# CLINICAL SPECTRUM OF OPPORTUNISTIC INFECTIONS IN HIV POSITIVE PATIENTS

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ABSTRACT: The human immunodeficiency virus (HIV) infection leading to Acquired Immunodeficiency Syndrome (AIDS) causes progressive decline in immunological response in people living with HIV/AIDS, making them susceptible to a variety opportunistic infections (OIs) which are responsible for morbidity and mortality. Therefore early diagnosis and management of opportunistic infections reduce the mortality and morbidity in HIV positive patients. **CONTEXT: AIMS:** To study the demographic variables; spectrum of opportunistic infections and its correlation with CD4 count in HIV patients. SETTING AND DESIGN: The study was conducted on 200 HIV patients either admitted to Sanjay Gandhi Memorial Hospital or attending ART Center, Shyam Shah Medical College, Rewa (M.P) from January 2013 to October 2014. METHODS AND MATERIAL: A detailed history was recorded with emphasis on personal history, high risk behavior, history of migration, mode of transmission of infection and complete thorough clinical examination was done. Data analysis was done by calculating P value using Chi Square test. **RESULTS:** Out of 200 HIV patients, most of them (88%) belonged to the age group 20-49 years, 66% were males and 34% were females. 45% were illiterates, 62% were from low socioeconomic class. Majority of patients were married (79%) and 72.2% had seropositive spouse. Unprotected sexual route was the most common (85%) mode of transmission; among which heterosexual route was the only mode of transmission. 59.4% of males contracted infection through unprotected sex with either commercial sex workers (44.8%) or multiple sex partners (14.6%). 61% of patients had history of emigration. Tuberculosis was the most common opportunistic infection (51%), followed by oral candidiasis 30% and chronic diarrhea (9%).Pulmonary Tuberculosis was the most common form of Tuberculosis (64.7%), followed by tubercular lymphadenopathy (15.7%). CONCLUSION: HIV/AIDS has no vaccine or cure, so prevention is the only way to decrease its burden in the society. Health education, safe sex, and creating awareness among the people are the main tools in preventing HIV transmission. Treating physicians should have knowledge of spectrum of opportunistic infection in HIV patients.

**KEYWORDS:** HIV, AIDS, Opportunistic infection, Tuberculosis.

**MESHTERMS:** AIDS, HIV, tuberculosis, opportunistic infections, HIV related.

**INTRODUCTION:** Human Immunodeficiency Virus (HIV) infection is a global pandemic, with cases reported from virtually every country.<sup>1</sup> According to World Health Organization (WHO), globally 35 million (32.8-38.8 million) people were living with HIV at end of 2013.<sup>2</sup> According to National AIDS Control Organization (NACO), estimated number of people living with HIV/AIDS in India is 2.09 million in 2011, with estimated adult prevalence of 0.27%, 86% of whom were in 15-49 years age group.<sup>3</sup> Opportunistic infection cause significant morbidity and mortality in people with HIV infection. The spectrum of OI of a particular locality should be known to prevent these infections by giving adequate prophylaxis.

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The antiretroviral therapy (ART) has reduced the incidence of OI among HIV infected individuals.<sup>4</sup> At present the initiation of prophylactic therapies against opportunistic pathogens is mainly based on the absolute CD4 count, as it is generally accepted as the best indicator of the immediate state of immunologic competence of the patient with HIV infection.<sup>5</sup>

**AIMS AND OBJECTIVES:** To study the demographic variables; spectrum of opportunistic infections and its correlation with CD4 count in HIV patients.

**SETTINGS AND DESIGN:** The study was conducted on 200 HIV patients either admitted to Sanjay Gandhi Memorial Hospital or attending ART Center, Shyam Shah Medical College, Rewa (M.P.) from January 2013 to October 2014.

The present study was cross sectional study comprising of 200 HIV patients selected, according to following inclusion criteria and exclusion criteria, from those who either admitted to SGMH or attending ART Center, SSMC, Rewa.

### **MATERIALS AND METHODS:**

**INCLUSION CRITERIA:** HIV patients, with > 18 years of age, admitted to the Medical wards/ seen in the outpatient department and ART Centre at SGMH during course of the study.

### **EXCLUSION CRITERIA:**

- 1. Patients with less than 18 years of age.
- 2. Patients who did not give consent.

A detailed history was recorded with emphasis on personal history, high risk behavior, history of migration, mode of transmission of infection and complete thorough clinical examination was done. All patients were subjected to routine investigations and CD4 count. CD4 count was done by using following formula.

CD4 count = Total leukocyte count x lymphocytes % X CD4%/100.

