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Original Research Article

Spectrum of opportunistic infections in relation to CD4 counts in HIV/AIDS patients admitted in the department of general medicine of a tertiary care hospital

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ABSTRACT

Background: HIV/AIDS was first recognized in USA in 1981 when centre for disease control (CDC) reported unexplained occurrence of Pneumocystis carinii pneumonia in 5 healthy homosexuals. Soon it was recognized in drug abusers and blood transfusion recipients. The present study has been taken up with an aim to know the incidence of various opportunistic infections in HIV positive patients and to correlate different opportunistic infections (OIs) with the CD4+cellcount.
Methods: Sample of 132 cases admitted in Gandhi hospital during the study period were taken. CD4+ counting of blood samples was done by Flow cytometry as per manufacturer's instructions (FACS Calibur, Becton- Dickinson, Immunocytometry system). Correlation of CD4 cell counts was done with the respective opportunistic infections.
Results: TB (50%) is the most frequent OI followed by candidiasis (49%), pneumocystis (16%) and others. The mean CD4 cell count in TB was 110.80/mL and in candidiasis 97.84/mL. Low values were observed in CMV (27/mL) and in toxoplasmosis (61.66/mL).
Conclusions: In most of the patient's respiratory system was the most common system involved by OIs and had CD4 T cell count below 200/mL. Early diagnosis and prompt treatment of opportunistic infections is important. This study helps the clinicians in proper guidance to come up before development of severe immunodeficiency to prevent serious and fatal outcome.

Keywords: CD4 Count, HIV/AIDS, Opportunistic infections

INTRODUCTION

HIV/AIDS was first recognized in USA in 1981 when centre for disease control (CDC) reported unexplained occurrence of Pneumocystis carinii pneumonia in 5 healthy homosexuals. Soon it was recognized in drug abusers and blood transfusion recipients. In 1983, HIV was isolated from a patient with lymphadenopathy and by 1984; it was demonstrated clearly to be the causative agent of AIDS. In 1985 a sensitive enzyme linked immunosorbent assay (ELISA) was developed for helping in the screening of HIV.

The first documented case of Acquired immunodeficiency syndrome from India was reported in August 1986. The patient developed AIDS and AIDS dementia following blood transfusion received by him in USA during a coronary artery bypass graft operation in June l980.

According to 2017 statics 79% of people living with HIV were aware of their HIV status, of which 56% were on antiretroviral treatment (ART). The proportion of individuals on ART who are virally suppressed is not reported.

The total number of people living with HIV in India was estimated at 21.17 lakhs in 2015 compared with 22.26 lakhs in 2007. In India, the estimated number of new HIV infections in 2015 were around 86 (56-129) thousand. Around 66% decline was observed in new infections from 2000 and 32% decline from 2007, the year set as the baseline in NACP IV.

Since 2007, when the number of AIDS related deaths (ARD) started to show a declining trend, the annual number of AIDS related deaths has declined to 64% in 2015, an estimated 67.6 (46.4-106.0) thousand people died with AIDS related causes nationally. The decline is consistent with the rapid expansion to ART in the country.

Opportunistic infections (OIs) are infections that occur more often or are more severe in people with weakened immune systems than in people with healthy immune systems. People with weakened immune systems include people living with HIV or people receiving chemotherapy.

Most of these deaths recorded in cases of AIDS are because of opportunistic infections (OI's) and other malignancies.[1,2] The reason may be attributed to the effective destruction or decrease in CD4+ cells which play a pivotal role in immune system.

HIV infection leads to low levels of CD4 counts making the body more susceptible to OI. This leads to increased morbidity and mortality of the patients, which is actually due to the OI rather than HIV itself.[3,4] This study was therefore undertaken to evaluate the correlation between the patients CD4 counts and the presence of various OI's in patients with HIV.

METHODS

It is prospective study. The present study was conducted at Gandhi hospital, Patients with HIV/AIDS satisfying inclusion and exclusion criteria admitted in the Department of General Medicine, Gandhi hospital over a period of one year that is from August 2016 to July 2017.

One hundred and thirty two (n=132) of both sexes. Sample of 132 cases admitted in Gandhi hospital during the study period were taken. Ethical clearance has been obtained from the Ethical clearance committee chaired by the Principal Gandhi Medical College, Secunderabad, in a prescribed certificate. Upon enrollment in the study, written consent was obtained and duly signed by the patients in a prescribed format. There were 132 patients are participated in this study.

