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Profile of Opportunistic Infections Among HIV Patients on ART Attending at Tertiary Health Care Center

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ABSTRACT

Opportunistic infections (OIs) are a significant cause of morbidity and mortality among people living with HIV/AIDS (PLWHA) due to their compromised immune systems. The aim of the present study was to assess the clinical profile of opportunistic infections and malignancies in HIV patients receiving antiretroviral therapy (ART) and to examine the correlation between CD4 count and disease severity in these patients. A cross-sectional study was conducted at a tertiary care center in Maharashtra, India. The study included 296 HIV-positive patients on ART who were more than 12 years old and provided written consent. Exclusion criteria were immuno compromised individuals due to chronic illnesses or immunosuppressive medications. Data collection involved clinical examination, laboratory tests (CD4 counts, hemoglobin, ESR, etc.) and diagnostic evaluations (X-rays, FNAC, etc.). Males accounted for 76% of the study population. The most affected age group was 30-39 years (59%). Daily wage workers (51%) and illiterate patients (50%) were most commonly affected. Heterosexuality (97%) was the most common mode of transmission. Most common presentation was weight loss (80%), fever (77%) and loss of appetite (68%) which further leads to cachexic and emaciated built (80%). Tuberculosis (75%) was the most common OI, followed by candidiasis (23%). Pulmonary tuberculosis was the leading respiratory OI (52%) and pneumonia occurred in 81 cases. CD4 counts below 200 cells/µL were observed in 65% of cases. Candidiasis was the cause of dysphagia in all cases. Malignancies were observed in 17% of cases, with cervical cancer being the most common (32%). Mortality was more common in patients with CD4 count less than 200/microL. Opportunistic infections and lower CD4 counts are strongly associated with disease severity and mortality in HIV patients, highlighting the need for regular follow-up and adherence to ART.

OPEN ACCESS

Key Words
HIV, opportunistic infections, CD4 count, antiretroviral therapy, tuberculosis, malignancies, immunosuppression

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INTRODUCTION

Opportunistic infections (OIs) are the most common complication of Human immunodeficiency virus (HIV) infection causing significant morbidity and mortality in people with HIV infection[1]. opportunistic infections are still the only primary cause of HIV infection related illness and death[2]. Studies reveal that opportunistic infections account for around 90% of HIV-related morbidity and mortality, with opportunistic malignancies accounting for 7% and other causes for 3%[3]. The WHO clinical staging system (2007) categorizes opportunistic infections in HIV patients into four stages based on severity. The severity depends on immune function, pathogen virulence and exposure conditions. Severe infections are associated with a poor prognosis. Identifying the pathogens causing opportunistic infections is critical for effective treatment of HIV-positive individuals. Awareness of the spectrum of opportunistic infections in a particular region aids in the implementation of appropriate prophylactic measures. The prevalence of specific opportunistic infections varies by country and region. For example, tuberculosis is common among HIV-positive individuals in Bangladesh, Guatemala and sub-Saharan Africa[4,5], while Pneumocystis carinii pneumonia is prevalent in Malaysia, Hong Kong and China[6,7]. In Thailand, Penicillium marneffei is the most common opportunistic infection, whereas in western India, a study found an incidence of pulmonary tuberculosis of 5.7 per 100 person-years of follow-up. These variations highlight the importance of region-specific preventive strategies[8]. Antiretroviral therapy (ART) significantly reduces opportunistic infection-related mortality in HIV-positive individuals by boosting the immune system, inhibiting viral replication and decreasing the incidence of infections. However, therapeutic failure remains a common cause of persistent opportunistic infections, reflected in lower CD4 T cell counts and higher HIV viral loads. Notably, some patients still develop opportunistic infections despite having high CD4 counts and viral suppression, indicating that factors beyond low CD4 counts and high viral loads also contribute to infection risk[9]. Numerous reports exist on the opportunistic infection pattern in HIV-positive patients across various regions of India. Hence the aim of the study was to study the clinical profile of opportunistic infections among HIV patients on ART attending at a tertiary care health center and to study the risk factors associated with the same.

