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Original Research Article

Prospective study of opportunistic infections among HIV infected patients in VSS Institute of Medical Science and Research, Burla, Sambalpur, Odisha, India

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ABSTRACT

Background: HIV destroys the CD4+T cells progressively thus making the HIV infected persons susceptible to a number of opportunistic infections (OIs).
Methods: The study was conducted in the Medicine Department and ART Centre, VIMSAR. It is a prospective study from July 2016 to September 2017.
Results: 86 patients register, detail history, clinical examination and investigation were done and then the data is complying in detail. Most of the patients were male (72%) male female ratio is 2.6:1. The majority of patients presented with fever, weight loss and anorexia seen in more than 73% of the study population.
Conclusions: (42%) cases belonged to the CD4+T cell count range of 101-200/µl with aCD4+T cell count of 183/µl, so there is increased chance of hospitalization in patients having CD4+T cell count below 200/µl. The most common OI was tuberculosis (51%) with pleural effusion as its commonest manifestation. The second most common OI was candidiasis (43%) with most cases suffering from oral candidiasis was seen to occur at higher CD4+T cell counts than tuberculosis.

Keywords: Candidiasis, CD4 cell, HIV, Opportunistic infections (OIs), Tuberculosis

INTRODUCTION

HIV destroys the CD4+ T cells progressively and relentlessly thus making the HIV infected persons susceptible to a number of opportunistic infections (OIs). It was also noted that certain OIs manifest below a particular threshold of CD4+T ce1l count, many of these in a advanced stage of the HIV infection. Since the beginning of HIV epidemic, ols have been recognized as common complications of HIV infection. OIs cause substantial morbidity and hospitalization and expensive therapies and shorten the survival of PLHA Patients. The right diagnosis and proper treatment will improve the quality of life and survival in PLHA. The relative frequencies of specific OIs vary in different countries and even in different areas within the same country. While Pneunocystic jiroveci is the commonest in the Western part of world, Tutberculosis and Candidiasis are the common OIs in India reported by studies.[1,2]

METHODS

It is prospective study. The study included all HIV infected patients admitted to the Department of Medicine, VIMSAR from July 2016 to September 2017. Patient's with known HIV positive having suspected OIs or

patients with different OIs admitted to the hospital and later found to have HIV positive were included in the study.

Diagnosis of HIV infection in the included cases was done at ICTC (Integrated Counseling and Testing Centre) as per the NACO guidelines by three different methods Dot blot (combo AIDs), Agglutination (Nova HIV) and Immunochromatographic test (Retrochek). Those having reactive test results at other laboratories were sent to the ICTC for confirmation. Informed consent was taken in each case as per NACO ethical guidelines.

Detailed history, clinical examination and investigations were done as necessary like CD4+T cell count, CBC, ESR, Blood culture and sensitivity, Arterial Blood Gas analysis, HBsAg, Anti-HCV antibody, Urine routine and microscopy and culture amd sensitivity, Stool routine and microscopy and culture and sensitivity, Mantoux Test, Sputum AFB and Microscopy, Chest X-ray, USG Abdomen and Pelvis, CT scan Brain , CT scan of Thorax, MRI of Brain, MRI of Spine, Fundoscopy, Peritoneal fluid/Pleural fluid/CSF analysis, CSF for Indian Ink staining, CSF PCR, FNAC of Lymphnode, ELISA for Toxoplasma IgG and IgM, Latex Agglutination for Cryptococcal antigen, Oral Scraping for Microscopy of fungal element with KOH staining, UGI endoscopy and Bronchoalveolar lavage.[3-5]

RESULTS

The patients were in the age group of 31-45 years, 45 cases (52.3%), followed by 24 cases (28%) in the age group of 15-30 years and 17 cases (19.7%) in the age group of 46-65 years.

Table 1: Age and Sex distribution of the patients.

Age group	Male	Female	Number	%
15-30 years	18	06	24	28
31-45 years	32	13	45	52.3
46-65 years	12	05	17	19.7
Total	62	24	86	100

Out of (86) HIV infected patients with OIs were studied 62 cases (72%) are male and 24 cases (28%) are female with male: female ratio of 2.6:1. Table 2 shows labourers (31.3 %), drivers by occupation (30.7%) and had a past history of emigration to nearby states.

Table 2: Occupation of the patients.

