

## ORIGINAL ARTICLE

# Incidence and Spectrum of Opportunistic Infections Among HIV Infected Patients Attending Government Medical College, Kozhikode

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## Abstract

**Background:** People with advanced human immunodeficiency virus (HIV) infections are vulnerable to opportunistic infections because of a weakened immune system. Early diagnosis of Opportunistic infections and prompt treatment definitely contributes to increased life expectancy among infected patients and delays the progression to AIDS.

**Aims and Objectives:** are to study the incidence, clinical spectrum and outcome of opportunistic infections and relation between opportunistic infections and CD4 count.

**Materials and Methods:** The study was carried out in the Anti Retroviral Treatment (ART) clinic and medical wards of Government Medical College, Kozhikode. The study period was from January 2012 to January 2013 till 100 opportunistic infections are identified in newly diagnosed retro positive patients. This was a clinical observational study. 424 newly diagnosed retro positive patients were screened to identify 100 patients having opportunistic infections and they were studied in detail.

**Results:** Out of the 100 patients, 71 were males and 29 were females. 67% were in the age group of 30-49 years. The most common symptom of presentation was weight loss (77%) followed by fever (67%) and mucocutaneous lesions (60%). The commonest opportunistic infection detected was candidiasis (52%) followed by tuberculosis (50%). Majority of the patients had a CD4 count between 50-200/microL. Out of the 100 patients 19 patients expired. Among them 10 patients had disseminated tuberculosis. Incidence of opportunistic infection was 23.59/100 person years.

**Conclusions:** This study demonstrates that Oral candidiasis is the commonest opportunistic infection in HIV patients and Tuberculosis is the second most common. The incidence of opportunistic infection is higher in the older age groups, males and patients with low CD4 count.

## Introduction

People with advanced HIV infections are vulnerable to opportunistic infections (OI) because of a weakened immune system. OI cause substantial morbidity and mortality. The common OI that affecting people living with HIV infection in India are Tuberculosis, Candidiasis, Pneumocystis jirovecii pneumonia (PCP), Bacterial pneumonia, Herpes simplex, Herpes zoster and chronic diarrhea.

Early diagnosis of OI and prompt treatment definitely contributes to

increased life expectancy among infected patients and delays the progression to AIDS (Acquired immunodeficiency syndrome) and it also helps to stop the spread of Tuberculosis and other transmissible OI.<sup>1,2</sup> The relative frequencies of specific OI may vary in different countries and even in different areas within the same country. The pattern of OI in

HIV patients in south Indian context is relatively less studied. This study was done to estimate the burden of OI and its pattern in HIV patients in North Kerala.

## Materials and Methods

This is a clinical observational study carried out in the Anti retro viral treatment (ART) clinic and medical wards of Government Medical College, Kozhikode. The study was done after getting institutional ethics committee approval and informed consent from the patients. The study period was from January 2012 to January 2013 till 100 subjects with OI are enrolled. All patients above 12 yrs of age who found to be HIV positive after testing from ICTC (Integrated counseling and testing centre) during the study period were included in the study. Patients who were already had other immune compromised state before contracting HIV like diabetes mellitus and patients on chemotherapy were excluded from the study.

424 newly diagnosed consecutive retro positive patients were clinically assessed to identify 100 patients who had opportunistic infections and they were studied in detail. Data collected by thorough history taking, meticulous clinical examination and relevant investigations. All the investigations were routinely done in Kozhikode Medical College. Investigations included CBC with ESR, urine analysis, RFT, LFT, ECG, Chest X ray, FBG, PPBG, CD4 count, sputum examination, Tuberculin test, Ultra sonogram Abdomen, CT scan, MRI scan, pleural and ascitic fluid study, CSF study, FNAC, Biopsy and

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Received: 01.09.16; Accepted: 02.04.2018

**Table 1: Age and gender distribution**

Age group	Male	Female
<20	2	1
20-29	10	6
30-39	20	14
40-49	26	7
50-59	10	2
>59	3	0