MATERIALS AND METHODS

This cross-sectional study was conducted on 296 patients aged over 12 years who had documented HIV-positive status, opportunistic infections and were admitted to various medical wards and ART centers. Only those who provided written consent to participate were included in the study. Patients with opportunistic infections who were immuno compromised due to chronic illnesses such as diabetes, chronic liver disease, chronic kidney disease, autoimmune diseases, or connective tissue disorders, as well as individuals on immunosuppressive medications and patients under the age of 12 years were excluded from the study. Following a thorough explanation of the process, their consent was obtained and an HIV Elisa test was used to confirm their status. Elisa measures antibodies to all viral proteins and is regarded as a standard HIV screening test. The solid phase has a 98.6% specificity and a sensitivity of greater than 99.5%. The test was regarded as positive in titers of 5:1 and negative in titers of 3:1. It is determined that the test is indeterminate between 3:1 and 5:1. Every patient completed a series of questionnaires and a thorough clinical examination in accordance with the proforma. A probable diagnosis of opportunistic infections was maintained based on clinical suspicion, and numerous laboratory tests were conducted to corroborate the diagnosis. Investigations that were carried out includes the hemoglobin level, ESR level, peripheral smear evaluation and total and differential leucocytes count, CD4 counts, LFT, RFT, Blood sugar. In the pathology department, TLC, DLC and ESR were performed on a Coulter counter and Westergren's ESR tube, respectively. In the microbiology department, CD 4 counts were performed using a Beckton and Dickinson FACS caliber flowcytometer. Additionally, serum tests for viruses such as the CMV and toxoplasma were conducted. Additional bodily fluid samples were tested, such as sputum for gram stain, ZN stain, Giemsa stain, silver methanamine and culture sensitivity. Under a microscope, helminthic eggs, cysts, protozoa, trophozoites, pus cells and fungal elements were checked for in the stool. CSF samples were examined using microscopy for total and differential counts, as well as for ZN staining, India ink preparation and culture on a variety of medium, including Mc Conkeys' media, blood agar and chocolate agar. Pleural fluid and when necessary, ascitic fluid were other fluids that were studied. In accordance with the requirements of the clinical presentation, additional supportive investigations included FNAC from lymph nodes, USG abdomen and thorax, CT head and X-ray chest (Table 1). The following list of supportive studies was utilized to confirm the diagnosis of opportunistic infections when combined with the clinical profile:

RESULTS AND DISCUSSIONS

Males accounted for 76% of the study population. The most affected age group was 30-39 years (59%). Daily wage workers (51%) and illiterate patients (50%) were most commonly affected. Maximum number of HIV positivity with opportunistic infections were seen in

Table 1: Diagnosis of Opportunistic Infections when Combined with the Clinical Profile

Opportunistic infections	Supportive investigations
Pulmonary TB	ESR, Montoux, sputum for AFB, X ray chest.
Tuberculous adenitis	ESR, Montoux, sputum for AFB, X ray chest, FNAC from lymph nodes
Tuberculous meningitis	ESR, Montoux, sputum for AFB, X-ray chest, CT head, in presence of evidence of tuberculosis elsewhere in body
Cryptococcal meningitis	CT head, CSF for India ink preparation, Negative stain (Nigrosine carbol fuschin stain)
Cryptosporidiosis, Microspora, Isospora, Strongyloids	Stool examination and special staining (modified ZN stain /Kinyoun stain), wet mount /saline mount or Lugol's iodine mount for helminthic eggs
Toxoplasma	CT head, IgM capture Elisa
Cytomegalo virus	Ophthalmoscopy
Herpes simplex, Herpes zoster, molluscum	Clinical
Candidiasis	Oropharyngeal swab for KOH mounting to
Contagiosum	see pseudohyphae, upper GI endoscopy
Pneumocystis carinii	X ray chest, sputum for Giemsa stain or Silver methanamine stain
Progressive multifocal leukoencephalopathy	MRI /CT brain

Table 2: Socio-Demographic Data of Patients

Age group and Marital status		No of cases	Percentage
Age group (years)	12-29	58	19.59
	30-39	174	58.78
	40-49	44	14.86
	50-59	15	5.06
	>60	05	1.68
Gender	Male	225	76.0
	Female	71	23.98
Occupation	Daily wage worker	152	51.0
	Service men	54	18.0
	Drivers	30	11.0
	Businessmen	28	9.0
	CSWs	23	8.0
	School children	09	3.0
Level of education	<10th standard	148	50.0
	10th-12th standard	104	35.0
	Higher education	44	15.0
Marital status	Married	198	66.89
	Single	65	21.95
	Separated	33	11.14
Addiction history	Multiple addictions	100	34.0
	Alcohol	59	20.0
	Tobacco (smoking /chewing)	42	14.0
	Ganja and Afeem	18	6.0
Status of Sexual partners	Multiple	177	59.79
	Single	41	13.85
	None	78	26.35

