

Spectrum and Frequency of Opportunistic Infections among People Living with HIV in a Tertiary Care Hospital of Tripura: A Cross-Sectional Study

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ABSTRACT

Background: Opportunistic infections (OIs) remain an important cause of morbidity among people living with HIV (PLHIV), particularly in the presence of advanced immunosuppression. Understanding the spectrum and frequency of OIs in specific regional populations is essential for improving clinical surveillance and management. This study assessed the spectrum and frequency of OIs among PLHIV attending a tertiary care hospital in Tripura, India, and examined their clinical and sociodemographic characteristics in relation to CD4 cell count.

Methods: A hospital-based cross-sectional observational study was conducted at Agartala Government Medical College and G.B. Pant Hospital, Tripura, from June 2023 to May 2025. A total of 100 adults with confirmed HIV infection who attended the hospital or ART Centre were enrolled. Sociodemographic and clinical information, ART status, laboratory findings, and CD4 cell counts were recorded using a structured case record form. OIs were identified using appropriate clinical, microbiological, radiological, and histopathological criteria. Data were analysed using descriptive statistics, the chi-square test, and Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant.

Results: Forty-five of the 100 participants had at least one OI. Tuberculosis was the most frequently observed OI, accounting for 15 cases (33.3%), followed by respiratory infections in 11 (24.4%), oral candidiasis in 9 (20.0%), skin infections in 6 (13.3%), and genital infections in 4 (8.9%). Regarding CD4 cell counts, 40 participants (40.0%) had counts <200 cells/ μ L, 45 (45.0%) had counts of 200–500 cells/ μ L, and 15 (15.0%) had counts >500 cells/ μ L. No statistically significant associations were observed between OI status and the evaluated sociodemographic variables, including sex, age, religion, education, occupation, marital status, and ethnicity.

Conclusion: OIs represented a substantial clinical burden among PLHIV in this tertiary-care setting, with tuberculosis, respiratory infections, and oral candidiasis comprising the predominant presentations. The high proportion of participants with CD4 counts <200 cells/ μ L underscores the importance of early diagnosis, sustained ART, and regular immunological monitoring for reducing OI-related morbidity.

Keywords: HIV Infections; Opportunistic Infections; Tuberculosis; CD4 Lymphocyte Count; Antiretroviral Therapy; Cross-Sectional Studies

INTRODUCTION

Human Immunodeficiency Virus (HIV) infection continues to be a major global health challenge, particularly in low- and middle-income countries where access to comprehensive care remains limited. Opportunistic infections (OIs) are among the most important contributors to morbidity and mortality in people living with HIV (PLHIV). These infections, caused by bacteria, fungi, viruses, and parasites that are usually harmless in immunocompetent individuals, become pathogenic when the immune system is compromised. The burden of OIs is closely linked to the degree of immunosuppression, most commonly measured by CD4 lymphocyte counts, and remains a critical marker of disease progression and prognosis in HIV patients.^[1] Globally, despite significant advances in antiretroviral therapy (ART), OIs continue to account for a substantial proportion of hospitalisations and deaths among PLHIV.^[2] Tuberculosis (TB) remains the most common OI worldwide, followed by fungal infections such as candidiasis and cryptococcosis, viral infections including cytomegalovirus (CMV), and protozoal infections such as toxoplasmosis.^[3] The risk of developing these infections increases markedly when CD4 counts fall below 200 cells/ μ L, with certain infections such as *Pneumocystis jirovecii* pneumonia (PCP) and cryptococcal meningitis strongly associated with counts below 100 cells/ μ L.^[4] In India, HIV prevalence is estimated at 0.22% among adults, translating to approximately 2.4 million PLHIV.^[5] The northeastern states, including Tripura, report higher prevalence rates compared to the national average, largely due to factors such

as intravenous drug use and socioeconomic vulnerabilities.^[6] Recent surveillance data indicate that Tripura has an adult HIV prevalence of 0.33%, ranking fifth among northeastern states.^[7] This regional burden underscores the importance of studying the epidemiology of OIs in PLHIV within this context.