The clinical and microbiological diagnosis for Mycobacterium tuberculosis infection was diagnosed by detecting Acid fast bacillus (AFB) in smears, lymphocyte predominant body fluids, granulomas on biopsy, and chest x- ray. PCP was diagnosed by clinical features, chest x-ray findings, arterial blood gas analysis showing partial pressure of oxygen (pO2) less than 60mmHg and elevation of serum lactate dehydrogenase (LDH). Toxoplasmosis was diagnosed by computerised tomography (CT) scan of the brain and IgG Toxoplasma levels in serum. Fungal infections such as cryptococcosis was diagnosed by staining with Indian ink, cryptococcal antigen and by biopsy. The Candida infection was diagnosed clinically and potassium hydroxide (KOH) stain. Viral infections like Herpes Simplex and Herpes Zoster was diagnosed clinically and confirmed by Tzanck smear. CMV retinitis was diagnosed by opthalmologist. Data thus obtained was statistically analyzed.

#### **OBSERVATIONS AND RESULTS:**

Sl.	Sociodemographic	Μ	ale	Female		Total		%	
No.	Profile	No.	%	No.	%	No.		%	
		A	ge					•	
1	20-31years	60	30.0	24	12.0	84		42.0	
2	31-40 years	56	28.0	36	18.0	92		46.0	
3	41-50 years	12	6.0	6	3.0	18		9.0	
4	>50 years	4	2.0	2	1.0	6		3.0	
Educational Status									
1	Illiterate	52	39.4	38	55.9	90		45%	
2	Primary School	46	34.8	18	26.5	64		32%	
3	High School	24	18.2	12	17.6	36		18%	
4	Graduate	10	7.6	0	0	10		5%	
	Socio	econo	omic sta	atus					
1	Upper class	8	6.1	12	17.6	20		10	
2	Middle class	44	33.3	12	17.6	56		28	
3	Lower class	80	60.6	44	64.7	120		62	
	Ν	larita	l status	;					
1	Married	110	69.7	48	30.3	158		79	
2	Divorced/Separated	6	33.3	12	66.7	18		9	
3	Widower/Widows	10	55.6	8	44.4	18		9	
4	Unmarried	6	100	0	0	06		3	
		Occup	oation						
1	Farmers	58	43.9	2	2.9	60		30	
2	House Wife	0	0	60	88.3	60		30	
3	Driver	28	21.5	0	0	28		14	
4	Non-Agricultural Laborer	20	15.5	6	8.8	26		13	
5	Student	10	7.5	0	0	10		5	
6	Office job	10	7.5	0	0	0		5	
7	Unemployed	Unemployed 6 4.1 0 0 06		3					
	Н	1 <b>/0</b> Mi	gratior	1					
1	Present	92	75.4	30	24.6	122	1	61	
2	Absent	40	51.3	38	48.7	78		39	
	Table 1: Sociode	emogra	aphic pr	ofile o	of patie	nts			

Sl.	Mode of		Ma	ale	Fei	male	Total	
No.	Transmission		No.	%	No.	%	No.	%
1	Sexual	Homosexual	-	-	-	-	-	-
L	Sexual H	Heterosexual	116	87.8	54	79.4	170	85
2	Blood Transfusion		2	1.5	4	5.8	6	3
3	IV Drug A	IV Drug Abuser		4.5	0	0	6	3
4	Accidenta	Accidental Needle Pricking		0	0	0	0	0
5	Unknown		8	6.2	10	14.8	18	9
	Total		132	100	68	100	200	100
Т	Table 2: Distribution of Cases According to Mode of Transmission							

Sl.		Source of		ale	Fer	nale	Total	
No.	Infection		No.	%	No.	%	No.	%
1	Unsafe	Commercial Sex worker	52	44.8	00	00	52	30.6
T	Sex Multiple Sexual Partner		17	14.6	02	3.7	19	11.2
2	Married	Married spouse		17.3	50	92.6	70	41.1
3	Unrevea	aled	27	23.3	02	3.7	29	17.1
4	Total		116	100	54	100	170	100
Tab	Table 3: Distribution of Heterosexual Patients According to Source of Infectio							ection

Sl.	Spouse Status	N	lale	Fe	male	Total			
No.	spouse status	No	%	No	%	No	%		
1	Seropositive	83	65.8	57	83.8	140	72.2		
2	Seronegative	25	19.8	5	7.4	30	15.4		
3	Unknown	18	14.4	6	8.8	24	12.4		
	Total	126	100	68	100	194	100.0		
Table 4: Distribution of Cases According to HIV Status of Spouse									