Table 3: Clinical Symptomatology and DGeneral Examination Findings

Symptoms and general examination findings		No of cases	Percentage
Clinical symptomatology	Weight loss	237	80.0
	Fever	228	77.0
	Loss of appetite	201	68.0
	Dyspnoea	194	66.0
	Fatigue	186	63.0
	Cough	133	45.0
	Vomiting	104	35.0
	Headache	76	26.0
	Dysphagia	68	23.0
	Altered sensorium	65	22.0
	Convulsions	60	20.0
	Abdominal pain	53	18.0
	Diarrhoea	44	15.0
	Chest pain	34	11.0
	Abdominal distension	29	10.0
	Blurring of vision	26	9.0
	Recurrent aphthous ulcers	24	8.0
	Vaginitis with discharge	19	6.0
	Dermatological manifestations	221	75.0
General Examination	Emaciated built	237	80.0
Findings	Tachycardia	231	78.0
	Lymphadenopathy	207	70.0
	Pallor	204	69.0
	Tachypnoea	103	35.0
	Oral candidiasis	59	20.0
	Cyanosis	60	20.0
	Edema	31	10.0
	Clubbing	30	10.0
	Apthous ulcer	21	7.0
	Palpable lump	20	7.0
	Icterus	19	6.0
	Ascitis	12	4.0

Table 4: Opportunistic Infections and Malignancies in HIV Positive Pts with CD4 Count

Opportunistic infection	No. of cases	Percentage	Mean CD4 count	Mortality
Pulmonary Koch's	115	39.0	194	13
Candidiasis	69	23.0	177	00
Tinea	38	13.0	321	00
Abdo Koch's with lymphadenopathy	31	10.0	175	02
TB Meningitis	30	10.0	179	08
Scabies	27	9.0	236	00
TB Lymphadenitis	25	8.0	191	00
Cryptosporidiosis	24	8.0	96	00
Seborrheic dermatitis	24	8.0	72	00
Herpes simplex (Labialis and genitals)	22	7.0	187	00
TB pleural effusion	20	7.0	214	00
Herpes Zoster	18	6.0	416	00
Pneumocystis pneumonia	13	4.0	183	02
Viral meningitis	12	4.0	239	0100
Warts	11	4.0	368	00
Isosporosis	10	3.0	158	00
Strongyloidosis	09	3.0	183	00
Papules	09	3.0	341	00
Liver abscess	09	3.0	156	00
Bacterial and atypical pneumonia	08	3.0	372	01
Cryptococcal meningitis	05	2.0	81	02
Bacterial meningitis	05	2.0	262	01
Tuberculoma	03	1.0	229	00
Vesicles	03	1.0	376	00
Progressive multifocal leukoencephalopathy	02	1.0	77	00
Splenic microabscess	02	1.0	148	00
Microsporosis	01	0.3	89	00

Table 5: Malignancies with Mean CD4 Count and Mortality

Malignancy	No. of cases	Percentage	Mean CD4 count (per microL)	Mortality
Cervical cancer	16	32.0	151	08
Non-Hodgkins lymphoma	12	24.0	147	07
Hodgkins's lymphoma	05	10.0	237	01
Oral SCC	05	10.0	273	00
Multiple myeloma	02	4.0	266	00
Breast cancer	02	4.0	354	00
Colon cancer	01	2.0	232	01
Leomyoma	01	2.0	280	00
Carcinoma pancreas	01	2.0	258	01
Posterior pharyngeal wall carcinoma	01	2.0	216	00
Kaposi sarcoma	01	2.0	134	00
Tonsillar SCC	01	2.0	209	00
SCC of stomach	01	2.0	217	01
SCC of lung	01	2.0	146	01
Total	50	100.0	-	20

Squamous cell carcinoma- SCC

the married group (67%). Multiple addictions were seen in most of the cases (33.7%). Multiple sexual partners were seen in 59% of cases and single sexual partner was seen in 14% cases. But it was found that opportunistic infections were also common among those who do not have any sexual partner (27% cases), (Table 2).

