Original Research Article

Spectrums of opportunistic infections in HIV-infected patients at tertiary care hospital

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Abstract

Background: Literature on the spectrum of opportunistic disease in human immunodeficiency virus (HIV)-infected patients from developing countries is sparse. HIV-related opportunistic infections (OIs) continued to cause morbidity and mortality in HIV-infected individuals.

Objectives: The objective for this study was to elucidate the prevalence and spectrums of OIs in HIV-infected patients in the Gandhinagar Civil Hospital.

Material and methods: The evaluation of the prevalence and spectrums of OIs was conducted by using the clinical data of 834 HIV-infected patients in the Gandhinagar Civil hospital from November 2012 to December 2013 those who were attended physician OPD for OIs.

Results: The prevalence and spectrums of OIs varied contingent on sex, age, CD4 levels and treatment with ART. We found that tuberculosis was most common OI with prevalence being 20.50%, followed by Pneumocystis pneumonia (PCP) (5.16%) mycobacterium avium complex (MAC) (1.80%), candidiasis (1.56%), cytomegalovirus (CMV) infection (0.24%), progressive multifocal leukoencephalopathy (PML) (0.12%). Males (31.85%) were more prone to get OIs than females (27.85%). Pulmonary OI infections were the most prevalent morbidity and mortality in patients in the AIDS stage including pulmonary tuberculosis (7.43%) and PCP (5.16%). Fungal OIs were one of most prevalent morbidity in patients in the AIDS stage, including oral candidiasis (1.79). EPTB (13.07%) was more common than PTB (7.43%). OI in AIDS is more common in 41 to 60 years

(32.93%) of age group. OI was more common in patients with CD4 count from 51-100 (86.96%) followed by 101 to 150 (69.05%). OI was more common in patients who were not on ART (72.33%) than those on ART (27.67%).

Conclusion: The prevalence and spectrums of OIs, was discussed in this study. It would help to increase the awareness for physicians to make a diagnosis and empirical treatment sooner and plan good management strategies, especially in resource limited regions.

Key words

Opportunistic infections, HIV, Tertiary care hospital.

Introduction

The first case of human immunodeficiency virus/ acquired immunodeficiency syndrome (HIV/AIDS) in India was detected in 1986 in the state of Tamil Nadu [1] and since then the spread of HIV/AIDS across the nation has been relentless. Cases have been reported from all states and union territories of India. Though the majority of HIV-infected population lives in developing nations, there is a paucity of data on natural history, pattern of disease and survival of hospitalised patients with HIV/AIDS from these regions especially India. It is well established that manifestations of AIDS are influenced by factors such as endemic infections and malnutrition that are widely prevalent in these regions [2]. Conventional disease staging criteria, which were developed in western populations may not hold good in these settings [3]. Added to this, resource constraints prohibit evaluation and decision-making based on cost and labour-intensive methods such as CD4+ cell counts and viral RNA load estimation. Timely initiation of prophylaxis for opportunistic infections (OIs) and their prompt recognition and treatment are the only economically viable options [4]. In 2012, 35.3 million people were living with HIV/AIDS globally [5], HIV led to immunosuppression that allowed OIs to cause diseases in HIV-infected patients. OIs led to frequent morbidity and mortality among HIV-infected individuals, and it mostly depended on sex, age, CD4 levels and treatment with ART. Despite the availability of Antiretroviral Treatment through NACO in India [6], HIV-related clinical diseases including OIs continued to cause morbidity and mortality in HIV-infected individuals. Some HIV-infected patients were not aware of HIV infection until OIs became the first indicator of their disease; some patients were aware of HIV infection but did not administer antiretroviral (ART) regimens due to skepticism some social factors; and some HIV-infected patients were taking ART medications but experiencing virological and immunological failure due to poor adherence. HIV-related OIs increased morbidity and mortality, which shortened the lifespan of HIV-infected population and increased social-economic burdens on India. The clinico-epidemiological spectrums of OIs were important to promote awareness of physicians to make a right diagnosis and empirical treatment sooner, in particular, in resource limiting regions. The objective for this study is to elucidate prevalence and spectrums of OIs in HIV-infected patients in Gandhinagar Civil Hospital.

