CLINICAL STUDY

Spectrum of Opportunistic Infections in People Living with HIV: A Tertiary Care Center Experience from North India

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ABSTRACT

Introduction: Patients with human immunodeficiency virus and acquired immunodeficiency syndrome (HIV/AIDS) are prone to opportunistic infections (OIs) given their immunosuppressed state. OIs continue to cause morbidity and mortality in HIV/AIDS patients even after highly-active antiretroviral therapy (HAART); hence, attainment of the goals on health care programs, particularly in resource-poor countries, is hard to achieve. The prevalence of specific OIs varies in different countries and even in different areas within the same country. Little information is available about the prevalence of OI in HIV patients from developing countries, especially India. Early diagnosis and prompt treatment contribute to increased life expectancy among infected patients delaying progression to AIDS. Hence, the present study was carried out to elucidate current frequencies and spectrum of OIs in HIV seropositive adult patients in Haryana and to evaluate the associated risk factors for OIs. **Materials and methods:** This was a cross-sectional study carried out at the Dept. of General Medicine in a tertiary care hospital in North India. Basic demographic details, anthropometric measurements, symptoms of HIV/OI, clinical examination, biochemical investigations and treatment details were recorded. Patients aged 18 to 70 years and HIV seropositive subjects were included in the study. **Results:** The study found that about 53.21% of HIV/AIDS patients on ART had one or more OIs. Tuberculosis (TB) was the predominant OI identified, with a prevalence of 25.71%. Candidiasis and herpes zoster were the second and the third most prevalent OIs at 13.8% (101/731) and 7.25% (53/731), respectively. Age (43.4 ± 10.7 years), low income, illiteracy, low socioeconomic status, initial 4 months since initiation of ART, CD4 count <200/mm^3, body mass index of <18.5 kg/m^2, poor ART adherence, hemoglobin, albumin were strongly associated with OIs. **Conclusion:** The present study shows that TB is the commonest OI in adults and the overall population of people living with HIV (PLHIV) in Haryana and proves that OIs across different patient groups vary significantly. Various factors like adherence to HAART, socioeconomic and education status of patients can influence the occurrence and outcome of these deadly infections.

Keywords: Spectrum, opportunistic infections, PLHIV

Human immunodeficiency virus (HIV) infection is one of most studied infectious diseases since it was first recognized clinically in 1981 in the United States of America. HIV-related opportunistic infections (OIs) have been defined as infections that are more frequent or more severe because of HIV-mediated immunosuppression.[1] OIs are the first clinical manifestations that alert clinicians to the occurrence of the acquired immunodeficiency syndrome (AIDS). These OIs occurs on average 7 to 10 years after infection with HIV.[2,3] Until effective antiretroviral therapy (ART) was developed, patients generally survived for only 1 to 2 years after the initial manifestation of AIDS.[4] However, OIs continue to cause morbidity and mortality in HIV/AIDS patients even after highly-active antiretroviral therapy (HAART); hence, the attainment of the goals on health care programs, particularly in resource-poor countries, is hard to achieve. OIs shorten the life span of people with HIV infection and require expensive treatments, which carry a substantial financial burden, especially for a developing country like India. Timely intervention helps HIV-positive persons live longer and also helps to prevent transmission in the community.[5]

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Estimating the cost of necessary health care as accurately as possible must be the first step in planning specialized health services, which is only possible if we know how the OIs are distributed in a given place. Also, there is no denying that HIV-related OIs affect a person's quality of life and contributes to the overall disability-adjusted life years (DALY) caused by AIDS. The prevalence of specific OIs varies in different countries and even in other areas within the same country. Identifying such OIs is especially important for HIV and AIDS case management. Little information is available about the prevalence of OI in HIV patients from developing countries, especially India. Early diagnosis of OIs and prompt treatment contribute to increased life expectancy among infected patients delaying progression to AIDS. Hence, this study was carried out to elucidate current prevalence and spectrum of OIs infecting HIV-seropositive adult patients in Haryana, a northern state in India, and to evaluate the associated risk factors of OIs. Identifying such pathogens is very important for clinicians and health planners to tackle the AIDS epidemic more effectively.