Inclusion criteria

Patients who are HIV positive aged >18 years and admitted in Department of general medicine.

Exclusion criteria

Patient refusal or inability to provide informed consent.

Statistical analysis

All the data was entered in Microsoft excel data sheet and analyzed. The mean, median and STD deviation was calculated regarding continuous variables.

RESULTS

In this study a total of 132 HIV patients are taken, of the 132 individuals analyzed, 84 (64%) were males, 46 (34%) were females and 2 (2%) were Transgender. A total of 160 opportunistic infections were found comprising of bacterial, fungal, parasitic and viral infections. Among different opportunistic infections, bacterial infections were seen in 56.06% (74) patients, followed by fungal in 45.45% (60), viral in 10.6% (12) and parasitic in 90.9% (12) respectively. Most of the OIs i.e. 46.3% (61/160) were seen in CD4+ count <100 (cells/ l), 15.2% (20/160) were seen within 101-150 CD4+ cells/ l range followed by, 25.7% (34/160) in 151-200 CD4 cells/ l while 12.8% (17/160) OIs were observed >200 CD4+ cells/ l group.

Most of the individuals had a CD4+ count less than 200cells/dl (Table 1) (Figure 1).

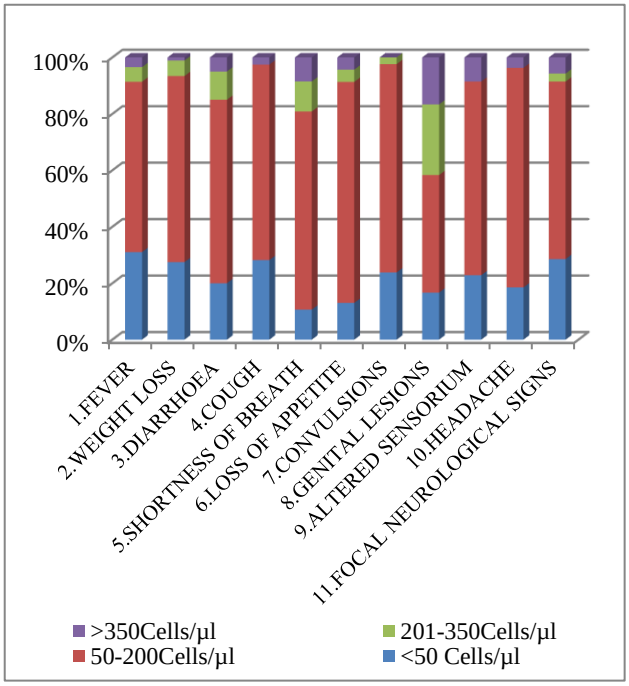

Figure 1: Distribution of the Symptoms based on CD4+ cell count

Only 17 individuals had CD4+ above 200 cells/dl. Majority of the patients were already on treatment and were using TLE regimen. The number of individuals who were not compliant were 24.3%.

The commonest infection among the opportunistic infections was Tuberculosis, followed by Candidiasis and Cryptosporidial diarrhea (Table 2 and 3) (Figure 2 and 3).

Herpes zoster was also seen in an increased frequency. Equal percentages of CMV *retinitis*, *Mooloscum contagiosum*, Progressive multifocal leuko encephalopathy, *Staphylococcus aureus* and *Entamoeba histolytica* were seen.

OI's association with CD4+ count <50 (cells/ l)

In this group, 27.05% (46/160) of opportunistic infections were seen which comprised of 43.47% (20/46) bacterial