Material and methods

Patient's selection

After taking permission with Ethical comity, Hospital superintendent as well as from AIDS Control Society, this retrospective observational study was carried out at the G.M.E.R.S. medical College, Gandhinagar, attached Civil Hospital. We reviewed a series of 834 HIV-infected patients, who were visiting to this Hospital between November, 2012 and December, 2013. The attended patients presented some symptoms presumed to be due to OIs, who needed evaluation and treatment of HIV-related diseases. Patients completed a face-to-face, paper-and-pencil questionnaire eliciting data on age,

gender, ethnicity, marital status, address, and transmission routes.

Diagnosis of OIs

Laboratory tests were performed for blood routine test, CD4 count liver and kidney functions, serum lipid panels and fasting plasma glucose. Blood, urine, stool, sputum, and even cerebrospinal fluid (CSF) were collected and used for culture and identification of species of pathogen depending on patients' symptoms and signs.

Pulmonary tuberculosis was confirmed by the isolation, culture and identification of mycobacterium tuberculosis, or positive acid-fast bacilli (AFB) in sputum samples. For patients with symptoms and signs of extra-pulmonary tuberculosis, pathological demonstration and AFB in samples of fine needle aspiration of lymph nodes and pleural fluid were required to be performed. The tuberculosis meningitis was diagnosed based on compatible systemic symptoms and signs, and cerebrospinal fluid (CSF) analysis indicated pleocytosis with mononuclear predominance, elevated protein and low glucose, and exclusion of cryptococcal meningitis.

The etiologic diagnosis of tuberculosis in HIV-infected patients was difficult, and some patients with negative samples underwent antibiotic treatment for 2 weeks so that bacterial infection could be cured, patients still having fever, cough and night sweat would underwent anti-tuberculosis treatment, tuberculosis was empirically diagnosed due to clinical improvement after empirical anti-tuberculosis treatment.

Oropharyngeal candidiasis was diagnosed based on its features with painless, creamy white, plaque-like lesions in tongue surface or oropharyngeal mucosa which can be scraped off with tongue depressor.

Pneumocystis pneumonia (PCP) was confirmed by compatible clinical symptoms such as subacute onset of progressive dyspnea, fever, non-productive cough and hypoxemia. In Pneumocystis jiroveci pneumonia (PCP) there was bilateral, diffuse interstitial infiltrates on chest radiograph or high-resolution CT, with hypoxaemia (PaO_2 <12 kPa) and sputum smears/cultures negative for aerobic bacteria and AFB and/or demonstration of Pneumocystis jiroveci in induced sputum. The etiologic diagnosis of PCP in HIV-infected patients sometimes was difficult, and some patients with compatible clinical symptoms and CT results but without positive BALF samples would underwent anti-PCP treatment, PCP was empirically diagnosed due to clinical improvement after empirical anti-PCP treatment. CMV retinitis was diagnosed according to recognition of characteristic retinal changes during an ophthalmoscopic examination.

Mycobacterium avium complex (MAC) disease was diagnosed based on isolation, culture and identification of MAC from culture of blood, focal infection sites and bone marrow. MAC infection should be suspected in patients with positive AFB but negative IGRA results who had poor response to anti-tuberculosis treatment. Due to lack of brain biopsy, Toxoplasmic encephalitis was empirically diagnosed by clinical symptoms and focal neurological abnormalities, identification of one or more mass lesions by CT scan or magnetic resonance imaging (MRI) of the brain, and seropositive anti-toxoplasma IgG. The data was subjected to statistical analysis using SPSS software package. Data was expressed as absolute numbers with or without percentages, as means with standard deviation or as medians with ranges. Frequency comparison was performed by chi-square test. A probability value less than 0.05 was considered to denote statistical significance.