MATERIALS AND METHODS

This was a cross-sectional study carried out at a tertiary care center in North India. Adult patients between 18 to 70 years attending the Nodal ART Centre, admitted under Dept. of Medicine PGIMS, Rohtak, Haryana, and admitted under clinics were enrolled in this study. Patients who did not consent to participate in the study, those with psychiatric illness taking regular medications, pregnant and lactating mothers, those with non-HIV/AIDS-related malignancy, known cases of chronic kidney and liver disease prior to diagnosis of HIV and patients with an altered sensorium or cognitive impairment severely affecting communication were excluded from the study. Our Nodal ART Centre has all the adequate facilities and investigations for detecting the OI before commencing ART.

Detailed information of all enrolled patients was filled in a proforma designed for the study purpose. This included basic demographic details, anthropometric measurements, symptoms of HIV/OI, clinical examination and treatment. At baseline, each patient underwent hematological and biochemical investigations. Patients were assessed for OI risk factors. These included age, weight at last visit, serum albumin at diagnosis of OI, World Health Organization (WHO) clinical stage III and IV, CD4 count at the time of diagnosis of OI, initiation of ART since diagnosis of HIV and adherence to ART. The Center for Adherence Support Evaluation (CASE) Adherence Index, a simple composite measure of self-reported ART adherence, was utilized to assess adherence to ART.[6] Informed consent was taken from all participants and study was approved from ethical committee of the institute and Haryana state division of National AIDS Control Society.

The diagnosis of OI was made following standard guidelines where possible and facilities available. Where diagnosis was based on clinical grounds alone, the opinion of two independent physicians involved in enrolled patient care and management was required before such diagnosis was accepted.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) Version 23 was used for all descriptive and statistical analysis. Association of OIs was done by subgroup analysis of WHO staging, CD4 count, demographic and biochemical/hematological profile and treatment adherence. The distribution of data was analyzed and appropriate parametric/nonparametric tests were used for statistical analysis. Continuous data were expressed as means ± standard deviation (SD), and the means were compared using a *t*-test. Nominal data were expressed as frequencies or proportions, and the Chi-square test and Fisher's exact test were used to compare the differences in frequency. For all tests, a p-value of <0.05 will be considered significant, and the confidence interval will be kept at 95%.

RESULTS AND OBSERVATIONS

The study was conducted in the Dept. of General Medicine, PGIMS, Rohtak, Haryana, India. A total of 731 patients aged 18 to 70 years and HIV seropositive subjects were included in the study. The baseline characteristic of the study participants is presented in Table 1.

The study found that about 53.21% of HIV/AIDS patients had one or more OIs compared to 46.79% who had no OI. Tuberculosis (TB) (48.32% of total OIs) was the predominant OI identified, with a prevalence of 25.71% (200/731). Of these, 71.80% (n = 135/188) were pulmonary TB and 31.3% were extrapulmonary TB (n = 59/188). Among the extrapulmonary TB cases, 35 were abdominal TB and 24 were TB meningitis. Candidiasis and herpes zoster were the second and the third most prevalent OIs in the present study, at 13.8% (101/731) and 7.25% (53/731), respectively (Table 2).

There were 63 co-infections of different OIs observed in the current study. Of these, 55 had 2 co-infections,

Table 1. Distribution of Demographic Characteristics of Study Subjects

Demographic characteristics	Frequency	Percentage (%)
Gender		
Female	284	38.85
Male	438	59.92
Transgender	9	1.23
Area of residence		
Rural	534	73.05
Urban	197	26.95
Religion		
Christian	3	0.41
Hindu	717	98.08
Muslim	10	1.37
Sikh	1	0.14
Income		
<2,000	135	18.47
2,000-5,000	232	31.74
5,001-20,000	298	40.77
>20,000	66	9.03
Socioeconomic status		
Lower	51	6.98
Upper lower	113	15.46
Lower middle	377	51.57
Upper middle	120	16.42
Upper	70	9.58
Education		
Illiterate	172	23.53
Primary school	271	37.07
Secondary school	208	28.45
College and Above	80	10.94
Marital status		
Married	655	89.60
Unmarried	23	3.15
Widow/Widower	53	7.25
Spouse		
Expired	52	9.65
Nonreactive	289	53.62
Reactive	198	36.73
Age (years)		
Mean ± SD	40.02 ± 11.17	
Median (25th-75th percentile)	38 (32-48)	
Range	19-70	