Occupation	Male (n = 62)		Female (n = 24)		Total (n=86)	%
	Number	%	Number	%		
Labourer	16	25.8	11	45.8	27	31.3
Driver	19	30.7	0	0	19	22.4
Farmer	14	22.5	4	16.6	18	21.0
Employee (government)	6	9.6	3	12.5	9	10.0
Student (upto graduation)	2	3.4	0	0	2	2.5
Housewife	0	0	4	16.6	4	4.6
Others*	5	8.0	2	8.5	7	8.2

Table 3: Modes of transmission.

Modes of transmission	Male (n= 62)		Female (n=24)		Number (n=86)	%
	Number	%	Number	%		
Heterosexual	48	77.4	15	62.5	63	73.3
Homosexual	0	0	0	0	0	0
Blood Transfusion	1	1.6	0	0	1	1.2
Injecting Drug Use	3	4.8	0	0	3	3.5
Frequent needle prick	0	0	0	0	0	0
Vertical transmission	0	0	0	0	0	0
Unknown modes	10	16.2	9	37.5	19	22

The mode of transmission is the heterosexual mode of transmission i.e., 73.3%.

One case of thalassemia with repeated blood transfusion is reported to have possible transmission by blood.

In nineteen cases (22%) mode of transmission remains unknown.

Figure 1 represents various presentation at the time of admission to the hospital.

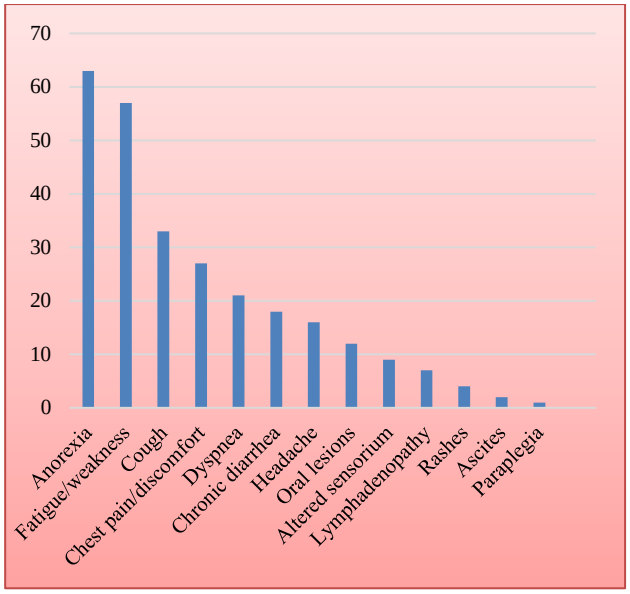

Figure 1: Clinical presentation of patients (in number).

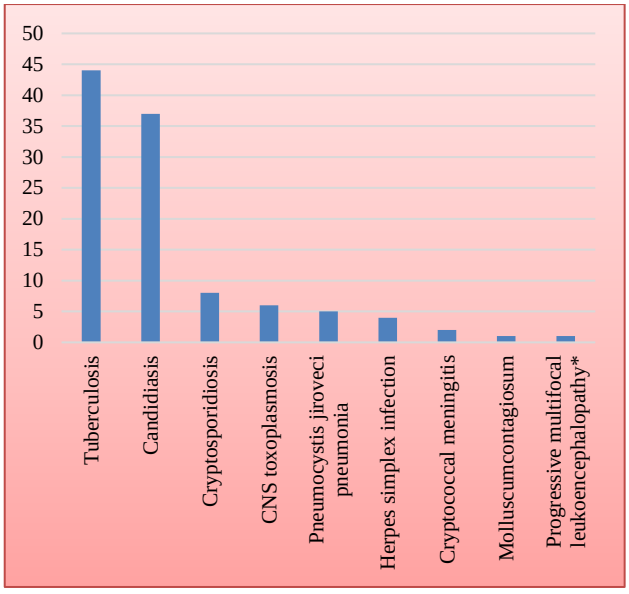

Figure 2: Prevalence of different OIs (in numbers).

The most common symptom was noted to be weight loss, fever and anorexia. 42% cases (n=36) belonged to CD4+T cell count of 101-200/µl, followed by 33% cases (n=29) having a CD4+ T cell count of > 200/µl. 18% of cases (n=15) had a count between 51-100/µl and 7% cases (n=6) had a very low CD4+ T cell count of ≤ 50/µl. Thus 57 cases (66.2%) had a CD4 count below 200/µl.