Results

Total 834 patients with HIV positive status were included in the study. Five hundred eighteen (62.11%) patients were male and 316 (37.88%) were female with mean age was 35.45±13.54

years. We observed that OIs were more common in males (31.85%) than females (27.85%) but there was no clinical significant difference (p = 0.222) had been found for OIs with gender distribution (**Table - 1**). We observed that OIs were more common in 41 to 60 years age group (66.88%) with p value being 0.0003 suggesting it to be significant. (**Table - 2**)

Table - 1: Distribution of OIs according to gender.

Gender	No. of Patients		
	With OIs	Without OIs	Total
Male	165 (31.85)	353 (68.15)	518 (100.00)
Female	88 (27.85)	228 (62.15)	316 (100.00)
Total	253 (30.33)	581 (69.67)	834 (100.00)

χ^2: 1.4898; p value: 0.222

Table - 2: Distribution of OIs according to age.

Age group (years)	With OIs (%)	Without OIs (%)	Total (%)
0 to 20	23 (27.38)	84 (72.62)	107 (100)
21 to 40	119 (37.42)	318 (62.58)	437 (100)
41 to 60	105 (66.88)	157 (33.12)	262 (100)
61 to 80	6 (27.27)	22 (72.73)	28 (100)
Total (%)	253 (30.33)	581 (69.67)	834 (100)

χ^2: 17.337; p value: 0.0003

Spectrum of OIs

Tuberculosis is a systemic disease and it was the most common OI in this study. Tuberculosis was most common OI among 834 clinical records analyzed, and the prevalence rate was 20.50%. In total 7.43% of these patients were diagnosed with pulmonary tuberculosis while 13.07% of the patients had extra-pulmonary tuberculosis. Extra-pulmonary tuberculosis (13.07%) was having higher prevalence rather than pulmonary tuberculosis (7.43%). This was followed by PCP (5.16%), MAC (1.80%), candidiasis (1.56%), Diarrhea (0.84%), CMV (0.24%), Toxoplasmosis (0.12%) and PML (0.12%). (**Figure - 1**)

Prevalence of OIs related to CD4 count

We observed that OIs are more common if CD4 count was less than 250 (48.41%) as compared to patients having CD4 count greater than 250 (21.42%). (**Figure - 2**)

Effect of anti-retroviral treatment

The prevalence of OIs decreased significantly (p = 0.002) in those who were on Anti-Retroviral Therapy (27.81%) as compared to those who were not on anti-retroviral therapy (Pre ART) (39.78%). (**Table - 3**)

Discussion

In India, HIV-infected patients were treated with antiretroviral therapy based on guideline by NACO, which was administered through ART centre, while OIs were treated by physician at tertiary care hospital. Civil Hospital attached with G.M.E.R.S. Medical College, Gandhinagar is having ICTC center for HIV/AIDS diagnosis ART CENTER for treatment and other specialized faculty like Physician and skin specialist to treat OIs and other complication. In this retrospective observational study, 834 HIV-infected patients came from different regions in Gandhinagar District. An accurate evaluation of the prevalence and spectrum of OIs helps to plan good management strategies. It was reported that [7], in a series of 135 hospitalized HIV-infected patients from north India, the five most common AIDS-defining illnesses were tuberculosis (71%), candidiasis (39.3%), PCP (7.4%), cryptococcal mentingitis (3.7%) and