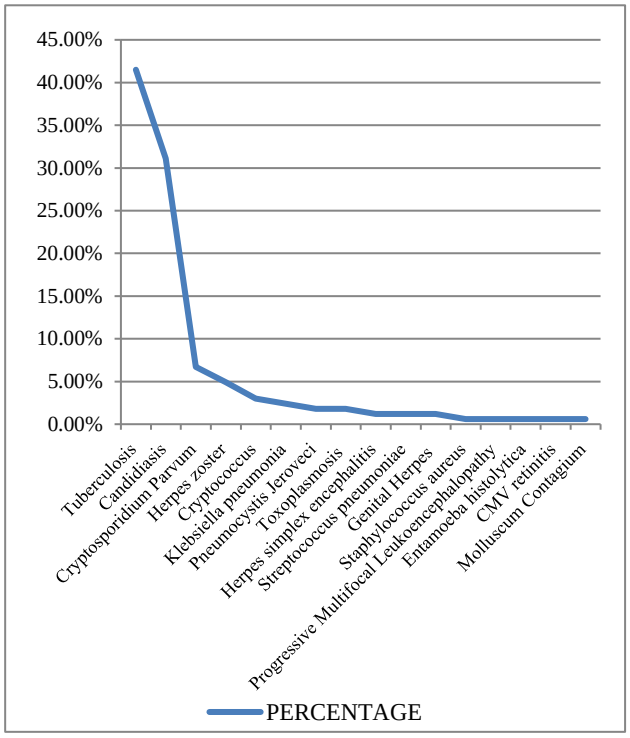

Figure 2: Percentage of each opportunistic infection

infections, 43.47% (20/46) fungal infections, 4.34% (2/46) parasitic infections and 8.6% (4/46) of viral infections.

Among bacterial infections, pulmonary tuberculosis and extra-pulmonary tuberculosis were seen with equal frequency i.e. 50% each (10/20). In fungal infections, most common was Candidiasis 80 % (16/20) followed by *Cryptococcal meningitis* 15% (3/20), and *Pneumocystis jiroveci* 5% (1/20). Parasitic infections included Cryptosporidium 100% (2/2). Viral infections included Herpes zoster 75% (3/4), and *Cytomegalovirus retinitis* in 25% (1/4) patients.

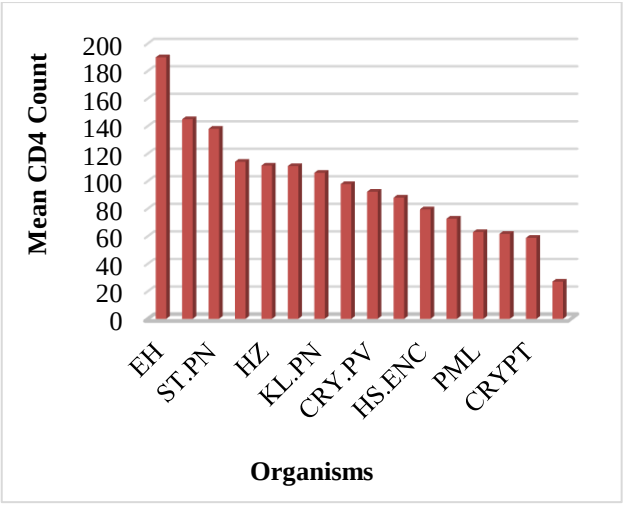

Figure 3: Relationship between CD4 cell counts and the organisms responsible for the opportunistic infections

OI's association with CD4+ count 50-99(cells/ l)

Most of the OI s i.e. 31.25% (50/160) were seen within 99-50 CD4 cells/µl range which comprised of 22% (11/50) bacterial infections, 48% (24/50) fungal infections, 16% (8/50) parasitic infections and 14% (7/50) of viral infections. In this group, among bacterial infections most common was extra-pulmonary tuberculosis followed by pulmonary tuberculosis, Klebsiella pneumoniae and Staphylococcus. In fungal infections, most common was Candidiasis followed by *Cryptococcal meningitis* and *Pneumocystis jiroveci.* Parasitic infections included Cryptosporidium and Toxoplasma gondii. Viral infections included Herpes Zoster, genital herpes, Herpes simplex encephalitis and Progressive multifocal leuko encephalopathy.

OI's association with CD4+ count 100-149(cells/ l)

In this group, 20% (32/160) of opportunistic infections were seen which comprised of 46% (15/32) bacterial infections, 40% (13/32) fungal infections, 9.3% (3/32) parasitic infections and 3.12% (1/32) of viral infections. In this group, among bacterial infections most common was extra-pulmonary tuberculosis and pulmonary tuberculosis, *Klebsiella pneumoniae*, *Streptococcus pneumoniae*, and *Staphylococcus aureus*. In fungal infections, only Candidiasis was seen. Parasitic infections included only *Cryptosporidium parvum*. Viral infections Molluscum contagiosum was observed in one patient.