**Table 2: Clinical manifestations of OI**

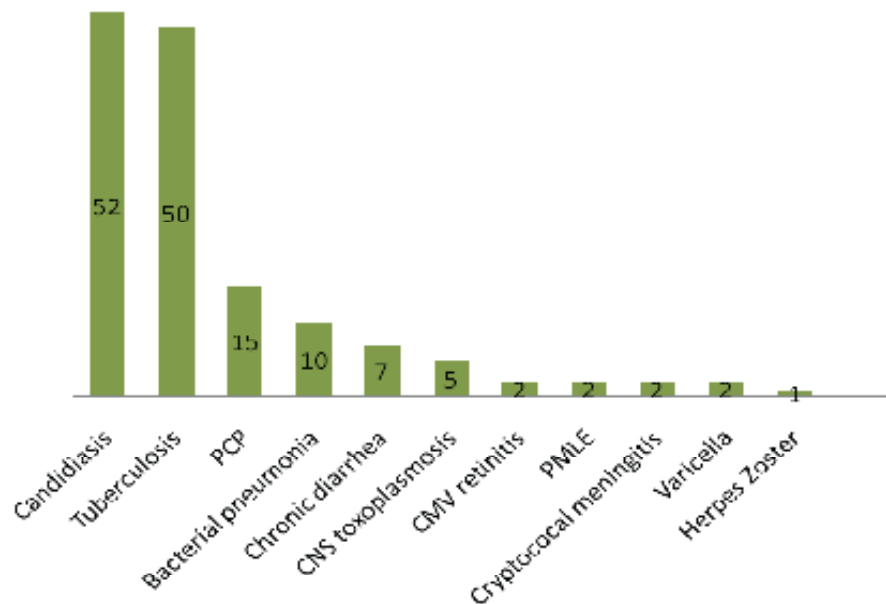
Clinical manifestations of OI	Diagnosis	No.	
Skin	Candidiasis	52	
	Seborrhic dermatitis	12	
	Herpes	7	
	Oral ulcer	6	
	Oral hairy leukoplakia	6	
	Genital warts	3	
	Scabies	2	
	Chickenpox	2	
	Respiratory	Tuberculosis	26
		PCP	15
Bacterial pneumonia		10	
Gastrointestinal system	Oral candidiasis	52	
	Chronic diarrhea	9	
	Chronic hepatitis B	9	
	Esophageal candidiasis	2	
CNS	Tuberculosis	14	
	Toxoplasmosis	5	
	Cryptococcal meningitis	2	
CVS	PMLE	2	
	Pericardial effusion	2	

Echocardiogram. The CD4 cell counting machine (Partec flow cytometer) is available in the Department of Microbiology, Government Medical College, Kozhikode sanctioned for ART clinic. The reagent used is CD4 m Ab PE and the result will be available on the next day. Investigations were done according to the clinical presentation and indication in each patient. OI were diagnosed as per the standard criteria.

Data was entered and analyzed by using SPSS software. Qualitative variables were presented as frequency and percentage. Strict confidentiality was maintained regarding the identity of each patient.

## Results

A total of 424 newly detected HIV patients were clinically assessed for opportunistic infections in the study. The source of the cases was either ART clinic of the Department of Medicine or Medicine wards in Government Medical College, Kozhikode. Of the 424 newly detected HIV patients screened, 100 patients had opportunistic infections

**Fig. 1: Spectrum of opportunistic infections**

and a detailed study of them was done.

In this study majority of the patients were male hetero sexuals. The age and gender distribution is shown in Table 1. It was observed that the majority were between the age groups of 30-49 yrs (67%) and 71% were males and 29% were females with a male to female ratio of 2.44:1.

All patients were presented with multiple symptoms. Symptoms at presentation were weight loss (77%), fever (67%), muco-cutaneous lesions (60%), cough (41%), breathlessness (33%) and diarrhea (16%). 22% patients had headache and 19% had seizure. Altered sensorium was present in 14% patients (Table 2).