Table 4: CD4+T CELL COUNT of the patients.

Cd4+ t cell range	Number	%
≤50/µl	6	7
51-100/µl	15	18
101-200/µl	36	42
>200/µl	29	33

Single and Multiple ois

Out of 86 cases single OI were seen in 57 cases (66%), while multiple OIs were found in 29 cases (34%).

Figure 2 indicates that Tuberculosis with candidiasis was the most common type of combination in patients admitted with multiple OIs.

Table 5: Different combinations of OIs.

Combinations of OIs	No. of cases (%)
Tuberculosis and Candidiasis	21(72.8)
Cryptosporidiosis and Candidiasis	2(6.8)
Toxoplasmosis and Candidiasis	2(6.8)
PCP* and Candidiasis	1(3.4)
Molluscumcontagiosum and Candidiasis	1(3.4)
Cryptosporidiosis and Tuberculosis	1(3.4)
Herpes simplex and Tuberculosis	1(3.4)

Figure 3 indicates Tuberculosis is the most common OIs (51% cases, n=44). Candidiasis is the second most common infection seen in 43% cases (n=37). TB in HIV infected patients is pleural effusion seen in 52.2% cases (n=23) pulmonary TB in 41% cases (n=18), 6 cases presented with both pleural effusion with parenchymal involvement of TB. Tubercular lymphadenitis, TB meningitis, peritoneal TB and TB spine were seen in 31.8% cases. The patients suffering from Candidiasis (43% cases, n=37), Oropharyngeal candidiasis was noted to be the most common type seen in 83.8% cases (n=31), followed by Oroesophageal candidiasis seen in 10.8% cases (n=4), and Vulvovaginal candidiasis in 5.4% cases (n=2).

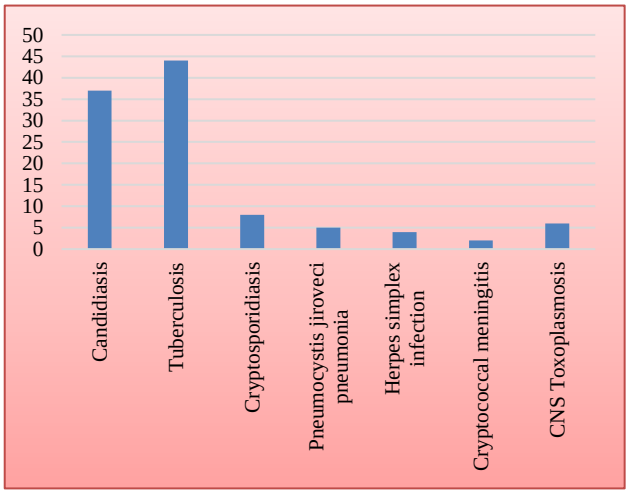

Figure 3: Distribution of tubercular manifestation (in numbers).

Figure 3 indicates CD4+T cell counts in tuberculosis. Oroesophageal candidiasis was seen with CD4+T cell count of 115 /µl and vulvovaginal candidiasis found with

CD+4T cell count of 181/µl thus showing lower CD4+T cell counts than cases with oral candidiasis which were noted with CD4 count of 286/µl.

Table 6: Types of candidial infections in patient (n=37).

Types of candidiasis	No. of patients	%
Oropharyngeal candidiasis	31	83.8
Oroesophageal candidiasis	4	10.8
Vulvovaginal candidiasis	2	5.4

The cases affected with TB exhibited a higher CD4+T cell count (227/µl) in cases with pulmonary TB, while pleural effusion displayed a relatively lower CD4+T cell count i.e., 193/µl and other cases of extra pulmonary TB showed a lower CD4+T cell count in the range of 109/µl-178/µl. The Table 7 the CD4 + T cell range of <51/µl and 51-100/µl.

Though in CD4+ T cell range of 101-200/µl, tuberculosis was almost affecting half of the population followed by candidiasis, in cases with CD4+ T cell counts of >200/µl, candidiasis was the commonest OI affecting 56.8% cases with tuberculosis lagging behind with 37.8 % of cases.