The heterosexual mode of transfer was the most prevalent form of transmission (287., 97%) followed by homosexuals (3., 1%), Needle prick (3., 1%) and materno-fetal (3., 1%). Weight loss (80%) was the most common symptom followed by Fever (77%) and loss of appetite (68%). Dermatological manifestations (more cases during summer season) 75% of cases. Fever was seen in 228 cases (77%). Majority of the patients had fever more to 1 month (69%) and 8% pts had fever <1 month. Weight loss was seen in 237 cases (80%). 50% of them had weight loss more than 10% of their body weight and 30% have weight loss less than 10%, while 20% pts have no weight loss. However, on general examination most common finding was emaciated built was seen in 237 cases (80%) followed by tachycardia 231 (78%), pallor in 204 cases (69%), fever in 228 cases (77%) and lymphadenopathy in 207 cases (70%), (Table 3).

Majority of the patients had their CD4 T cells in the range of <200/ microliter (65%), 35% of cases had their CD4 T cells in the range of 200-499/ microlitre (Fig.1). Mortality was seen in 50 cases of which 30 cases were of opportunistic infections and 20 of opportunistic malignancies. Mortality was maximum among cases with CD4 count less than 200/microlitre., 43 cases (27 cases of opportunistic infections and 16 cases of malignancies) and less with CD4 count between 200-500 /microlitre., 7 cases (3 cases of opportunistic infections and 4 cases of malignancies).

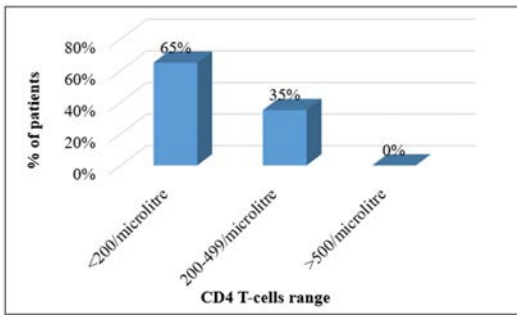

Fig. 1: CD4 T-Cells Count Variability

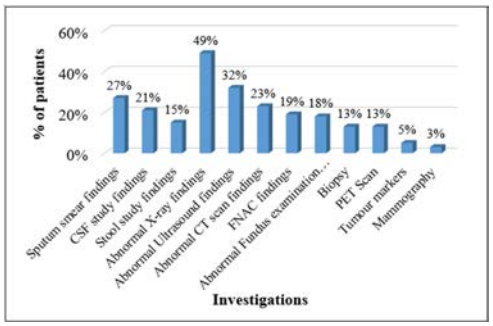

Fig. 3: Investigations

The most common opportunistic infection was Pulmonary tuberculosis 115 cases, followed by candidiasis 69 cases, Tinea 38 cases, abdo Koch's 31 cases and TB meningitis 30 cases. Mortality was seen in 30 cases with was highest among patients with CD4 count less than 200/microL. Deaths were more in Tuberculosis cases, either Pulmonary or Extrapulmonary. TB meningitis contract more deaths than other Extra pulmonary Tuberculosis manifestations, (Table 4). Respiratory system affected more in HIV associated opportunistic infections (46%) followed by Abdominal system (25%), CNS (23%), CVS (4%) and dermatological manifestations present in 75% of the subjects, (Fig. 2).

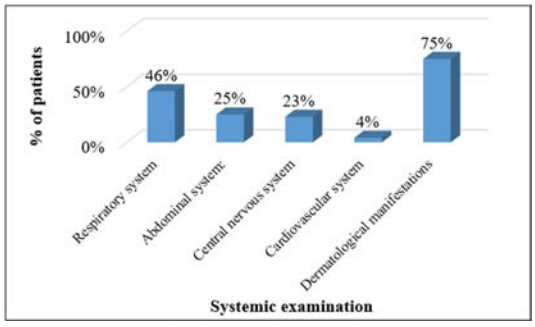

Fig. 2: Systemic Examination Findings

In this study, 27% of cases were sputum positive, with 74% diagnosed with pulmonary Koch's, 16% with Pneumocystis pneumonia and 10% with bacterial/ atypical pneumonia. Stool positivity was observed in 15% of cases, identifying cryptosporidium cysts (55%), isospora cysts (23%), strongyloides larvae (20%) and microsporidia (1%). CSF study positivity was found in 21% of cases, with TB meningitis in 48%, bacterial meningitis in 24%, viral meningitis in 20% and cryptococcal meningitis in 8%. Abnormal X-ray findings occurred in 59% of cases, with consolidation (56%), fibrosis (14%) and pleural effusion (14%) being most common. CT scans were abnormal in 23%, primarily showing TB meningitis (45%). Ultrasound abnormalities were present in 32%, most commonly abdominal Koch's (33%) and pleural effusion (21%), (Fig. 3).