Most common skin manifestation was candidiasis (52%) followed by seborrhoeic dermatitis (12%). Tuberculosis (26%) was the frequent respiratory problem followed by PCP (15%). 15 patients had isolated pulmonary tuberculosis and 11 patients had disseminated tuberculosis (DTB). Eight patients had extra pulmonary tuberculosis. Fourteen patients had CNS tuberculosis and 2 patients had pericardial effusion which was tuberculous in aetiology. Sputum AFB was negative in 76% of pulmonary tuberculosis cases. Among the patients with tuberculosis 11 patients had non homogenous opacity in chest x-ray and 5 had miliary mottling, 6 had pleural effusion. Oral candidiasis (52%) was the commonest gastrointestinal

manifestation. Chronic diarrhea was present in 9 patients. There were 9 patients with HBsAg positivity. Stool examination of the patients with chronic diarrhea showed cryptosporidium in 5 patients and *Isospora belli* (Figure 5) in 2 patients. Most frequent CNS manifestation was tuberculosis (14 patients). CNS toxoplasmosis was present in 5 persons and 2 patients had Cryptococcal meningitis (Figure 4). The various clinical manifestations were shown in Table 2.

Oral candidiasis (Figure 3) was the commonest opportunistic infection. It was present in 52 patients. Among the 100 patients with OI, 50 patients had tuberculosis. Pneumocystis carinii. Pneumonia (PCP) was present in 15 patients. Ten patients had bacterial pneumonia. Other infections are shown in Figure 1.

CD4 count ranged between 2/microL to 892/microL. Majority of the patients had a CD4 count between 50-200/microL. The CD4 count at various OI presented were shown in Table 3.

Out of the 100 patients 19 patients expired. Most common cause of death was tuberculosis (10 patients). 3 patients with PCP expired. All cases of PMLE (2) and cryptococcal meningitis (2) died. 2 patients with toxoplasmosis also did not survive (Figure 2).

Out of the 424 cases with newly detected HIV infection 100 patients

**Table 3: Relation between CD4 count and OI**

CD4 count	OI	Number
>500	Bacterial pneumonia	2
200-500	Pulmonary tuberculosis	8
200-500	Bacterial pneumonia	8
200-500	Oral candidiasis	7
200-500	Extrapulmonary tuberculosis	7
200-500	PCP	2
200-500	Varicella	2
100-200	Oral candidiasis	21
100-200	Pulmonary tuberculosis	7
100-200	PCP	7
100-200	CNS TB	5
100-200	Extrapulmonary tuberculosis	4
100-200	Chronic diarrhea	4
100-200	Disseminated tuberculosis	3
100-200	Toxoplasmosis	2
100-200	CMV retinitis	1
100-200	Esophageal candidiasis	1
100-200	PMLE	1
50-100	Oral candidiasis	12
50-100	CNS TB	5
50-100	PCP	5
50-100	Disseminated tuberculosis	3
50-100	Toxoplasmosis	2
50-100	Chronic diarrhea	2
50-100	CMV retinitis	1
50-100	PMLE	1
<50	Oral candidiasis	12
<50	CNS TB	5
<50	Disseminated tuberculosis	5
<50	Cryptococcal meningitis	2
<50	Toxoplasmosis	1
<50	Chronic diarrhea	1
<50	PCP	1

had opportunistic infections. Incidence calculated as 23.59/100 person years in this study.

## Discussion

In the present study, among OI in HIV infected people at presentation, age group ranged from 20-50 yrs which represents the most active and productive group of the society. Majority were males (79%). These observations are comparable to another study from India by Nilanjan Chakraborty et al.<sup>3</sup> In the present study most common symptom of presentation was weight loss (77%) followed by fever (67%) and skin and mucosal lesions (60%) which is similar to a study by Singh A et al.<sup>4</sup> The high proportion of weight loss, fever and cough can be due to the high incidence of tuberculosis in this study group.