OI's association with CD4+ count 150-199(cells/ l)

In this group 24% (39/160) OI s were observed which consisted of 35.3% (28/39) bacterial infections, 23.5% (8/39) fungal infections, 29.4% (1/39) parasitic infections and 11.8% (2/39) of viral infections. In this group, among bacterial infections most common was pulmonary tuberculosis followed by extra-pulmonary tuberculosis. In

fungal infections, only member was Candidiasis 100% (8/8). Parasitic infections included *Entamoeba histolytica* each. Viral infections included Herpes zoster alone.

Table 1: Distribution of study subjects based on CD4+ cell count

		Gender						Total (n=132)
		Male		Female		Transgender		
		Count	Column N %	Count	Column N %	Count	Column N %	Count (%)
CD4 Range	<50	19	22.6%	10	21.7%	0	0.0%	29 (22)
	51-100	20	23.8%	10	21.7%	2	100.0%	32 (24.3)
	101-149	14	16.7%	6	13.0%	0	0.0%	20 (15.2)
	150-199	25	29.8%	9	19.6%	0	0.0%	34 (25.7)
	>200	6	7.1%	11	23.9%	0	0.0%	17 (12.8)
Total		84	100.0%	46	100.0%	2	100.0%	132 (100)

Table 2: Mean CD4 count in infections caused by various organisms alone and in combination

Sr.no	Organisms	N	Percentage	Mean
1	Cryptococcus	5	3%	58.8
2	Tuberculosis	68	41.5%	110.89
3	Cryptosporidium Parvum	11	6.7%	92.27
4	Herpes zoster	8	4.9%	111.25
5	Herpes simplex encephalitis	2	1.2%	79.5
6	Streptococcus pneumoniae	2	1.2%	138
7	Candidiasis	51	31.1%	97.84
8	Progressive Multifocal Leukoencephalopathy	1	0.6%	63
9	Entamoeba histolytica	1	0.6%	190
10	Klebsiella pneumonia	4	2.4%	106
11	Pneumocystis Jeroveci	3	1.8%	72.66
12	Genital Herpes	2	1.2%	88
13	Toxoplasmosis	3	1.8%	61.66
14	CMV retinitis	1	0.6%	27
15	Staphylococcus aureus	1	0.6%	114
16	Molluscum Contagium	1	0.6%	145
Total		164	100.0%	97.24

Table 3: The distribution of the subjects based on opportunistic infections and also CD4+ cell level.

	Outcome	N	Mean	Std. Deviation	Std. Error Mean	P value
CD4 Count	Discharge	103	149.85	115.979	11.428	0.042*
	Death	29	101.86	92.253	17.131	

OI's association with CD4+ count >200(cells/ l)

Only 1.8% (3/160) OIs were seen above 200 CD4+ cells/µl group. Only infections were tuberculosis, Candida species and Herpes zoster. Acquired Immunodeficiency Syndrome (AIDS) is a pandemic of 21st century presenting with severe immunodeficiency in which patients present with symptoms of different opportunistic infections. HIV presently accounts for the highest number of deaths attributable to any single infective agent. India has an estimated 5.2 million HIV-infected people. The threat to their life is not from the virus alone. Opportunistic infections (OI's) and associated complications account for a considerable proportion of such mortality (Table 4).

Table 4: Independent sample t-test for Outcome Vs CD4 count

	Outcome	N	Mean	Std. Deviation	Std. Error Mean	P value
CD4 Count	Discharge	103	149.85	115.979	11.428	0.042*
	Death	29	101.86	92.253	17.131	

Thus, it is very important to identify and start appropriate management of the off ending agent at an earliest so that OI s can be managed appropriately to prevent mortality and morbidity among HIV-infected persons.

DISCUSSION

In the study of opportunistic infections, we found bacterial infections as prominent opportunistic infection followed by fungal, viral and parasitic in decreasing order. Out of total 132 patients under study, 160 events of opportunistic infections were seen in the present study singly/ in mixed form.

