

Profile of Opportunistic Infections among *HIV* Patients Prior to Start of ART in a Tertiary Care Hospital in Rajasthan

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ABSTRACT

Introduction: *HIV* infection is a global pandemic causing immunodeficiency resulting in various opportunistic infections among patients suffering from *HIV* infection. The chances of developing opportunistic infections increases with decreasing CD4 counts, and incidence rates of opportunistic infections are six times higher in patients with CD4 counts below 200/mm³. The pattern and sequence of opportunistic infections varies as the total CD4 cell count decreases and also differ between different geographical regions. Hence, knowing local pattern is must for the treating physician before starting any empirical therapy.

Methodology: The present study was carried out at the ART Centre of a Government Medical College in Rajasthan. The study duration was four years from July 2013 to July 2017. A total of 274 patients prior to start of ART were investigated for the profile of opportunistic infections associated with *HIV*.

Results: Among these 274 *HIV* patients, a total of 690 opportunistic infections were found with chronic diarrhea as the most common symptom in 169 (61.9%) patients, followed by oral candidiasis which was present in 139 (50.7%) patients, other opportunistic infections like tuberculosis (TB), *Pneumocystis jirovecii* (*PJ*), lower respiratory tract infections (LRTI), *Herpes simplex virus* (*HSV*) and *Herpes zoster virus* (*HZV*) were present in 131(47.8%), 126 (45.9%), 86 (31.3%), 34 (12.4%), and 5 (1.8%) of patients, respectively.

Conclusion: Chronic diarrhea and oral candidiasis were the most common opportunistic infections prior to starting ART, with a total of 84.7% of patients having

opportunistic infections. This data will be useful in planning research cum intervention for improving patient care in *HIV* patients in this region.

INTRODUCTION

Opportunistic infections (OIs) are the most common complication of *Human immunodeficiency virus* (*HIV*) infection¹ causing significant morbidity and mortality in people with *HIV* infection.^{1, 2} OIs remain the single main cause of ill-health and death among *HIV*-infected patients.³ Research shows that about 90% of *HIV*-related morbidity and mortality are caused by opportunistic infections compared to 7% due to opportunistic cancers and 3% due to other causes.⁴

The identification of pathogens responsible for OIs is very important in managing the *HIV* infected individual. The spectrum of OIs of a particular locality should be known to prevent these infections by giving adequate prophylaxis. The relative frequencies of specific OIs may vary in different countries and even in different areas within the same country.^{5,6} Knowledge of the most common OI of a geographical area will help in implementing the preventive measures against that pathogen. Tuberculosis is the most common OI among *HIV* infected individuals of Guatemala, sub-Saharan Africa,⁷ and Bangladesh.⁸ *Pneumocystis carinii* pneumonia is the most common cause of OI in Malaysia,⁹ Hong Kong,¹⁰ and China.¹¹ *Penicillium marneffei* is the commonest cause of OI in Thailand.⁷ A natural history study from western India (Mumbai) reported the incidence of pulmonary tuberculosis to be 5.7 per 100 person-years of follow-up.¹² In another Indian study, the overall incidence of tuberculosis was found to be 15.4 per 100 person-years of

follow-up (95% CI 12.219.2). The incidence of extrapulmonary tuberculosis was higher (7.9 per 100 person-years) than pulmonary tuberculosis (6.9 per 100 person-years), resulting in the reporting of 45 and 39 cases of extrapulmonary and pulmonary tuberculosis, respectively^{13,14} among the study participants during the follow-up. There are many reports available regarding the pattern of OIs in *HIV* infected individuals.

In a study from eastern India, incidence of oral candidiasis (88%) was found to be the most common OIs, followed by tuberculosis (57%), enteropathogenic vibrio (47%), *Cytomegalovirus* infection (45%), cryptosporidial diarrhea (43%), *Escherichia coli* infection (42%), and other infections among the study subjects.¹⁵ There are many reports available regarding the pattern of OIs in *HIV* infected individuals from different parts of India, but no study is published with profile of OI's from Rajasthan. Hence, we are reporting the recent profile of OIs and their respective CD4 count among patients prior to start of ART.