The most common muco-cutaneous manifestation was oral candidiasis. This

was present in 52% of patients. In many of the unsuspected cases of retroviral infection oral candidiasis prompted the diagnosis. Some of the patients had multiple muco-cutaneous lesions like candidiasis, oral ulcers, seborrheic dermatitis. Kaposi's sarcoma was not detected in any of the subjects in the present study. This may be due to the decreased prevalence of the causative organism HHV-8 which predominantly spreads through homosexual contact. Homosexual mode of transmission is reported only in 6 patients in our study.

Pulmonary tuberculosis was the commonest respiratory infection. Eleven patients had disseminated tuberculosis (DTB) and 8 had extra pulmonary tuberculosis.<sup>5</sup> The major symptoms at presentation were weight loss, fever and cough. 75% of patients with tuberculosis were Mantoux test negative. This can be attributed to the immune suppression in HIV-TB co-infection and Mantoux test will not be a useful aid in tuberculosis in HIV infection. Sputum AFB was negative in 76% of the tuberculosis cases. It was observed that many patients became positive for AFB in sputum after starting on HAART. This shows the improving immunity of these patients. Patients with high CD4 count have classical findings in chest x-ray. When CD4 count is low X-rays have lower zone involvement, miliary shadows and pleural effusion.<sup>6</sup>

Most of the patients with PCP infection had a lower CD4 count and it was diagnosed clinically. Main symptoms were dry cough and breathlessness. Typical interstitial pattern of chest x-ray, high serum LDH (Lactate dehydrogenase) and ABG (Arterial blood gas) abnormality were present in these patients. There is a 5-7 fold increase in bacterial pneumonia in HIV patients compared to the general population. The clinical presentation was similar as in the HIV non infected patients.<sup>7</sup>

Chronic diarrhea was present in 9 patients, which is much less when compared to the incidences reported by other Indian studies. This could be the reflection of better sanitary and environmental hygiene present in Kerala. In a study by Anant A Takalkar et al<sup>8</sup> about OI in HIV 30.1% patients had chronic diarrhea. The mainstay of therapy in chronic diarrhea of HIV positive individuals in countries where

it is economically and socially feasible is with highly active ART (HAART) which was instituted in our patients also. In our study, most common organism was cryptosporidium. In a study on chronic diarrhea in HIV patients by S.V. Kulkarni et al<sup>9</sup> showed that commonest organism was cryptosporidium. Nine patients had HBsAg positivity. HIV infection increases the risk of chronic carriage of HBV infection and we need to ensure the screening of Hepatitis B in HIV patients.<sup>10</sup>

Neurological manifestations were present in 23% of the cases. There was higher incidence of tuberculous meningitis when compared to western reports due to the increased incidence of this disease in general population. The clinical course of CNS tuberculosis in HIV patients is different from HIV negative patients. Cryptococcal meningitis was present in 8.7% of patients with neurological manifestation. The world wide incidence is 6-12%. Toxoplasmosis was present in 5% of the patients with opportunistic infections. In Europe the most common OI involving CNS is toxoplasmosis affects 20-40% of all the AIDS patients.

Progressive multifocal leuco-encephalopathy (PMLE) was present in 2%. The worldwide incidence is 2-3%. Patients with this disease showed cognitive impairment and a sequence of variable focal deficits. Various studies showed that PMLE is exclusively seen in immune compromised groups. It is currently one of the AIDS defining illnesses in HIV infected patients.

The CD4 cell count is an important investigation in the clinical evaluation of any patient with HIV infection as it helps to decide the stage of the disease and in decisions regarding anti retroviral treatment and prophylaxis against OI. As the tuberculosis is endemic in India it may occur at any CD4 count. Most of the disseminated tuberculosis and CNS tuberculosis had a CD4 count below 100.