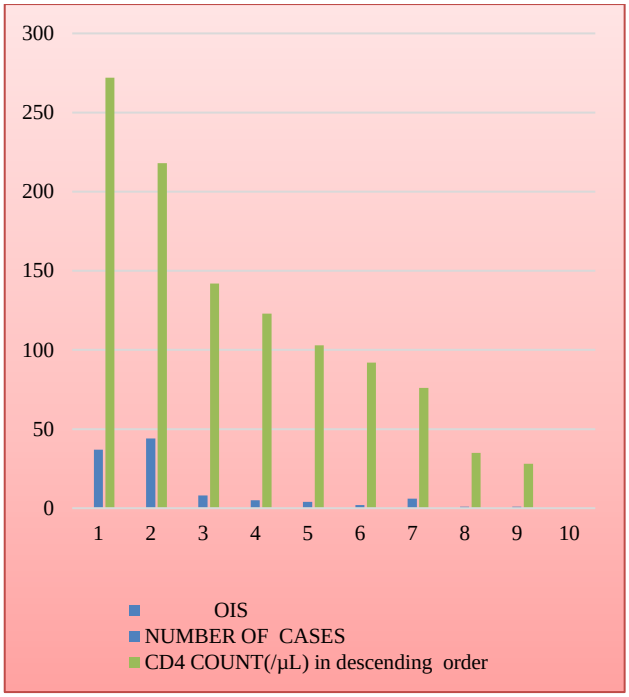

Figure 4: CD4 count of different OIs in study population (in numbers).

Table 7: Prevalence of different OIs of the patients with CD4+ T cell range.

Type of OI	<51/µl	51-100/µl	101-200/µl	>200/µl
Tuberculosis	25%	29.4%	50%	37.8%
Candidiasis	12.5%	11.7%	28.2%	56.8%
Cryptosporidiosis	0	17.6%	8.6%	2.7%
CNS toxoplasmosis	25%	17.6%	2.3%	0
Pneumocystis jiroveci pneumonia	12.5%	11.7%	4.3%	0
Herpes simplex infection	0	6%	4.3%	2.7%
Cryptococcal meningitis	0	6%	2.3%	0
Molluscumcontagiosum	12.5%	0	0	0
PML	12.5%	0	0	0

DISCUSSION

In the present study 86 patients were included and data compiled. among 86 hospitalized 72% were male and 28% were female, which is compare with other studies (75% male), (80.8% male), (68% male) and (83.58% male).[6-9]

Most of the patient belonged to the age group 31-45 years (52.3%) as compared to (55% were in 31-40 year) and (54% were in 31-40 year).[1,10] But the study (76.11%) and (77.9%) shows a substantial number of patients were in younger age group i.e., 20-39 yr. The study shows involvement of still younger age group i.e., 20-29 years in 61%.[6,7,9] Majority of patients were labourers by occupation which is comparable to that reported (majority were migrant worker).[7] Most of the patients were from low socioeconomic status.[10] They were working as hotel waiters, taxi drivers, panwallas and mechanics. This could be due to illiteracy and low level of awareness about mode of transmission of HIV amongst them. In the present study the distribution of male patients was noted to be almost homogenous amongst labourers, drivers and farmers, whereas almost half of female patients were daily labourers by occupation. Most of the male patients were drivers by occupation (30.7%) and had a past history of emigration to nearby states. the commonest mode of transmission is heterosexual mode of transmission (73.3%) in this study) like that of (80.4%), (90%), (80%), (86%), (94%) as well as the annual report in 2010-11 (87.4%).[1,5-8,11]

Possible transmission by blood and blood products is seen in 1.2% of cases In the present study which is similar to that of (1%).[5] But other Indian studies show blood transfusion like (7%), (3%) and (2.5%).[6,7,11] Vertical transmission was not observed in study. But other studies (2%) and (1.8%) show a significant percentage of transmission from mother to child. The national rate of vertical transmission reported in 5.4%.[5-7] Mode of transmission could not be ascertained in a significant number of cases (22%) like that reported in literature in which risk factor for HIV transmission could not be elicited in 14.1% and 12% respectively.[7,11]

Majority of patients presented with more than one symptom like weight loss (91%), fever (86%) and anorexia (73.2%) which is similar to the study done that showed most common presentation was fever (71%) and weight loss (65%).[2] Although the mode of presentation is almost similar in all studies the frequency of various presentations varies showed that common presentation was fever (70.6%), weight loss (53.3%) and chronic diarrhea (43.9%).[11] fever (82.2%), weight loss (65.5%) and cough (45.5%) was the common presentation of hospitalized patients study, fever (56%), cough (50%) and oral lesions (50%) were the common presentation of the patients attending the ART centre.[12] The higher frequency of weight loss and fever In the present study could be due to inclusion of PLHA who needed hospitalization and were in WHO clinical stage 3 or 4.