Sl.				CD4 Cou	nt		Mean		
31. No.	Disease		51- 150	151- 250	251- 350	>350	CD4	То	otal
1	Tuberculosis	20	36	40	6	0	154	102	51%
2	Oral Candidiasis	6	26	20	8	0	112	60	30%
3	Chronic Diarrhea	0	12	6	0	0	114	18	9%
4	Pneumonia	0	8	4	0	0	146	12	6%
5	Herpes Zoster	0	0	4	0	0	204	4	2%
6	CMV Retinitis	2	0	0	0	0	40	2	1%
7	Pneumocystis jirovecii pneumonia(PCP)	0	2	0	0	0	77	2	1%

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The Relationship Between CD4 Count Level and Type of Tuberculosis										
1	Pulmonary TB (PTB)		20	26	16	4	0	120	66	64.7
	2 Extra Pulmonary	Pleural effusion	0	0	6	2	0	199	08	7.9
2		TB Lymphadenopathy	0	4	12	0	0	149	16	15.7
		TB Abdomen	0	2	4	0	0	204	06	5.8
		Meningitis	0	4	2	0	0	98	06	5.8
	Table 5: Frequency Distribution of Opportunistic Infection in Relation to CD4 count									

**DISCUSSION:** In present study, majority of patients (88%) were in the age group 21-40 years. The findings are comparable with study by Patel Yet al<sup>6</sup> who reported 94% of patients from the age group of 15-49 years. HIV being a sexually transmitted disease is more prevalent in reproductive age group (20-40 years). Any suffering of this population will not only adversely affect the family but also the national economy and development. So interventions should be targeted to this vulnerable age group to create awareness, in prevention of transmission of HIV disease. Males (66%) outnumbered females (34%) with male to female ratio of 1.9:1. The findings are in accordance with those of Pandey A et al<sup>7</sup> who reported 61.5% males and 38.5% females with male to female ratio 1.6:1. The male preponderance may be due to the fact that in the existing social milieu, females do not seek medical care fearing ostracism, social stigma, lack of awareness, gender bias and low accessibility to health care which decreases the number of females attending the HIV clinic. So the lower number of females in the study may not be the true representation of proportion of females in general population.

In the present study, a significant number of patients were illiterates (45%), followed by 32% who studied up to primary school, 18% patients were educated up to high school, while least number of patients were graduates (5%). These findings are similar to study by Baig Vaseem et al<sup>8</sup> who reported that 31% were illiterates, 28% were studied up to primary school and 25% had secondary schooling. In present study, female illiterates (59.9%) were more than male illiterates (39.4%), no females were graduates. Poor literacy among females may be associated with high rate of infection, because of low level of knowledge and awareness about risk factors and route of HIV transmission.

In the present study, maximum numbers of patients were from lower socioeconomic class (62%), followed by 28% patients from middle and least number of patients were from upper socioeconomic class (10%). In the present study, 90% of patients belonged to middle and lower socioeconomic class. The findings well correlated to study by Pandey S et al<sup>9</sup> who reported that 97.5% of patients were from low and middle socioeconomic strata. The people from low socioeconomic status are poor and illiterate, so they tend to migrate to larger cities in search of job opportunities where they are consequently exposed to the risk of contracting HIV disease.

In the present study, maximum numbers of patients were married (79%), followed by 9% who were divorced or separated, same number (9%) were widowers or widows and least number of patients were unmarried (3%). The findings are comparable to the study by Baig Vaseem et al<sup>8</sup> among whose subjects 75.5% were married, 15.5% were widows/widowers, 7% were unmarried and 4% were separated. Marriage reduces promiscuous activity of the individual and is protective if the partners practice monogamous relationship. Marriage may be protective if the partners know their serostatus before the marriage and protect each other thereafter.

In the present study, a significant number of patients had seropositive spouse (72.2%), while 15.4% patients had seronegative spouse while status of rest 12.4% patients' spouse was unknown. The findings are comparable to the study by JogeU et al<sup>10</sup> who reported that 62.94% patients had seropositive spouse and 17.29% had HIV seronegative spouse and status of rest (19.6%) was unknown.

In the present study, majority of females (83.8%) had seropositive spouse. It appears that, as males were more mobile and often migrate to larger cities for jobs and stay there longer, exposure to unsafe sex is more frequent in males. Therefore, husbands may be the source of infection for the female.