Pulmonary tuberculosis was present in 52% of cases, while extrapulmonary tuberculosis was seen in 48%, with 92 cases showing a combination of both forms. The most common extrapulmonary manifestations included abdominal Koch's (25%), TB meningitis (23%), TB lymphadenitis (20%), tubercular pleural effusion (16%), TB ascites (10%) and TB pericardial effusion (6%). Among HIV patients, malignancies included cervical cancer (32%), non-Hodgkin lymphoma (24%), Hodgkin lymphoma (10%), oral squamous cell carcinoma (10%), multiple myeloma (4%), breast cancer (4%), colon cancer (2%), leiomyoma (2%), pancreatic carcinoma (2%), post-pharyngeal carcinoma (2%), Kaposi sarcoma (2%), tonsillar carcinoma (2%), squamous cell carcinoma of the stomach (2%) and squamous cell carcinoma of the lung (2%). Mortality occurred in 20 out of 50 malignancy cases, primarily in cervical carcinoma (8 cases) and non-Hodgkin lymphoma (7 cases), with the highest mortality rates observed in patients with a CD4 count below 200 cells/microL, (Table 5).

In the present study, the demographic profile of patients with HIV revealed a major prevalence in the 30-39 age group (59%), aligning with findings from Garcia[10] who reported a mean age of 33.2 years, with 88% under 55 years. This trend reflects the higher vulnerability of sexually active individuals in this age bracket. The predominance of male patients (76%) corroborates similar findings by Sirohi[11] and Ngulani[12], suggesting a consistent gender disparity in HIV infection rates. The majority of patients were married (67%), followed by single individuals (22%), with the least being separated (11%) which is comparable with the study done by Naik[13]. In current study, daily wage workers made up 51% of cases, followed by service workers (18%), drivers (10%), businessmen (9%) and casual sex workers (8%). These occupations are typically at higher risk of unprotected sex and HIV infection, as also noted by Malta[14] and Shilpa[15]. The heterosexual exposure was the most common mode of transmission (97%), while a small portion of cases were attributed to homosexual