Several Indian studies have highlighted the predominance of TB, PCP, and candidiasis among PLHIV, with strong correlations to declining CD4 counts.^[8] Earlier studies from northern India reported that 53.2% of PLHIV developed one or more OI during follow-up, with tuberculosis accounting for a major proportion of cases.^[9] Nutritional status, low body mass index (BMI), and hypoalbuminemia were also identified as predictors of OI occurrence, in addition to immunological decline.^[10] In Northeast India, intestinal parasitic infections such as *Cryptosporidium* and *Cystoisospora* have been reported as major causes of chronic diarrhoea in HIV patients, further complicating disease management.^[11]

The introduction of ART has significantly reduced OI incidence; however, gaps in access, adherence, and early diagnosis persist.^[12] In resource-limited settings, PLHIV often present late to healthcare facilities, already suffering from advanced immunosuppression and multiple OIs. This not only increases the risk of mortality but also places a heavy burden on healthcare systems.^[13] Moreover, stigma, poor awareness, and limited laboratory infrastructure in rural and semi-urban regions exacerbate the challenge of timely diagnosis and management.

Understanding the epidemiological profile of OIs in PLHIV is therefore crucial for

tailoring interventions, strengthening ART programs, and guiding prophylactic strategies. Regional data from Tripura and other northeastern states can provide valuable insights into the spectrum of infections, their frequency, and their correlation with CD4 counts. Such evidence is essential for clinicians, policymakers, and public health authorities to design effective strategies for reducing HIV-related morbidity and mortality.

This study aimed to describe the prevalence and spectrum of OIs among PLHIV attending a tertiary care hospital in Tripura and to analyse their relationship with CD4 counts. By documenting the epidemiological profile of OIs in this high-burden region, the study aims to contribute to improved clinical management, early detection, and targeted preventive measures for PLHIV.

MATERIALS AND METHODS

Study Design and Setting: This cross-sectional observational study was conducted in the Department of General Medicine at Agartala Government Medical College and GBP Hospital, Tripura. The study was conducted in collaboration with the Department of Microbiology and the institution's ART Centre.

Study Period: Data collection was undertaken over a two-year period, from June 2023 to May 2025.

Study Population: The study included adult patients diagnosed with HIV infection who were admitted to the General Medicine ward or attending the ART Centre during the study period.

Sample Size Determination: The required sample size was calculated using the Kish Leslie formula (1965) for cross-sectional studies:

$$N = \frac{Z^2 \cdot P(1 - P)}{L^2}$$

Where:

- N= sample size
- Z= 1.96 (standard normal deviate at 5% significance level)
- P= estimated prevalence of OIs among PLHIV on ART (60%)

- L= margin of error (10%)

The calculated sample size was approximately 92 participants; therefore, a total of 100 participants were included in the study.

Inclusion Criteria

Participants were eligible for enrolment if they met the following conditions:

- Confirmed diagnosis of HIV infection.
- Provided written informed consent and expressed willingness to participate in the study.
- Age ≥ 18 years.
- Both male and female patients were considered.

Exclusion Criteria

Participants were excluded from the study if they met any of the following conditions:

- Age < 18 years.
- Declined to provide informed consent.
- Pregnant or lactating women.

Diagnosis of Opportunistic Infections

Diagnosis of OIs was based on clinical evaluation and appropriate laboratory, microbiological, radiological, or histopathological investigations, as clinically indicated. An infection was classified as an OI only when it met the study's predefined clinical and/or microbiological diagnostic criteria. The diagnostic methods used for individual infections were as follows:

A. Bacterial Infections: HIV-associated bacterial infections considered in this study included tuberculosis and other clinically significant bacterial infections meeting the study's predefined diagnostic criteria.

- **Tuberculosis:** Chest X-ray, sputum smear/culture, CBNAAT, TRUENAT, LPA, and liquid/solid culture.
- **Pneumococcal pneumonia:** Chest X-ray and blood culture.
- **Bacterial meningitis:** Lumbar puncture with CSF analysis and culture.
- **Skin/soft tissue infections:** Wound swab or biopsy with culture and sensitivity.

B. Fungal Infections: Major fungal infections included candidiasis, cryptococcal meningitis, histoplasmosis, and aspergillosis.