In the present study, a greater number of patients were laborers (43%), followed by house wives (30%), drivers (14%), students (5%), officers (5%) while 3% were unemployed. The findings are comparable to the study of Madakar SS etal<sup>11</sup> who reported that laborers (50%) were most common group affected, followed by house wives (20.8%) and drivers (13.5%). Among laborers, farmers (30%) were more than non-agricultural laborers (13%) because major population resides in rural area, where main occupation is agriculture. In present study majority (88.3%) of females were housewives, as females were not allowed to workout side because most of them were from low socioeconomic status and rural background. Among study group, 14% were drivers who often travel and indulge in unprotected sexual activity. In the present study, a significant number (61%) of patients had history of emigration and it was more common among males (75.4%) than females (24.6%). The findings are comparable to study by Pandey S et al<sup>9</sup> who reported that 55% of patients had history of emigration for work for extended periods of time takes migrants away from the social environment provided by their families and community. This can place them outside the usual normative constraints and thus they are more likely to engage in promiscuous activity.

In the present study, the predominant mode of transmission was unprotected heterosexual intercourse (85%), followed by unknown routes (9%), 3% through blood transfusion, while 3% through intravenous drug usage. The findings are comparable to the study of Umesh S. Joge et al<sup>10</sup> who reported that 94.39% of patients contracted HIV through the sexual intercourse, 2.99% through blood transfusion and 2.62% by unknown routes. As per exclusion criteria, children were not included in the study therefore maternal to child transmission was not observed. HIV infection is most commonly transmitted through the sexual contact. In the present study, heterosexual route was the only mode of transmission, none of patients had given history of homosexuality and reason could be the social taboos associated with practice of this risky behavior. Among the heterosexual group of patients, highest number of males (59.4%) contracted infection by having unprotected sex with either commercial sex worker (44.8%) or multiple sexual partners (14.6%), followed by 23.2% males who denied revealing their partner, while 17.2% males practiced monogamous sex with spouse.

Majority of females (92.6%) had monogamous relationship with spouse, while 7.8% females who denied revealing their partner and only 3.4% females contracted infection by having unprotected sex with multiple partners. No females gave history of contact with commercial sex worker. The findings are comparable to the study by Patel Yet al<sup>6</sup> who reported that 47.37% of males had unprotected sex with commercial worker, while 25% of males had multiple sexual partners and 23.68% of males gave history of monogamous relationship.

The study by Patel Yet al<sup>6</sup> also reported that 91.67% of females had monogamous relationship with spouse, while 8.33% of females had multiple sexual partners. The most of males had

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unprotected sex with either commercial worker or with multiple sexual partners. This exposed their spouse to risk of HIV infection even though she practice monogamy and they are silent suffers.

In present study, tuberculosis (51%) was the most common opportunistic infection, followed by oral candidiasis (30%), chronic diarrhea (9%), pneumonia (6%) and herpes zoster (2%). CMV retinitis and pneumocystis jirovecii pneumonia were least encountered infection each accounting for 1%.

In our study, 51% of patients had tuberculosis. This is comparable to studies of Goud GT et  $al^{12}$  (56%) and Chakraborty N et  $al^{13}$  (57%) who reported tuberculosis as most common opportunistic infection. Owing to the environmental conditions prevailing in India like malnutrition, poverty and overpopulation, the incidence of TB in the India is high as compared to other parts of the world. The incidence increases in patients with HIV infection, due to re-infection and relapses. In the present study, the mean CD4 count for tuberculosis was 154 cells/µl. This finding is comparable to the study of Goud GT et  $al^{12}$  who reported a mean CD4 count of 118cells/µl.

In the present study, oral candidiasis (30%) was the second most common opportunistic infection. This finding is in conformity with studies of Madkar SSet al<sup>11</sup> and Wadhwa Aet al<sup>14</sup> who reported candidiasis in 37.6% and 41.7% of patients respectively. The patients with oral candidiasis had a mean CD4 count of 112cells/µl while a significant number (43.3%) of patients had CD4 counts in the range of 51-150 cell/µl. The findings are comparable to the study by Goel R et al<sup>16</sup> who reported a mean CD4 count of 82cells/µl for oral candidiasis. Oral candidiasis commonly occurs below the CD4 count of 300cells/µl.

In the present study, chronic diarrhea was seen in 9% of patients. This finding is different from the study by Vinay K V et al<sup>16</sup> who reported diarrhea in 22% of patients. The majority of chronic diarrhea (66.67%) patients had CD4 count below 150cells/ $\mu$ l with a mean CD4 count of 114cell/ $\mu$ l. The findings are comparable to the study of Goel R et al<sup>15</sup> who reported mean CD4 count of 101cells/ $\mu$ l for diarrhea. The patients are exposed to causative organism very often because of poor living conditions and sanitations. So the importance of hygiene and hand washing should be emphasized to patients.