transmission (1%), needle prick (1%), materno-fetal transmission (1%) and none to blood transfusion as similar to Patel[16]. study. The majority of patients had an education level below the 10th standard (50%) and only 15% had completed higher education which is correlated with the study conducted by Naik[13]. In the present study, the most common symptom was weight loss (80%), followed by fever (77%), loss of appetite (68%), fatigue (63%) and dyspnea (66%). Similarly, Shilpa[15], Patel[16] and Korzeniewska-Kosela[17] reported weight loss, fever and diarrhea as common presentations. Additionally, multiple addictions were seen in 34% of our cases, with alcohol addiction in 20%, while 26% had no addictions. Malta[14] noted that alcohol and drug use among truckers influenced unsafe sex practices. Tuberculosis was the most common opportunistic infection (75%), followed by candidiasis (23%). Other infections included cryptosporidiasis (8%), scabies (9%), herpes simplex (7%), herpes zoster (6%), bacterial/atypical pneumonia (3%) and pneumocystis (2%). These findings are consistent with studies by Sharma[1] and Patel[16] where tuberculosis and candidiasis were predominant opportunistic infections. In current study, pulmonary tuberculosis was found in 52% of cases, while extra-pulmonary tuberculosis was observed in 48%. Among extra-pulmonary manifestations, abdominal tuberculosis was seen in 25%, TB meningitis in 23% and TB lymphadenitis in 20%. TB pleural effusion and ascites were present in 16% and 10% of cases, respectively. Sputum smear positivity was noted in 37% of cases, with 74% of those being pulmonary tuberculosis. These aligns with findings from Garcia Ordonez[10] and Robles[18] study. Additionally, diarrhea was reported in 15% of patients, with Cryptosporidium (55%) being the most common pathogen, consistent with studies by César Cárcamo[19] and Guk[20] that identified Cryptosporidium as a prevalent opportunistic pathogen in HIV patients. In present study, altered sensorium was observed in 65 cases, while convulsions were noted in 60 cases. Focal neurological deficits were present in 5 cases, including 2 cases of PML. Meningitis was diagnosed in 62 cases: tuberculosis in 30 (48%), bacterial in 15 (24%), viral in 12 (19%) and cryptococcal in 5 (8%). Similar findings are reported in Satishchandra[21]. Central nervous system manifestations were seen in 23% of our cases, compared to 12% reported by Shilpa[15]. The respiratory system manifestations were observed in 166 cases (56%). Pneumonia was seen in 81 cases (68%), with 60 cases attributed to tuberculosis (81%), 13 to Pneumocystis (12%) and 8 to bacterial/atypical pneumonia (7%). Pleural effusion was present in 20 cases (12%), cavities in 12 cases (7%) and fibrosis in 21 cases (13%). Miliary shadows were noted in 2 cases, all of which were tuberculosis. X-ray findings were positive in 145 cases (49%), showing consolidation in 81 (56%), pleural effusion in 20 (14%), pericardial effusion in 8 (6%), fibrosis in 21 (14%), cavities in 12 (8%) and a mediastinal mass in 1 case. These findings are correlated with the study done by Sirohi[11] and Shilpa[15]. In our study, we correlated CD4 lymphocyte counts with various opportunistic infections. A majority of cases (192, or 65%) presented with CD4 counts <200/microL, while 35% (104 cases) had counts between 200-499/microL. Specific counts included tuberculosis at 194/microL, cryptococcosis at 81/microL, cryptosporidiasis at 96/microL, pneumocystis at 183/microL and candidiasis at 177/ microL. Korzeniewska-Kosela[17] reported a mean CD4 count of 200/microL in tuberculosis patients, while Patel[16] found that 93% of cases had CD4 counts <200/mm³, consistent with our findings. Infections like cryptococcosis and pneumocystis carinii were linked to much lower counts, with pneumocystis occurring at a CD4 count of 6 cells/mm³. Other studies[13-15] also indicated significant proportions of patients with CD4 counts <200/microL, highlighting the strong correlation between low CD4 counts and opportunistic infections. However, in our study, 35% of patients with opportunistic infections had CD4+counts between 200-499/microL, while 65% had counts below 200/microL, with no patients presenting counts above 500/microL. This indicates that the risk of developing opportunistic infections (OIs) increases as CD4 counts decrease, consistent with findings from both developed[22] and developing countries[5]. For example, a study in Brazil reported a 51% incidence of OIs per year in patients with CD4 counts below 100/mm³ on either monotherapy or dual therapy antiretroviral regimens[22]. Similarly, a study in southern India found an incidence of OIs of up to 10 per 100 person-years of follow-up before the initiation of ART[5]. In the present study, cervical cancer was the most common malignancy, followed by non-Hodgkin lymphoma (NHL). This finding aligns with Phatak[23], who also identified NHL as the most prevalent cancer. Additionally, 65% of our patients had CD4 counts less than 200, suggesting that immunodeficiency may trigger malignancy development, a finding echoed by Prosperi[24]. Notably, mortality was observed in 22 out of 50 malignancy cases, with cervical carcinoma (8 cases) and NHL (7 cases) contributing most to mortality, which was more common in patients with CD4 counts below 200/microL. This study faced several limitations that may have impacted the findings. Firstly, many patients were reluctant to undergo special investigations due to financial constraints, limiting the comprehensiveness of the data collected.

Secondly, social stigma associated with HIV led to a significant number of patients concealing their HIV status from relatives, colleagues and healthcare providers.

CONCLUSION

The present study highlights the significant impact of opportunistic infections on morbidity and mortality among HIV patients, particularly affecting males and younger, sexually active individuals. Daily wage workers and illiterate individuals are disproportionately impacted, indicating that socioeconomic and educational factors contribute to HIV vulnerability. Contrary to previous beliefs, married individuals now show a higher prevalence of HIV, possibly due to unsatisfied marriages and social media influences. Patients with substance abuse issues are at increased risk, with heterosexuality being the primary mode of transmission in India. Common clinical manifestations include weight loss, fever and loss of appetite, particularly in patients with CD4 counts below 200/microL. Cervical carcinoma is the most prevalent malignancy with the highest mortality rates, while pulmonary tuberculosis, often presenting as pneumonia, poses a significant risk, especially in those with low CD4 counts. The direct correlation between CD4 count and the severity of opportunistic infections underscores the importance of regular follow-up and adherence to antiretroviral therapy (ART). Despite advances in treatment, the stigma surrounding HIV remains, necessitating ongoing community education and support.

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