- **Candidiasis:** Direct microscopy and culture from oral/mucosal lesions.
- **Cryptococcal meningitis:** CSF antigen detection and culture.
- **Histoplasmosis/aspergillosis:** Serology, biopsy, and fungal culture (SDA $\pm$ antibiotics, Bird Seed Agar).

C. Viral Infections: Viral OIs considered in this study included cytomegalovirus (CMV) end-organ disease. Hepatitis B virus (HBV), hepatitis C virus (HCV), and human papillomavirus (HPV) were treated as comorbid viral infections rather than automatically classified as OIs, unless they met the study's predefined OI criteria.

- **CMV:** Antigen detection, ELISA, ICT, or RT-PCR from blood/fluids.
- **Hepatitis B/C:** Serological assays for viral antigens and antibodies.
- **HPV:** Pap smear and HPV DNA testing.

D. Protozoal Infections: Protozoal infections considered included toxoplasmosis, cryptosporidiosis, and *Cystoisospora belli* infection.

- **Toxoplasmosis:** Serological tests.
- **Cryptosporidiosis/isosporiasis:** Stool microscopy (Kinyoun Carbol Fuchsin stain), saline/iodine mount, and DNA detection.

E. Other Opportunistic Infections: Other OIs considered included PCP, Kaposi sarcoma, progressive multifocal leukoencephalopathy (PML), and *Salmonella* septicaemia, according to predefined diagnostic criteria.

- **PCP:** Examination of lung fluid or lung tissue.
- **Kaposi's sarcoma:** Biopsy with histopathology.
- **PML:** Brain MRI and CSF JC virus detection.
- **Salmonella septicaemia:** Blood culture.

Data Collection: A structured case record form was used to collect socio-demographic details, clinical history, ART status, and

laboratory findings. CD4 counts were obtained from the ART Centre records.

Statistical Analysis: We entered data into Microsoft Excel and analysed them in SPSS. We used descriptive statistics to summarise demographic and clinical variables. We analysed the data using chi-square and Fisher's exact tests as required. A p-value <0.05 was considered statistically significant.

Ethical Considerations: The Institutional Review Board (IRB) of Agartala Government Medical College & GBP Hospital approved the study before initiation. We obtained written informed consent from all participants before enrolment. Throughout the study, we took strict measures to safeguard participant privacy and maintain the confidentiality of all collected data.

RESULTS

Out of 100 PLHIV enrolled in the study, 45 (45%) developed OIs, while 55 (55%) did not. This highlights that nearly half of the study population experienced at least one OI. Most patients were on ART at enrolment; however, this study did not analyse ART status as a primary variable.

Spectrum of Opportunistic Infections

Among the 45 patients who developed OIs, the distribution was as follows:

- **Tuberculosis:** The most common OI, affecting 15 patients (33.3%). The predominant organisms were *Mycobacterium tuberculosis* and *Mycobacterium avium*.
- **Respiratory infections:** Documented in 11 patients (24.4%), caused mainly by *Streptococcus pneumoniae*, *Pneumocystis jirovecii*, and *Aspergillus fumigatus*.
- **Oral thrush:** Observed in 9 patients (20.0%), with *Candida albicans* and *Candida tropicalis* as the common pathogens.
- **Skin infections:** Found in 6 patients (13.3%), most frequently due to

Staphylococcus aureus, *Trichophyton rubrum*, and *Candida albicans*.

- **Genital infections:** Reported in 4 patients (8.9%), associated with *Candida*

albicans, herpes simplex virus type-2 (HSV-2), and human papillomavirus (HPV).

Table 1: Spectrum of Opportunistic Infections and Causative Organisms

OI Type	Frequency	Common Organisms
Tuberculosis	15 (33.3%)	Mycobacterium tuberculosis, M. avium
Respiratory infection	11 (24.4%)	S. pneumoniae, P. jirovecii, A. fumigatus
Oral thrush	9 (20.0%)	Candida albicans, C., tropicalis
Skin infection	6 (13.3%)	S. aureus, T. rubrum, C., albicans
Genital infection	4 (8.9%)	Candida albicans, HSV-2, HPV

Frequency in Relation to CD4 Counts

CD4 counts were strongly associated with OIs.