Table 2. Distribution of Opportunistic Infections of Study Subjects

Opportunistic infections	Frequency	Percentage (%)	Percentage (%) from total OI
No OI	**342**	**46.79**	**-**
Skin	73	9.99	18.77
Herpes zoster	53	7.25	13.62
Kaposi sarcoma	20	2.74	5.14
CNS	56	7.66	14.40
TBM	24	3.28	6.17
Primary CNS lymphoma	3	0.41	0.77
PMLE	2	0.27	0.51
Cryptococcal meningitis	15	2.05	3.86
Cerebral toxoplasmosis	12	1.64	3.08
GIT	166	22.71	42.67
Abdominal TB	35	4.79	9.00
Chronic mucocutaneous candidiasis	100	13.68	25.71
Candidal esophagitis	1	0.14	0.26
HSV oral ulcers	16	2.19	4.11
Chronic diarrhea	20	2.74	5.14
Cryptosporidiosis	14	1.92	3.60
Giardiasis	1	0.14	0.26
Isosporiasis	2	0.27	0.51
Schistosomiasis	3	0.41	0.77
Respiratory	161	22.02	41.39
Pulmonary TB	135	18.47	34.70
Other bacterial	12	1.64	3.08
Klebsiella pneumoniae	3	0.41	0.77
Pseudomonas aeruginosa pneumonia	1	0.14	0.26
Streptococcus pneumoniae	8	1.09	2.06
Fungal	8	1.09	2.06
Aspergillus fumigatus pneumonia	1	0.14	0.26
Histoplasma capsulatum pneumonia	1	0.14	0.26
Cryptococcus neoformans pneumonia	1	0.14	0.26
Pneumocystis jirovecii pneumonia	5	0.68	1.29

Table 2. Distribution of Opportunistic Infections of Study Subjects

Opportunistic infections	Frequency	Percentage (%)	Percentage (%) from total OI
Hematology	10	1.37	2.57
Diffuse large B-cell lymphoma	10	1.37	2.57
Eye	1	0.14	0.26
CMV retinitis	1	0.14	0.26
Total pulmonary and extrapulmonary	188	25.71	48.32

OI = Opportunistic infection; TB = Tuberculosis; CNS = Central nervous system; TBM = Tuberculosis meningitis; PMLE = Polymorphous light eruption; GIT = Gastrointestinal tract; HSV = Herpes simplex virus; CMV = Cytomegalovirus.

7 had 3 co-infections and 1 patient had 4 co-infections. TB with candidiasis were the most common co-infection (32 cases) followed by TB with cryptosporidiosis (4 cases).

The mean ± SD of age (years) in patients with OI was 43.4 ± 10.7, which was significantly higher than patients without OI (36.18 ± 10.43). The proportion of patients with OI was significantly higher in patients with income (in Rupees) (<2,000 [68.15.52%] and 2,000-5,000 [60.34%]) as compared to 5,000-20,000 (45.97%) and >20,000 (30.30%). OIs were significantly higher in illiterate people (66.86%) as compared to those with primary school education (52.40%), secondary school education (54.33%) and college and higher education (23.75%) with a p-value of <0.0001. It was found that 90.20% of patients in the lower Kuppuswamy class had OIs as compared to upper-lower (57.52%), lower-middle (52.25%), upper-middle (41.67%) and upper class (44.29%) with a p-value <0.0001. OIs were significantly higher in patients with body mass index (BMI) (kg/m^2) of <18.5 (underweight; 83.94%) as compared to 18.5-24.99 (normal BMI; 44.23%), 25-29.99 (overweight; 3.85%), ≥30 (obese; 0%) with p value of <0.0001. Significant association was seen between weight (kg) and OIs. Mean ± SD of weight (kg) in patients without OI was 58.7 ± 9.17, which was significantly higher as compared to patients with OI (52.72 ± 7.21) with p value of <0.0001.

The proportion of patients with OI was significantly higher in time since ART initiation (months) ≤12 months (71.84%) as compared to 13 to 24 months (30.19%), 25 to 36 months (26.67%), 37 to 48 months (57.64%), 49 to 60 months (53.33%), 61 to 72 months (55.56%) and ≥73 months (52.21%) (p < 0.0001). The proportion of patients with OI was significantly higher within 1 to 4 months (83.33%) as compared to 5 to 8 months (66.67%), 9 to 12 months (50%) after HAART initiation with p value of 0.011. This signifies that as the viral load decreases and CD4 count improves, the risk of OIs reduces significantly.

The highest prevalence was seen in patients categorized as WHO clinical stage IV and III (n = 135/135, 100%) and (n = 193/193, 100%), respectively, while the lowest prevalence was observed among clinical stage I patients (n = 1/342, 0.29%). Statistically, a significant association was depicted between the prevalence of OIs and WHO clinical stages II, III and IV.