Significant number of cases (42%) belonged to the CD4+ T cell count range of 101-200/µl and 66.2% cases had CD4 count less than 200/µl; with CD4 count of 183/µl which is almost comparable to other Indian studies. In the study it was observed that 82.6% had CD4 count <200/µl from which 46% had CD4 count <50/µl. In the present study only 7% cases had CD4+T cell count below 50/µl.[2] In another study it was noted that 51% patients had CD4count less than 200/µl.[11] But the study showed 36.8% belonged to CD4 range of 101-200/µl, with lower CD4 count i.e., 120/µl.[1] The study reported a differently, in which the mean CD4 count in male was 179±9.3/µl whereas CD4 count in female was 323±28.26/µl.[7] OI was found in 66% and multiple OIs in 34% cases. The study reported multiple OIs in 30% cases, but study observed multiple OIs in 50% cases.[6,12]

Most common OIs was tuberculosis (51%) with pleural effusion as its commonest manifestation. The second most common OIs was candidiasis (43%) with most cases suffering from oral candidiasis which was seen to occur at higher CD4 counts than tuberculosis. The other OIs found in descending order of their prevalence were Cryptosporidiosis, CNS toxoplasmosis, (Figure 2). The prevalence of different OIs varied in different studies. Most of the studies show that tuberculosis contributes to about half of all cases presenting with OIs except that reported.[9,6,12] Tuberculosis, Candidiasis and Crypyosporidiosis emerged to be three most common OIs in studies with variable frequencies depending upon the type of study (whether hospitalized patients or patients attending OPD and ART centre). But study showed that none of patient presented with diarrhea out of 135 cases.[2,13]

Among other OIs, bacterial pneumonias were seen in 4.3% to 12.6% of patients in the studies, which is not consistent with our study. Bacterial pneumonias occur at a higher CD4+T cell count and screening of HIV status is not a usual practice.[4,12,14] This could be the reason of exclusion of cases from our study. Inclusion of larger patients with OIs may represent with Bacterial pneumonia in the studies which were not found in the present study. Herpes zoster was seen in most patients in other studies but not seen in the present study.[9,12] Diagnosed based upon sputum AFB, Chest X- ray, Mantoux test, TB ELISA and other body fluid and tissue specimen examination.[14] Tuberculosis was the commonest infection In the present study and it matches with the findings by other authors. This is because tuberculosis is endemic in India and patients with HIV and TB rapidly downgrade with high mortality and multidrug resistance.[15]

Tuberculosis infection, 27.2% cases of pulmonary tuberculosis (PTB), 13.8% cases had both pulmonary and extra pulmonary tuberculosis and 59% cases had only extra pulmonary tuberculosis (EPTB) with pleural effusion or pleural TB being the commonest tubercular manifestation seen in 52.2% cases. Two cases presented with disseminated TB. In the present study EPTB is more common than PTB like that of the study which showed that 47.6% EPTB and 41.8% PTB.[7] But most of the Indian studies show a differently with PTB commoner than EPTB reported (35% PTB vs 21% EPTB), (70% PTB vs 30% EPTB with 18% CNS TB, 6% Pleural TB and 6% Abdominal TB), (40% PTB vs 10% EPTB) majority of the patients (i.e., 64%) presented with disseminated TB which was seen in only 4.5% cases In the present study.[2,10,16,17] Candidiasis is the second most common OI In the present study like other Indian studies. But some of the studies reported that candidiasis was the commonest OI. Oral candidiasis was the commonest manifestation seen in 83.8% cases like all other Indian studies.[2,5]

Among the 37 cases Candida albicans was seen in the studied. But in the study Candida albicans was isolated in 62.5% cases which was well comparable with the study of other workers.[12,18] Non-albicans Candida isolates were found in 37.5% cases which has also been reported by others.[19] In this study the isolation of Candida dubiliniensis (9.37%) was also noted, a new species, which was consistent with the findings of other study.[20]