- **Normal CD4 (>500 cells/ μ L):** 15 patients (15.0%) fell into this category. These individuals had relatively preserved immunity and a lower risk of OIs.
- **Low CD4 (200–500 cells/ μ L):** 45 patients (45.0%) were in this range. This group represented the largest proportion of the study population, and many of them developed OIs, reflecting moderate immunosuppression.
- **Very Low CD4 (<200 cells/ μ L):** 40 patients (40.0%) had severe immunosuppression. OIs were most frequent in this group, and several patients presented with multiple infections simultaneously.

Table 2: CD4 Count Distribution among PLHIV

CD4 Category	Frequency	Percent
Normal (>500)	15	15.0%
Low (200–500)	45	45.0%
Very Low (<200)	40	40.0%

Socio-Demographic Factors Associated with OIs

Socio-demographic factors such as sex, age, religion, education, occupation, marital status, and ethnicity were analysed (Table 3), but none showed statistically significant associations with OI occurrence (all $p > 0.05$).

- **Sex:** Among the 45 patients with OIs, 36 (80.0%) were male, and 9 (20.0%) were female. In the non-OI group, 41 (74.5%)

were male, and 14 (25.5%) were female. The difference was not statistically significant ($\chi^2 = 0.415$, $p = 0.51$).

- **Age:** OIs were most frequent in patients ≤ 30 years (33.3%) and 41–50 years (22.2%). Notably, all 4 patients above 60 years had OIs. The association was not statistically significant ($p = 0.16$).
- **Religion:** OIs were distributed across all religious groups: Hindu (31.1%), Christian (28.9%), Buddhist (20.0%), and Muslim (20.0%). No significant association was observed ($\chi^2 = 1.314$, $p = 0.72$).
- **Education:** Patients without formal education had the highest proportion of OIs (31.1%), followed by secondary education (33.3%). Those with higher education had fewer OIs (11.1%). The difference was not statistically significant ($\chi^2 = 5.445$, $p = 0.14$).
- **Occupation:** OIs were observed across all occupational categories, with students (24.4%) and unemployed individuals (22.2%) contributing notable proportions. No significant association was found ($\chi^2 = 1.341$, $p = 0.85$).
- **Marital Status:** Widowed/divorced participants had the highest burden of OIs (44.4%), followed by married (35.6%) and single (20.0%). The association was not statistically significant ($\chi^2 = 1.113$, $p = 0.57$).
- **Ethnicity:** OIs were present in both non-tribal (55.6%) and tribal (44.4%) groups, with no significant difference ($\chi^2 = 0.214$, $p = 0.64$).

Table 3: Socio-Demographic Factors Associated with Opportunistic Infections (N=100)

Socio-demographic factors	Presence of OIs (n=45)	Absence of OIs (n=55)	χ ² value	P value
Sex:				
Male	36 (80.0)	41 (74.5)	0.415	0.51
Female	9 (20.0)	14 (25.5)		
Age group[#]:				
30 years or less	15 (33.3)	14 (25.5)	-	0.16
31 – 40 years	8 (17.8)	10 (18.2)		
41 – 50 years	10 (22.2)	17 (30.9)		
51 – 60 years	8 (17.8)	14 (25.5)		
Above 60 years	4 (8.9)	0 (0.0)		
Religion:				
Buddhist	9 (20.0)	13 (23.6)	1.314	0.72
Christian	13 (28.9)	14 (25.5)		
Hindu	14 (31.1)	13 (23.6)		
Muslim	9 (20.0)	15 (27.3)		
Education:				
No formal education	14 (31.1)	8 (14.5)	5.445	0.14
Primary	11 (24.4)	16 (29.1)		
Secondary	15 (33.3)	18 (32.7)		
Higher	5 (11.1)	13 (23.6)		
Occupation:				
Professional	10 (22.2)	12 (21.8)	1.341	0.85
Skilled worker	7 (15.6)	9 (16.4)		
Student	11 (24.4)	12 (21.8)		
Unemployed	10 (22.2)	9 (16.4)		
Unskilled worker	7 (15.6)	13 (23.6)		
Marital status:				
Single	9 (20.0)	16 (29.1)	1.113	0.57
Married	16 (35.6)	18 (32.7)		
Widow/Divorce	20 (44.4)	21 (38.2)		
Ethnicity:				
Non-Tribal	25 (55.6)	28 (50.9)	0.214	0.64
Tribal	20 (44.4)	27 (49.1)		

[#] Fisher's exact test was used because cell counts were less than 5.