METHODS

The present study was carried out at the ART centre of a government medical college and associated group of hospitals, Rajasthan. Study period was for four years from July 2013 to July 2017. A total of 274 patients prior to start of ART attending ART centre were screened for OIs

infection associated with *HIV* to note the pattern of OIs. The individuals were interviewed in detail and their socio-demographic data were collected with the help of a proforma. CD4 cells estimation was done. In ART center, free ART was issued based on their CD4 count and National Acquired Immunodeficiency Syndrome (AIDS) Control Organization (NACO) guidelines.¹⁶ These patients were investigated in hospital for initiation of therapy and any complications thereafter.

All adult patients admitted, with newly diagnosed *HIV/AIDS*, in medicine wards and referrals from other departments during the study period were included in this study. Patients admitted to pediatric wards, patients with all other immune compromised states such as malignancies, organ transplant, patients on steroids therapy or immunosuppressive therapy, and diabetes mellitus were excluded.

RESULTS

The current study revealed that the maximum number of patients who had OIs were in the age group of 28-37 years (54.9%), followed by the age group 18-27 years (29.3%) and 38-59 years (15.8%). No patients were found in the age group above 60 years. There was higher proportion of males (73.6%) as compared to females (26.4%). The male to female ratio was 2.8:1. Patients who had OIs prior to start of ART were 74.3%.

Table 1: Profile of opportunistic infections among patients of *HIV* in relation to CD4 level before start of ART

OIs	CD4 levels (per mm ³)						Total
	<50	51-100	101-150	151-200	201-250	>250	
CHR DIA	17	37	59	10	39	7	169
HSV	8	0	18	2	6	0	34
HZV	1	0	2	0	2	0	5
LRTI	6	26	27	5	19	3	86
OC	13	31	36	9	37	13	139
PJ	12	32	43	7	27	5	126
TB	20	21	23	5	60	2	131
Total	77	147	208	38	190	30	690
infections							
Total number of patients	29	66	91	14	61	13	274
%	10.5	24.1	33.2	5.1	22.2	4.7	100

(CHR DIA) Chronic diarrhea; (HSV) *Herpes simplex virus*; (HZV) *Herpes zoster virus*; (TB) Tuberculosis; (PJ) *Pneumocystis jiroveci*; (LRTI) Lower respiratory tract infections; (OC) Oral Candidiasis.

A total of 690 OIs were found in 274 patients with chronic diarrhea as the most common infection in 169 (61.9%) patients, followed by oral candidiasis which was present in 139 (50.7%) patients, other OIs like tuberculosis (TB), *Pneumocystis jiroveci* (PJ), lower respiratory tract infections (LRTI), *Herpes simplex virus* (HSV), and *Herpes zoster virus* (HZV) were present in 131 (47.8%), 126 (45.9%), 86 (31.3%), 34 (12.4%), and 5 (1.8%) of patients respectively as shown in table 1. Maximum patients were having CD4 level of less than 150. Two patients of HZV and 18 patients with HSV as primary OIs had CD4 count between 100-150 while patients with LRTI had CD4 level below 200, with 24, 27, and 26 patients with CD4 values falling between 150-250, 100-150, and 51-100, respectively. The maximum numbers of patients with PJ as OIs were having CD4 count less than 150 and those with TB fell in 201-250 group.

The median CD4 count for chronic diarrhea (CD), *Herpes simplex virus* (HSV), *Herpes zoster virus* (HZV), lower respiratory tract infections (LRTI), oral candidiasis (OC), *Pneumocystis jiroveci* (PJ), and tuberculosis (TB) were 140, 120, 114, 127, 154, 117, and 194, respectively. The lower median CD4 count of 138 cells/cu.mm in our study may be on account of late detection of the infections due to inadequate laboratory facilities at the peripheral health centers where treatment might be held up until significant immunosuppression has already set in, at which point patients are referred to tertiary care hospitals.

DISCUSSION

Many research studies have described the types and prevalence of OIs in HIV-infected individuals globally.^{5,6,8,9,11} It has also been reported that the incidence of OIs has decreased in developed countries due to the availability of ART. However, in India being in the present phase of transition of the epidemic from HIV infection to AIDS, a rise in the burden of OIs is anticipated.

The HIV epidemic in India is geographically diverse and there are regional differences, not only in the incidence and prevalence of HIV infection, but also in the burden of background communicable diseases. Facilities and access to healthcare in rural areas are limited. While preparing appropriate strategies for the effective management of AIDS patients, significant effort and investment will have to be made to build infrastructure, diagnostic facilities, and clinical expertise to manage OIs. If the public health managers are provided with accurate estimates of the

existing burden and the rate of occurrence of OIs among HIV-infected individuals, they will be able to plan and implement appropriate management strategies and interventions. The highlight of this study was reporting the incidence rates of four commonly observed OIs at various levels of immunosuppression in HIV-infected patients enrolled in a prospective study in North West Rajasthan.