Majority of the bacterial pneumonia had a CD4 count 200-500/microL and the clinical presentation was similar to general population. Oral candidiasis was occurred in a wide range of CD4 counts and the incidence is very high when CD4 count is below 200. Patients with CD4 count below 100 had OI like cryptococcal meningitis and



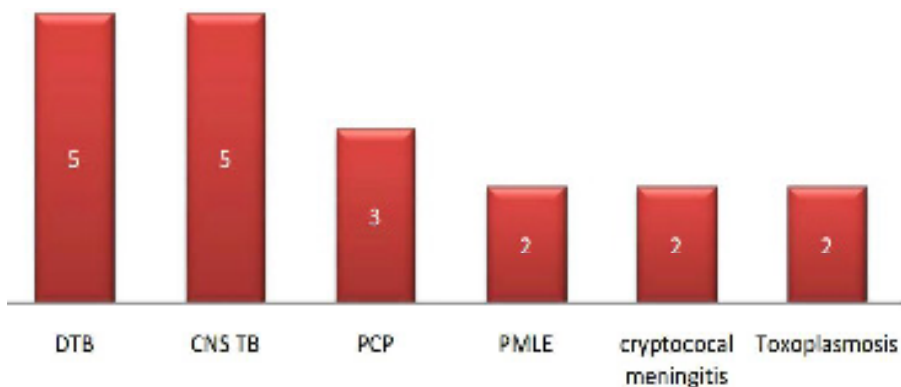


Fig. 2: Cause of death

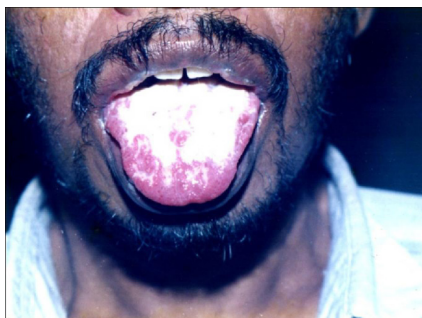


Fig. 3: Oral candidiasis

Toxoplasmosis. These observations are comparable to another study by Vinay KV et al.<sup>11</sup>

Out of the 100 patients 19 patients expired. In this study most of the expired patients had lower CD4 count. Cryptococcal meningitis and PMLE had 100% mortality. Disseminated tuberculosis had a high mortality rate in this study. Most of the patients with CNS tuberculosis expired. Toxoplasmosis also had a high mortality. Even if initiation of ART results in the suppression of OI, issues of non adherence, ART drug resistance and treatment failure also exist and might not be able to totally prevent or avert OI among the HIV infected patients. In this study incidence calculated as 23.59/100 person years. In a study by Manisha Ghate et al<sup>12</sup> the incidence was 36.8.

In another study from Brazil, had an incidence 51/100 person years. In other studies incidence ranges from 10.7-

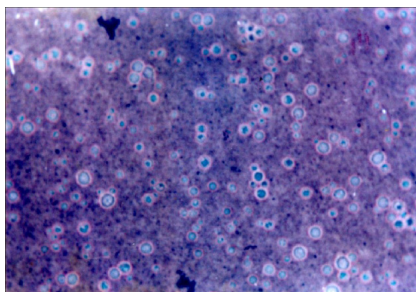


Fig. 4: Indian ink staining of Cryptococcus culture

69.7/100 person years. Oral candidiasis and tuberculosis had a high incidence rate in this study. The incidence of OI is higher in the older age group, in males and among patients with low CD4 count.

### Conclusion

Oral candidiasis is the commonest opportunistic infection in HIV infected patients and is the first indicator of underlying immunodeficiency in majority of the cases. Tuberculosis is the second most common opportunistic infection and major cause for meningitis, lymphadenitis and respiratory disease. Chronic diarrhea is rare in our people compared to other states of India and HBV co-infection is common in HIV patients. The incidence of opportunistic infection is higher in the older age groups, males and patients with low CD4 count.

Limitations of the study are PCP is diagnosed mainly by clinical assessment



Fig. 5: Isosporabelli

### Recommendations

There should be skilled staff and adequate medications needed for prophylaxis and management of OI. Strengthening of the TB-HIV collaboration activity is very important.

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