DISCUSSION

The present study highlights that OIs remain a major contributor to morbidity among PLHIV in Tripura, with tuberculosis, respiratory infections, and candidiasis forming the predominant spectrum. Nearly half of the study population developed at least one OI, underscoring the persistent burden despite widespread availability of ART. These findings are consistent with national and international reports that continue to identify OIs as a leading cause of hospitalisation and mortality in HIV-infected individuals, particularly in resource-limited settings. [14,15,16]

Tuberculosis was the most common OI in this cohort, affecting one-third of patients.

This aligns with evidence from multiple Indian studies where TB remains the dominant opportunistic pathogen, often presenting in extrapulmonary forms due to advanced immunosuppression. [17] The high prevalence of TB in Tripura may be explained by regional epidemiology, socioeconomic vulnerabilities, and delayed health-seeking behaviour. Respiratory infections, including *Pneumocystis jirovecii* pneumonia (PCP) and bacterial pneumonias, were also frequent, reflecting the susceptibility of HIV-infected lungs to both opportunistic and community-acquired pathogens. [18,19]

Oral candidiasis was the third most common OI, affecting 20% of patients. This condition

is widely recognised as an early clinical marker of HIV progression and correlates strongly with declining CD4 counts.^[20] The occurrence of skin and genital infections further illustrates the broad spectrum of pathogens that exploit immunosuppression, ranging from *Staphylococcus aureus* to herpes simplex virus type 2. Such diversity of infections highlights the need for comprehensive diagnostic capacity in tertiary centres.

This study showed a clear relationship between CD4 counts and OI occurrence. Patients with counts below 200 cells/ μ L were disproportionately affected and often presented with multiple infections simultaneously. This threshold has been consistently identified as critical for the emergence of severe OIs such as PCP, cryptococcal meningitis, and toxoplasmosis.^[21] The finding reinforces the importance of routine CD4 monitoring and timely initiation of prophylaxis. For instance, trimethoprim-sulfamethoxazole prophylaxis is recommended when CD4 counts fall below 200, while fluconazole prophylaxis may be considered in high-burden fungal regions.^[22] Interestingly, socio-demographic variables such as sex, age, education, and occupation did not show statistically significant associations with OI occurrence. This suggests that immunological decline, rather than social determinants, is the primary driver of OI risk in this population. However, the higher burden among widowed or divorced individuals may reflect psychosocial vulnerabilities and reduced adherence to ART. Similar patterns have been reported in other Indian cohorts, where stigma and social isolation negatively influence treatment outcomes.^[23]

The study also underscores challenges in resource-limited settings. Many patients present late to healthcare facilities, already suffering from advanced immunosuppression. Limited laboratory infrastructure hampers early diagnosis of infections such as cryptococcosis and CMV, while nutritional deficiencies exacerbate vulnerability.^[24] Strengthening ART

adherence, expanding diagnostic capacity, and integrating nutritional support are therefore essential strategies. Moreover, Tripura's relatively high HIV prevalence compared to the national average necessitates region-specific interventions, particularly targeting injecting drug users and socioeconomically disadvantaged groups.^[25]

Limitations

- The study was conducted in a single tertiary care hospital, which may limit generalizability to the wider population of Tripura.
- OIs were diagnosed based on available clinical and laboratory facilities; advanced diagnostic modalities (e.g., molecular assays for fungal/viral OIs) were not uniformly accessible.
- ART adherence and duration were not analysed as primary variables, which may have influenced OI occurrence.
- The cross-sectional design precludes assessment of temporal relationships or causality between CD4 decline and OI development.

CONCLUSION

This study demonstrates that OIs remain a significant burden among PLHIV in Tripura, with tuberculosis, respiratory infections, and candidiasis dominating the spectrum. Their occurrence is strongly linked to declining CD4 counts, highlighting the need for early diagnosis, prophylaxis, and strict ART adherence. Public health strategies must focus on strengthening HIV care infrastructure, reducing diagnostic delays, and addressing social vulnerabilities to mitigate the impact of OIs in this high-burden region.

Declaration

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