Stool specimens examined showed the presence of only Cryptosporidium. The study noted that intestinal parasitic pathogens were detected in 44% patients, and the major pathogens included Cryptosporidium parvum (20%), the most common, followed by Isospora belli (10%),

Entamoeba histolytica (8%).[20] The study stated that Cryptosporidium parvum (13.6%)was the most common enteric parasite followed by *Giardia lambia* (3.8%) and *Entamoeba histolytica* (2.3%).[13] In the study it was observed that the most common pathogen in stool specimen was enteropathogenic Vibrio (47%) followed by Cryptosporidium parvum (43%) and *Eischerichia coli* (42%).[10] The study showed that the commonest organism in HIV infected persons with diarrhea was Cryptosporidium parvum(36.7%) followed by *Entamoeba histolytica* (13.3%) and *Strongyl odesstercoralis* (3.3%).[22]

Low socioeconomic status, poor hygiene, unavailability of safe drinking water may be responsible for the high percentage of cryptosporidiosis. Provision of safe drinking water and maintaining good hygiene is important in prevention.[11] CNS toxoplasmosis was seen in 6.9% cases In the present study which is comparatively higher than other Indian studies 3.7%(2), 3.8%.[5]

Five of the HIV seropositive patients (5.8%) were co-infected with (PCP) in the present study. PCP is one of the common opportunistic infections in HIV but the cases are relatively less documented, may be due to the lack of routine testing facility.[23] But relatively higher prevalence was seen in following two studies. The study reported PCP in 14.2% cases and in the study, it was seen in 13% cases.[5,12] Even though pneumonia due to Pneumocystis carinii is one of the most common opportunistic infection in AIDS patients, the frequency with which it is recognized among HIV patients in tropical and developing countries is generally much lower than that in industrialized nations.[11,24] The incidence has decreased in part due to cotrimoxazole prophylaxis. It has often been the AIDS defining illness, with up to 80% of patients noted,

Cryptococcal meningitis was confirmed by clinically as well as from detection of cryptococcal capsular antigen (Cryptococcus antigen latex agglutination test) and Indian ink staining of CSF.[25] Cryptococcal meningitis was seen in 2.3% cases In the present study, which was comparatively lower than the studies (7%) (9%).[5,11] 4.6% cases herpes simplex In the present study. But prevalence of Herpes simplex was very rare in other Indian studies except that of study (7.2%). Rather Herpes zoster was seen in a significant number of patients in other Indian studies including report (14%).[2,5,7,10,11,26,27] *Molluscum contagiosum* and PML both were seen, one case each. *Molluscum contagiosum* were also found in 8 cases in the study.[7] But PML was seen in none of the Indian studies.[5] The above patient was probable case of PML because the patient died before complete evaluation (CSF PCR study). Cytomegalovirus infection was seen in significant number of patients which was not seen in the present study. In the study, CMV retinitis was seen in 45% cases. 18.7% cases presented with CMV retinitis in the study.[28,29] CD4+T cell count for different OIs in this study was observed to be 272/µl for candidiasis, 218/µl for tuberculosis and 142/µl for cryptosporidiosis. But this observation was different than the study [13] which stated that CD4+T cell count for candidiasis was 189/µl, for tuberculosis was also 189/µl and for cryptosporidiosis was 227/µl. In the present study the CD4+T cell count was found to be below 100/µl in cases of Cryptococcal meningitis and CNS toxoplasmosis whereas it is below 50/µl in each case of *Molluscum contagiosum* and Progressive multifocal leucoencephalopathy. The CD4+T cell count for esophageal candidiasis (115/µl) was lower than that of oral candidiasis (286/µl), which was lower than that of vulvovaginal candidiasis [30] (312/µl).

CONCLUSION

Among the studied 86 cases (42%) belonged to the CD4+T cell count range of 101-200/µl with aCD4+T cell count of 183/µl, so there is increased chance of hospitalization in patients having CD4+T cell count below 200/µl. The most common OIs was tuberculosis (51%) with pleural effusion as its commonest manifestation. The second most common OIs was candidiasis (43%) with most cases suffering from oral candidiasis was seen to occur at higher CD4+T cell counts than tuberculosis.

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