OIs are the major cause of morbidity and mortality in immune-compromised individuals as cellular and humoral defenses are compromised in these patients. In this study, all the patients presented with most of the constitutional symptoms of the disease. The 28-37 years age group was found to be most commonly (54.9%) involved. All the females participating in the study were married monoandrous. This observation explains the shift of the epidemic from high risk groups like sexually transmitted diseases and injectable drug users, to low risk groups like married monoandrous women. This finding is based on the interview with the study group female patients, but polyandrous relation cannot be ruled out. In this study, chronic diarrhea was the most common infection found in 169 (61.9%) patients, followed by oral candidiasis which was present in 139 (50.7%) study participants.

The overall incidence of OIs in our study population was 74.3%. The chances of developing OIs increased with decreasing CD4 counts, and incidence rates of OIs were six times higher in patients with CD4 counts below 200/mm³ as compared to others. These findings are consistent with observations from other developed and developing countries.¹⁷ A study from Brazil reported an incidence of 51% OIs per year in patients with CD4 counts below 100/mm³ who were either on monotherapy or dual therapy antiretroviral regimens.¹⁷ In a study in southern India, the incidence of OIs before initiation of ART was up to 10 per 100 person-years of follow-up.^{18,19} This is low compared to present study, and may be due to the difference in the profile of the study population, study design, and differential follow-up rates. On an average globally, TB prevalence among HIV positive individuals slightly reduced from around 25% in 2007 to 21% in 2010.²⁰ In the present study, we have observed a significant declining trend in mean annual prevalence of *Mycobacterium tuberculosis*. This is consistent with the study in the USA that evaluated annual trends for 13 most common AIDS-

defining opportunistic infections by examining medical records in more than 90 hospitals and clinics in 9 US cities before HAART showed decreasing trends in tuberculosis³, however study of NACO has also reported tuberculosis as the major OI with 62% incidence followed by candidiasis (57%), and chronic diarrhea (47%).¹⁵

A study reported that the median CD4 count at the development of pulmonary tuberculosis was 194/mm³, which is higher than that reported in a natural history study in southern India (111/mm³).^{18, 19} The diagnosis and management of tuberculosis, especially, extrapulmonary tuberculosis, is likely to pose unique challenges for medical practitioners from the diagnostic viewpoint, particularly in resource-limited settings. Although early diagnosis of extrapulmonary tuberculosis can be a challenge, if accomplished it can significantly reduce associated morbidity and mortality. The issue of prophylaxis against tuberculosis in *HIV*-infected individuals, especially using a potent drug like isoniazid, is debatable. However, it is certainly important that studies be undertaken to evaluate various drugs that can be used as prophylactic agents against tuberculosis in *HIV*-infected persons in settings like India, Herpes zoster showed a significant declining trend²¹ though the effect of HAART seems to be relatively less compared to other OIs. Oral candidiasis is a commonly described OI globally and has been reported as a marker of immunosuppression. The high incidence of oral candidiasis, especially at low CD4 counts, necessitates the introduction of appropriate intervention for the same. The median CD4 counts at the time of diagnosis of oral candidiasis in this study were lower than those determined elsewhere, but in India this condition is shown to have an association with low CD4 counts.²² Oral candidiasis is one of the clinical markers of immunosuppression, and antiretroviral therapy should be initiated in patients with persistent oral candidiasis if facilities for performing CD4 counts are not available. Another important observation in the present study was that 74.3% of the study subjects were suffering from at least on single OIs before initiation of HAART.

CONCLUSION

The high prevalence rate of OIs in the present study may also be due to the fact that this study was conducted at a major tertiary-care government hospital where patients seeking care are mostly referred from peripheral health care centers. This high OI burden could be partly

secondary to associated malnutrition, overcrowding, poor hygiene, and lack of a good public health infra-structure. However, this aspect needs indepth investigations. A greater prevalence of OIs was observed in those with CD4 counts below 200 cells/cu.mm. Clinicians should carefully investigate those patients with very low CD4 counts presenting with symptoms suggestive of meningitis. Early diagnosis and effective treatment may considerably reduce the morbidity and mortality associated with this condition.

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