(2):100–6.
18. Fatimatuzzahra DSL, Ganiem AR, Cahyani A, Gunadharma S, Dian S. Prevalence of Opportunistic Infection in Central Nervous System among Patients with HIV/AIDS at Dr. Hasan Sadikin General Hospital Bandung, Indonesia. Althea Med J. 2022 Jun;9(2):100–5.
19. Chemoh W, Sawangjaroen N, Siripaitoon P, Andiappan H, Hortiwakul T, Sermwittayawong N, Charoenmak B and Nissapatorn V (2015) Toxoplasma gondii – Prevalence and Risk Factors in HIV-infected Patients from Songklanagarind Hospital, Southern Thailand. Front. Microbiol. 6:1304. doi: 10.3389/fmicb.2015.01304.
20. Vidal JE. HIV-Related Cerebral Toxoplasmosis Revisited: Current Concepts and Controversies of an Old Disease. *J Int Assoc Provid AIDS Care.* 2019;18.
21. Tewachew AS, Mekonnen WN, Mekuria AD, Amare YE. Determinants of Opportunistic Infections Among HIV-Positive Patients on HAART in Debre Berhan Referral Hospital, North Shoa Zone, Ethiopia, 2020: A Case–Control Study. HIV/AIDS - Res Palliat Care. 2021 Mar;Volume 13:337–47.
22. Lestari A, Dian S, Chrysanti C. Predictor of Mortality in Acquired Immunodeficiency Syndrome Patients with Central Nervous System Opportunistic Infections. althea Med J. 2016;3(4):577–82.
23. Zhao Y. Wei L. Zhao D, Gan X, Wu Y, Han M, Changing Mortality and Patterns of Death Causes in HIV Infected Patients — China, 2013–2022, CCDC Weekly / Vol. 5 / No. 48.
24. Gunda DW, Nkandala I, Kilonzo SB, Kilangi BB, Mpondo BC. Prevalence and Risk Factors of Mortality among Adult HIV Patients Initiating ART in Rural Setting of HIV Care and Treatment Services in North Western Tanzania: A Retrospective Cohort Study. J Sex Transm Dis. 2017 Jun 15;2017:1–8.