The prevalence of OIs was found to be highest (n = 225/225, 100%) among HIV-infected patients with CD4 count <200/mm^3 followed by CD4 count 200-349/mm^3 and count 350-499/mm^3 with a prevalence of (n = 122/157, 77.71%) and (n = 30/127, 23.62%), respectively whereas, the prevalence was significantly lower in patients with CD4 count more than 500/mm^3 with a prevalence of only 5.41% (Fig. 1). The mean ± SD CD4 count/mm^3 in patients without OI was 600.37 ± 246.8, which was significantly higher than patients with OI (199.07 ± 116.88).

Good adherence to ART was seen in 503 (68.81%) patients, and poor adherence was present in 228 patients (31.19%). OIs were significantly higher in patients with poor ART adherence (99.12%) as compared to good adherence (32.41%).

A significant association was seen between low hemoglobin, protein (g/dL), albumin (g/dL) and OI. Mean ± SD protein (g/dL) and albumin (g/dL) in patients without OI was 7.51 ± 0.86, 3.9 ± 0.51, respectively, which was significantly higher as compared to patients with OI (7.29 ± 0.88 (p = 0.0006), 3.63 ± 0.6 (p < 0.0001)), respectively.

On univariate analysis, co-factors that had significant association with OIs were low-income education/socio-economic status, age, weight/BMI, hemoglobin, albumin, CD4 count, WHO staging, adherence to ART (Table 3).

On performing multivariate regression, CD4 count, low case adherence index score (poor adherence) and WHO staging (stage II, stage III and stage IV) were significant independent risk factors of OI after adjusting for confounding factors. Patients with low case adherence index score (poor adherence), WHO staging (stage II, stage III, stage IV) had significantly high risk of OI with adjusted odds ratio (OR) of 913.992 (21.282-39,252.803), 20.188.208 (678.408-60,0764.698), 26.264.032 (640.880-1076331.334), respectively. With the increase in CD4, risk of OI significantly decreased with adjusted OR of 0.989 (0.98-0.999) (Table 3).

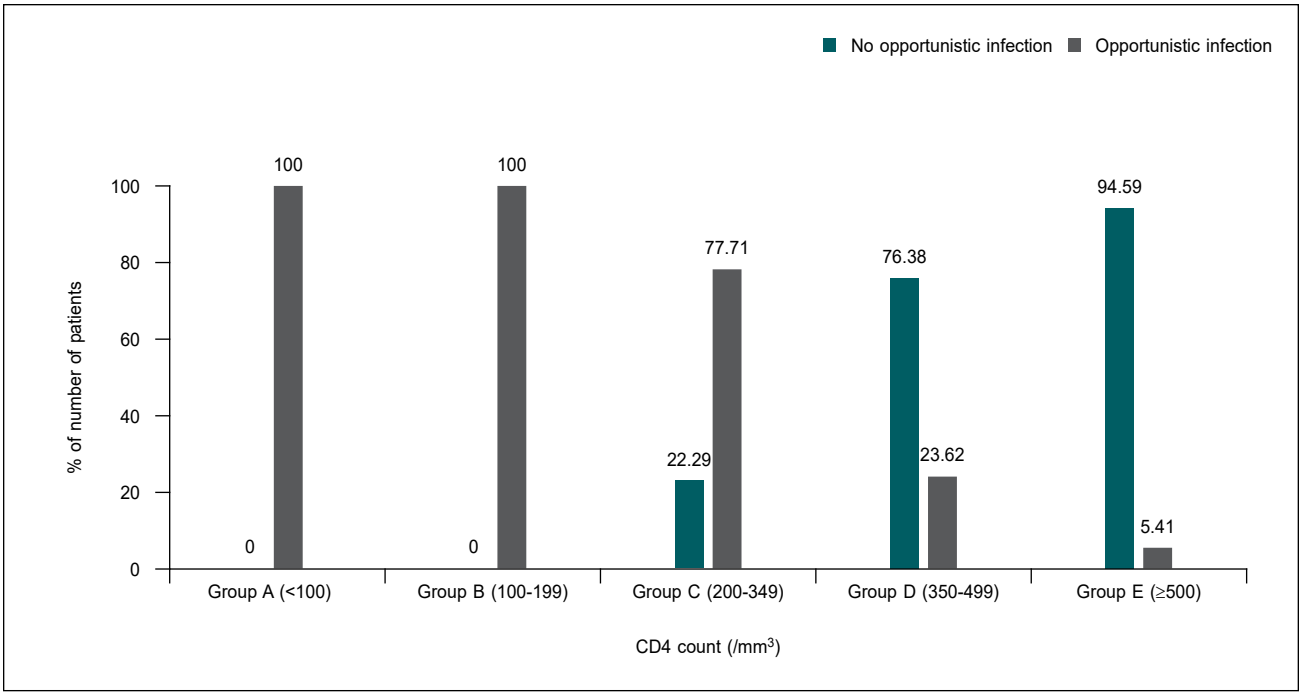

Figure 1. Association of CD4 count (/mm³) with opportunistic infection.