The present study of 132 HIV patients deals with wide spectrum of opportunistic infections and their correlation with CD4+ cell counts. Among bacterial infections, tuberculosis was found to be most common bacterial infection. It was seen in 41.5% of all the 132 patients out of which 49.2% were of pulmonary tuberculosis and 50.8% were of extrapulmonary tuberculosis. As far as tuberculosis is concerned, we found almost equal distribution of pulmonary tuberculosis and extra-pulmonary tuberculosis in the study group with slightly more number of extra-pulmonary tuberculosis cases. Equal distribution of pulmonary tuberculosis and extra-pulmonary tuberculosis has also been observed by Ayyagariet al although in small number of cases.[5] Our findings are nearly similar to findings reported by Sunderam G. et al, Kumara samy N et al Misra SN et al, Veeranoot et al, M. Vajpayee et al, Singh A et al.[6-11]

Correlation of opportunistic infections with CD4+ cell count

As the immunodeficiency advances, HIV positive patient becomes susceptible to variety of opportunistic infections because of profound immune suppression. There have been many reports showing the correlation between CD4+ cell count and occurrence of opportunistic infections in HIV patients. We also tried to correlate the same in the present study. To correlate the opportunistic infection with CD4+ cell count, for the convenience we divided the study cases into five groups based on CD4 cell count (cells/mm^3) i.e.<500-200, 199-150, 149-100, 99-50 and <50 cells/mm^3.It was observed in the present study that when CD4+ count starts falling below 500 cells/mm^3, first indication of immunodeficiency is seen in the form of oral thrush and pulmonary tuberculosis however other opportunistic infections are seen when the severity of immunodeficiency increases as CD4 cell count becomes less than 200 cells/mm^3.Theonly infections seen in the CD4 count range (200-500) was Candida infection and tuberculosis. No other opportunistic infections were seen in this group in the present study. Crowe et al, Giri TK et al and Merle A et al reported the pulmonary tuberculosis to be the commonest opportunistic infection inCD4+ cell count range (200-500).[12-14] Whereas Merle A et al, Chien-ChingHung et al and NACO also reported the similar findings in their studies did not get a single case of tuberculosis in this range of CD4+ cell count.[15-17]

However, when immunodeficiency further progresses and CD4+ cell count falls below 200 cells/mm^3 i.e. (199-150), the most common infections after pulmonary tuberculosis were Candidiasis followed by viral and parasitic infection. Parasitic infections found in the form of Cryptosporidium parvum in this range of CD4 cell count. Reactivation of Herpes zoster was also observed.

When CD4+ cell count further drops to below 149 cells/ mm^3 i.e. in the group (149-100), the spectrum of opportunistic infections changes. At this level of CD4+ cell count the infections comprised in the order of frequency i.e. Candidiasis followed by extra-pulmonary tuberculosis and pulmonary tuberculosis, and Cryptosporidium. At this level tuberculosis dominated with addition of bacterial pneumonia.

Most of the reports by other workers did not classify the CD4+ cell count in the range 100-149 cells/mm^3 as they had taken in to consideration the CD4+ cell count <200 cells/mm^3 as a group in place of 149-100 cells/mm.

In the present study, with further increase in degree of immunodeficiency and simultaneous decrease in CD4+ cell count i.e. below 100cells/mm^3 or in the group (99-50), tuberculosis both pulmonary and extra pulmonary dominated the spectrum of opportunistic infections which was followed by Candidiasis, Cryptosporidium and Herpes zoster. At this level of immunodeficiency, two new infections, Cryptococcus meningitis and cerebral toxoplasmosis were seen.

When severe immunodeficiency occurs i.e.CD4+ cell count <50 cells/mm^3 almost all opportunistic infections become manifest at this terminal stage of AIDS. In this scenario, the existing infections are seen with increasing frequency and in disseminated form. In the present study with increasing infections with both forms of tuberculosis, Candida and Cryptococcus, we also found *Cytomegalovirus retinitis* and *Pneumocystis jiroveci*.

CONCLUSION

There exists definite CD4+ cell count correlation with the opportunistic infections in HIV-AIDS patients starting with Pulmonary tuberculosis, Candidiasis, *Cryptosporidiosis, Herpes, Cryptococcal meningitis, Pneumocystis jiroveci pneumonia, Toxoplasma gondii* and interminal stage of immunodeficiency, bacterial pneumonia along with Molluscum contagiosum and Cytomegalovirus retinitis in the order of increasing immunodeficiency.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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