In the present study, 2% of patients had herpes zoster infection with a mean CD4 count of 204cells/ $\mu$ l. The findings are comparable to the study by Goud GT et al<sup>12</sup> who reported herpes zoster in 5% of patients. In the present study, pneumonia was seen in 6% of patients with a mean CD4 count of 146cells/ $\mu$ l. The findings are comparable to study by Vinay KV et al<sup>16</sup> who reported pneumonia in 16% of patients.

In the present study, pneumocystis jirovecii pneumonia was seen only in 1% of patients with a mean CD4 Count of 77cell/µl. This finding differs from study by Vinay KV et al<sup>16</sup> who reported pneumocystis jirovecii pneumonia in 16% of patients with a mean CD4 count of 79cells/µl. This difference may be due to the under diagnosis of pneumocystis jirovecii pneumonia because of lack of sophisticated diagnostic facilities and affordability of patients. Pneumocystis jirovecii pneumonia commonly occurs below the CD4 count of 200cells/µl. In present study, CMV retinitis was seen in only 1% of patients, all of them had CD4 count below 50cells/µl with a mean CD4 count of 40cells/µl. The findings are comparable to the study of Vinay KV et al<sup>16</sup> who reported CMV retinitis in 4% of patients with mean CD4 count of 52cells/µl. According to WHO the leading cause of blindness in HIV patients is CMV retinitis and it is seen only below the CD4 count of 50cells/µl. Therefore ophthalmic examination should be the part of routine check-up for any patient with CD4 count of less than 50cells/µl.

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In the present study, pulmonary tuberculosis (64.7%) was the most common form of tuberculosis, followed by TB lymphadenopathy (15.7%), and pleural effusion (7.9%). TB meningitis and Abdominal TB each accounted for 5.8%. The findings are comparable to the study by Deivanayagam et al<sup>17</sup> who reported pulmonary tuberculosis (83.9%) as most common form of tuberculosis, followed by TB lymphadenopathy (7%), pleural effusion (6%), pericardial disease (6%) and meningitis (6%). In the present study, pulmonary tuberculosis (PTB) was seen in 64.7% of patients with a mean CD4 count of 120cells/µl. The findings are comparable to study by Goel R et al<sup>15</sup> who reported pulmonary tuberculosis in 61.8% of patients with a mean CD4 count of 110cells/µl.

The majority of PTB patients (75%) had CD4 count below 200cells/ $\mu$ l. The findings are comparable to study of Vinay K V et al<sup>16</sup> who reported that 72% of PTB patients had CD4 count below 200cells/ $\mu$ l. Pulmonary tuberculosis can occur in wide range of CD4 count but more common below 200cells/ $\mu$ l. As background prevalence of tuberculosis is high in general population, any immunodeficiency state like HIV infection leads to reactivation of latent infection resulting in active disease.

In the present study, tubercular lymphadenopathy was the most common extra pulmonary tuberculosis (15.7%) with a mean CD4 count of 149cells/ $\mu$ l. The finding differs from the study by Goel Ret al<sup>15</sup> who reported extra pulmonary tuberculosis in 2% of patients with a mean CD4 count of 100cells/ $\mu$ l. In present study, the majority of patients with TB meningitis (66%) had CD4 counts in the range of 51-150 cell/ $\mu$ l and a mean CD4 count of 98cells/ $\mu$ l. The findings are comparable to study of Vinay K V et al<sup>16</sup> who reported that majority of patients with TB meningitis (80%) had CD4 count below 200cells/ $\mu$ l with a mean CD4 count of 114cells/ $\mu$ l.

In the present study, a significant number of patients with abdominal tuberculosis (66.7%) had CD4 count in the range of in range of 151-250 cells/ $\mu$ l and a mean CD4 count of 204cells/ $\mu$ l. The findings are comparable to study of Vinay K V et al<sup>16</sup> who reported that majority of patients with Abdominal tuberculosis (80%) had CD4 count below 200cells/ $\mu$ l with a mean CD4 count of 201cells/ $\mu$ l.

**CONCLUSIONS:** Most of HIV positive patients are from sexually active group and were more often illiterate, having extra martial and multiple sexual partners. Until a vaccine or cure for AIDS is found, the only means at present available is health education to enable people to make life saving choices avoiding multiple sexual relation and use of Candom. To reduce mortality and morbidity due to opportunistic infection, one should know its spectrum and range of CD4 count at which it occurs.

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