Table 3. Baseline Characteristics and Univariate and Multivariate Risk Factor Analysis for Opportunistic Infection

Characteristics	No OI (n = 342)	OI (n = 389)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P value	OR	P value
Age (years)						
Mean ± SD	36.18 ± 10.43	43.39 ± 10.73	1.066 (1.05-1.082)	<0.0001		
Income						
<2,000	43 (31.85%)	92 (68.15%)	1	<0.0001		
2,000-5,000	92 (39.66%)	140 (60.34%)	0.714 (0.457-1.117)			
5,001-20,000	161 (54.03%)	137 (45.97%)	0.4 (0.261-0.614)			
>20,000	46 (69.70%)	20 (30.30%)	0.207 (0.11-0.392)			
Socioeconomic status						
Lower	5 (9.80%)	46 (90.20%)	1	<0.0001		
Upper lower	48 (42.48%)	65 (57.52%)	0.16 (0.061-0.42)			
Lower middle	180 (47.75%)	197 (52.25%)	0.129 (0.052-0.323)			
Upper middle	70 (58.33%)	50 (41.67%)	0.085 (0.032-0.222)			
Upper	39 (55.71%)	31 (44.29%)	0.094 (0.034-0.259)			
Education						
Illiterate	57 (33.14%)	115 (66.86%)	1	<0.0001		
Primary school	129 (47.60%)	142 (52.40%)	0.548 (0.368-0.815)			
Secondary school	95 (45.67%)	113 (54.33%)	0.592 (0.389-0.899)			
College and above	61 (76.25%)	19 (23.75%)	0.158 (0.086-0.288)			
Weight (kg)						
Mean ± SD	58.7 ± 9.17	52.72 ± 7.21	0.913 (0.895-0.932)	<0.0001		

Table 3. Baseline Characteristics and Univariate and Multivariate Risk Factor Analysis for Opportunistic Infection

Characteristics	No OI (n = 342)	OI (n = 389)	Univariate analysis		Multivariate analysis	
			OR (95% CI)	P value	OR	P value
BMI (kg/m²)						
18.5-24.99 (Normal)	285 (55.77%)	226 (44.23%)	1	<0.0001		
<18.5 (Underweight)	31 (16.06%)	162 (83.94%)	0.15 (0.101- 0.234)			
25-29.99 (Overweight)	25 (96.15%)	1 (3.85%)	0.01 (0.002-0.064)			
≥30 (Obese)	1 (100%)	0 (0%)	0.06 (0.001-6.069)			
WHO clinical staging						
I	341 (99.71%)	1 (0.29%)	1	<0.0001	1.000	
II	1 (1.64%)	60 (98.36%)	9182.5 (929.2-90739.2)		20188.20	<0.0001
III	0 (0%)	193 (100%)	88107 (3545.5-2189448.1)		26264.03	<0.0001
IV	0 (0%)	135 (100%)	61697.667 (2472.9-1539321.7)		116.37	0.050
CD4 count (/mm³)						
Group A (<100)	0 (0%)	60 (100%)	1	<0.0001		
Group B (100-199)	0 (0%)	165 (100%)	2.73 (0.05-142.5)		0.98	0.02
Group C (200-349)	35 (22.29%)	122 (77.71%)	0.029 (0.002-0.48)			
Group D (350-499)	97 (76.38%)	30 (23.62%)	0.003 (0-0.04)			
Group E (≥500)	210 (94.59%)	12 (5.41%)	0 (0-0.009)			
Hemoglobin (g/dL)	12.51 ± 2.31	9.87 ± 1.83	0.56 (0.5-0.6)	<0.0001		
ART adherence						
Good adherence	340 (67.59%)	163 (32.41%)	1	<0.0001	-	-
Poor adherence	2 (0.88%)	226 (99.12%)	188.681 (53.3- 667.1)		913.992	0.0004
Albumin (g/dL)	3.9 ± 0.51	3.63 ± 0.6	0.412 (0.3-0.5)	<0.0001		

DISCUSSION

HIV is a major global public health issue, which has claimed more than 40 million lives so far with ongoing transmission globally. Despite the availability of ART, it is not a 100% curable disease. OIs and associated complications account for considerable morbidity and mortality in people living with HIV (PLHIV). The present study involving 731 patients on ART was carried out to elucidate current frequencies and spectrum of OIs infecting HIV seropositive adult patients in Haryana and to evaluate the associated risk factors of OIs.

The most common self-reported risk factor for the occurrence of HIV was the heterosexual route of transmission (94.53%), followed by unsafe sex with high-risk partners 6.16% and men who have sex with men (MSM) 3.01%. This can be explained by the mode of sexual activity practiced in the population. The study found that about 53.21% of HIV/AIDS patients on ART had one or more OIs compared to 46.79% who had no OI. This agrees with the prevalence of 48%, 46.7% and 58% documented by Mitiku et al, Sun et al and Balkhair et al, respectively.[7-9] However, prevalence in the present study is higher than various studies conducted in Nigeria and Southern India, which documented 22.4%, 35.7% and 8.3% prevalence, respectively.[10-12] This might be due to methodological differences in selecting study subjects. Moreover, South India's literacy rate is comparatively higher as compared to Haryana's; the present study found a significant association between education and OIs. This may explain the lower prevalence of OIs in the South. Also, it was lower as compared to the South Ethiopia study with a prevalence of 88.4%.[13] This could be due to differences in availability and duration of HAART, the difference in CD4 level, clinical staging and the difference in host immunity of study subjects.

Table 4. Comparison Between Different Studies Vis-a-Vis Present Study

Study	Prevalence of OIs	Most common OIs		
		Most common	2nd most common	3rd most common
Our study (2022)	53.21%	Tuberculosis (48.32%)	Candidiasis (25.7%)	Herpes zoster (13.6%)
International studies				
Mitiku et al[7] (2015)	48%	Tuberculosis (21.23%)	Herpes zoster (11.2%)	Oral candidiasis (9.5%)
Solomon et al[13] (2018)	88.4%	Tuberculosis (18%)	Community-acquired pneumonia (16.3%)	Oral candidiasis (15.3%)
Balkhair et al[9] (2012)	58%	*Pneumocystis jirovecii* pneumonia (25%)	Cryptococcal meningitis (22%)	CMV retinitis (17%)
Iroezindu et al[10] (2013)	22.4% (76/339)	Candidiasis (8.6%)	Tuberculosis (7.7%)	Dermatitis (5.6%)
Chanie et al (in children)[17] (2021)	5.53%	Pneumonia (35.63%)	Tuberculosis (28.74%)	Oral Candidiasis (10.34%)
Indian studies				
Vinod et al[15] (2018)	23.5%	Candidiasis (52%)	Tuberculosis (50%)	
Ghate et al[11] (2009)	35.7%	Tuberculosis (15.4%)	Oral Candidiasis (11.3%)	Herpes zoster (10.1%)
Srirangaraj et al[12] (2011)	8.3%	Tuberculosis (53.4%)	Oral Candidiasis (27.2%)	Herpes zoster (14.7%)
Singh et al[16] (2003)		Oral candidiasis (59%)	Tuberculosis (56%)	Cryptosporidiosis (47%)
Bariha et al[18] (2018)		Tuberculosis (51%)	Oral Candidiasis (43%)	Cryptosporidiosis (6.8%)
Saldanha et al[19] (2008)		Tuberculosis (45.3%)	Candidiasis (34.5%)	Cryptosporidiosis (17.5%)
Sharma[20] (2004)		Tuberculosis (71%)	Candidiasis (39.3%)	*Pneumocystis jirovecii* pneumonia (7.4%)

The present study revealed that TB (48.32% of total OIs) is the predominant OI identified, with a prevalence of 25.71% (188/731). Other studies done worldwide also had the same observation and TB was the most common OI found in PLHIV.[7,13,14] TB enhances the progression of HIV infection by inducing immune activation. Candidiasis and herpes zoster were the second and the third most prevalent OIs in the present study, at 13.8% (101/731) and 7.25% (53/731), respectively. However, in many other studies, Candidiasis was found to be the most common OI as summarized in Table 4.[7,9-13,15-20]

In the present study, the prevalence of cryptococcal meningitis was 2.05%, significantly higher than in the study conducted by Mitiku, with a prevalence of 0.28%.[7] This could be due to increasing diagnostic availability (radiological and serology) and high suspicion of disease. There were 63 co-infections of different OIs observed in the present study. Of these, 55 had 2 co-infections, 7 had 3 co-infections and 1 patient had 4 co-infections. Also, TB with candidiasis was the most common co-infection (32 cases), followed by TB with cryptosporidiosis (4 cases). This was similar to studies conducted in Eastern Ethiopia and Northwest Ethiopia.[7,21]

A higher proportion of TB and candidiasis co-infection in the present study may be explained by a higher prevalence of these two OIs among the study participants. Double and triple OIs have also been reported from studies in India and Nigeria.[5,10] Prevalence of OIs among patients with comorbid viral hepatitis was comparable. No statistically significant association was observed ($p = 0.053$). This could be due to the small sample size of hepatitis B virus (HBV) and hepatitis C virus (HCV) reactive patients. However, the highest prevalence of OIs was depicted among hepatitis B surface antigen (HBsAg) reactive patients (n = 14/18, 77.78%).

The present study was conducted among HIV patients taking ART for 1 month or more. The prevalence of OIs was significantly higher in patients on ART for <4 months (83.33%), and the prevalence decreased in the subsequent months. This was similar to various previous studies and may be because HAART improves patient's CD4 count and therefore the prevalence of OIs decreases overtime.[22,23] HIV-associated OIs and other related infections continue to occur in HIV-positive patients, but since the introduction of HAART, most infections occur at rates that are substantially lower than those seen in the pre-HAART era.

WHO clinical stage IV and III showed highest prevalence while least prevalence was observed among clinical stage I patients. This was similar to study in Northwest Ethiopia.[21] In WHO stages II, III and IV, there is marked reduction in CD4 count, which may be the reason for the increased prevalence of OIs as in our study. The prevalence of OIs was highest (n = 225/225, 100%) among HIV-infected patients with CD4 count <200/mm^3. In contrast, the prevalence was significantly lower in patients with a CD4 count of >500/mm^3, with a prevalence of only 5.41%. Other studies from India have also reported a high risk of developing OIs such as TB, *Pneumocystis jirovecii* pneumonia and cryptococcal meningitis among patients with CD4 counts <200 cells/mm^3.[23] This finding appears accurate since CD4 cells play a central role in the activation of humoral and cellular immune response in the fight against infection. Hence, low CD4 count increases susceptibility to OIs.[21]

In the present study, OI was significantly higher in patients with BMI (kg/m^2) of <18.5 (underweight; 83.94%). BMI is an important indicator of nutritional status in patients with HIV infection. Emaciation is a common condition during the early period of HIV, and there is some evidence that higher BMI is associated with more robust CD4+ T-cell recovery in HAART-treated patients.[24] Li et al demonstrated that HIV-infected patients with higher BMI at pre-treatment exhibit better immune reconstitution overtime after HAART initiation.[25] Also, patients with body weight <52.72 ± 7.21 kg were more prone to develop OIs. This finding was similar to a study conducted by Inamdar et al.[14]

Opportunistic infections were significantly higher in patients with poor adherence to ART (99.12%). This was similar to the findings in the study conducted by Iroezindu et al.[10] Fonsah et al conducted a study where subjects with CD4 cell counts <200 cells/μL had a lower proportion of good adherence than subjects with CD4 cell counts ≥200 cells /μL.[26] Therefore, people with poor adherence have a low CD4 count that translates to an increased incidence of OIs. Poor adherence to ART also causes progression of HIV, decreased CD4 count and hence can result in more OIs as already discussed.

Significant association was seen between hemoglobin (g/dL) and patients with OI with mean ± SD of hemoglobin (g/dL) <9.87 ± 1.83 g/dL. This was similar to a study by Iroezindu et al.[10] Srikantia et al demonstrated that both the cell-mediated immune response and bactericidal capacity of leukocytes in children with hemoglobin levels below 10 g/dL were significantly depressed.[27]

Significant association was seen between protein, albumin and OIs. Studies in the past decade have suggested that low albumin levels in HIV-infected patients are associated with rapid progression to AIDS and may account for increased mortality. Studies have suggested baseline albumin levels to be a good predictor of survival in patients with low CD4 count.[28-30] This may be attributable to nutritional factors, enteropathy and acute phase reactant proteins. Hence, the National AIDS Control Organization (NACO) in India provides nutritional supplements to those HIV-infected cases inducted for ART and nutritional counseling for others as a part of a national policy.[31] In developing countries where many people live below the poverty line, serum albumin would be a useful surrogate test for predicting the severity of HIV infection and the clinical monitoring of response to ART.

There were some limitations of the present study. As a cross-sectional study, cause-effect relationships cannot be assessed. Therefore, the data on the natural history pattern of disease and survival of hospitalized patients with HIV/AIDS could not be established. The study's endpoint is restricted to the in-hospital period; hence, the full access to patient's follow-up clinical data after being discharged was not always available.

The present study shows TB as the commonest OI in overall population of PLHIVs in Haryana followed by candidiasis and herpes zoster. Baseline CD4 cell count <200 cells/mm^3, baseline WHO clinical stages III and IV and ART nonadherence were strongly associated with the prevalence of OIs. Lower income, education and socioeconomic status were also associated with a higher prevalence of OIs. Weight, BMI, albumin, hemoglobin level are strong predictors for the occurrence of OIs.

CONCLUSION

Presently, India has the third-largest population of HIV-infected individuals after South Africa and Nigeria. HIV patients are susceptible to a variety of OIs depending upon clinical status, WHO grading and CD4 count. It is noteworthy that OIs can have atypical presentations and multisystem involvement. Various factors like adherence to ART, socioeconomic and education status of patients can influence the occurrence and outcome of these deadly infections. Hence, there is a need for surveillance and a high degree of suspicion of these infections in HIV patients to ensure early diagnosis and intervention. Moreover, interventions need to be designed to promote easy and early access to HIV testing and early enrollment of HIV-infected individuals into ART services seeing that the use of ART was found to reduce the prevalence of

OIs by 4th month. Individuals who continue to have low CD4 cell counts while on ART should be aggressively evaluated for OIs and practical efforts to optimize their immunological recovery should be made.

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Carotid Plaque in Type 2 Diabetes Patients

Older type 2 diabetes patients and those with long diabetes duration, increased waist-to-hip ratio and high lipoprotein(a) [Lip(a)] levels have a higher likelihood of developing carotid atherosclerotic plaque, according to a study published in the *Journal of Translational Medicine*.[1]

In the study, a total of 949 hospitalized patients with type 2 diabetes were included. Carotid ultrasound was performed to identify the presence of carotid atherosclerotic plaque in these patients, and it was found that 531 patients had such plaques, while 418 did not. The participants were assessed for waist-to-hip ratio, blood glucose levels, liver and kidney function, blood lipid profile, islet function, among other relevant indicators to determine the risk factors that contribute to the development of carotid plaque and to evaluate the predictive significance of carotid plaques in patients with type 2 diabetes. It was observed that the carotid plaques were significantly more prevalent in male patients with type 2 diabetes. The prevalence of diabetic nephropathy and hypertension was also significantly higher in patients with carotid plaque compared to those without carotid plaque. Patients with carotid plaque were older and had long-standing diabetes than those without carotid plaque. They also had higher waist-to-hip ratio, elevated postprandial glucose, increased Lp(a), higher levels of carcinoembryonic antigen and lower estimated glomerular filtration rate (eGFR) compared to those without plaque.

Furthermore, age, waist-to-hip ratio, duration of diabetes, hypertension, male gender and Lp(a) were identified as independent risk factors. After adjustment for confounding variables, eGFR was not found to be a risk factor for carotid plaque. Age, waist-to-hip ratio, duration of diabetes and Lp(a) demonstrated higher area under the curve (AUC) values for predicting the presence of carotid artery plaque in this group of patients (AUC: 0.750, 0.640, 0.678, 0.552, respectively). By constructing the logit (P) value using the aforementioned risk factors, the area under the receiver operating characteristic (ROC) curve was calculated to be 0.816, indicating a relatively good predictive ability for the presence of carotid plaque in patients with type 2 diabetes.

Cardiovascular disease is a major cause of death in patients with type 2 diabetes. Carotid atherosclerosis has shown significant correlation with cardiovascular events in these patients. Hence, early prediction of these macrovascular complications is critical. In this study of type 2 diabetes patients, several risk factors have been identified as being significantly predictive of the risk of formation of carotid plaque. These factors can be evaluated clinically and include advanced age, waist-to-hip ratio, duration of diabetes, hypertension, male gender and Lp(a) levels. Identification of these risk factors and their collective assessment allows better prediction of likelihood of carotid plaque formation in these patients and devise strategies for its prevention and management.

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