toxoplasmosis (3.7%). Another retrospective study in 89 cases in Lebanon with OIs reported [8] that the most common OIs were cerebral toxoplasmosis (21%) and fungal infection (17%). In this study, we found that most common OIs were tuberculosis, candidiasis, PCP, CMV infection, other fungal infection, MAC and Cryptococcosis. In this study, the majority of the patients (52.39%) were in the age group of 21-40 years, and men were predominantly affected, which was consistent with the findings in Indian [9] and Euro-American [10] studies. Thus OIs occurred in economically productive years in these HIV-infected individuals that increased social-economic burden in India. The culture, isolation and identification of species of pathogens such as mycobacterium tuberculosis, Pneumocyst, some invasive fungi and Mycobacterium avium complex in some HIV-infected patients were difficult, and due to lack of brain biopsy, pathological diagnosis of Toxoplasmic encephalitis and PML was also difficult, empiric diagnosis and treatment was taken in patients with compatible clinical and radiographic results, which helped us minimize the false negative diagnosis. The important finding in this study revealed that pulmonary OI infections were the most prevalent morbidity cause in patients in the AIDS stage, and tuberculosis and PCP were most common OIs in respiratory system, which was similar with results in Indian studies [11]. The process of diagnosis of pulmonary OI infections was well planned, and HIV-infected patients with symptoms in respiratory tract underwent mycobacterium tuberculosis culture in induced sputum and BALF samples, pathological demonstration and thin-section computerized tomography scan. Empiric diagnosis and anti-tuberculosis treatment was taken in some patients with negative samples who were suspected of being infected with tuberculosis. The prevalence of mycobacterium tuberculosis infection was 20.50% in this study, which was similar to reports in Indian studies [12]. Tuberculosis infection was a systemic disease, and with increasing degrees of immunodeficiency, extra-pulmonary tuberculosis was more common. In this study, we found that Extra-pulmonary tuberculosis was the most widespread (13.07%) then pulmonary tuberculosis (7.43%). This indicated that that tuberculosis infection was one of most widespread OIs in HIV-infected patients. We also found that tuberculosis infection was prevalent at any levels of CD4 counts. These findings indicated that appropriate tuberculosis management strategies should be planned and implemented in HIV-infected population. PCP was found in 5.16% of patients in this study, which was diagnosed based on etiology and empirical treatment. Pneumocystis jirovecii can't be cultivated routinely; cytopathologic demonstration of this organism in BALF was required for etiologic diagnosis. Empirical diagnosis was based on compatible clinical symptoms and CT results, negative cytopathologic demonstration of organism and clinical improvement after empirical anti-PCP treatment. The findings in this study revealed that CMV retinitis also common viral infection. Most of CMV infection occurred in HIV-infected patients with immune suppression, typically in those with CD4 count less than 50 cells/ul. In this study, 0.22% of the patients were found to have CMV retinitis. The occurrence of oral candidiasis was recognized as an indicator of immune suppression, and those were often found in HIV-infected patients with CD4 counts fewer than 200 cells/ul. The prevalence of oral candidiasis in this study was 1.56%. Except Candidiasis, Cryptococcosis, the culture, isolation and identification of species of other fungi in HIV-infected patients were difficult. We diagnosed candidiasis based on its features with painless, creamy white, plaque-like lesions in tongue surface or oropharyngeal mucosa which can be scraped off with tongue depressor. In our study we found candidiasis in 1.56% of patients. We found the low prevalence of AIDS-defining illnesses in central neural system in this study, including PML (0.12%), cerebral toxoplasmosis (0.12%), which contributed to increased mortality in HIV-infected patients. Lumbar puncture and MRI scan were required in HIV-infected patients with central nervous system (CNS) manifestation and different pathogen

detections were performed in cerebrospinal fluid to differentiate various OI infections.

Table - 3: Effect of anti-retroviral treatment.

ART status	With OIs (%)	Without OIs (%)	Total (%)
On ART	183 (27.81)	475 (72.19)	658 (100)
Pre ART	70 (39.78)	106 (60.22)	176 (100)
Total (%)	253 (30.33)	581 (69.67)	834 (100)

χ^2: 9.401; p value: 0.002

Figure - 1: Spectrum of OIs.

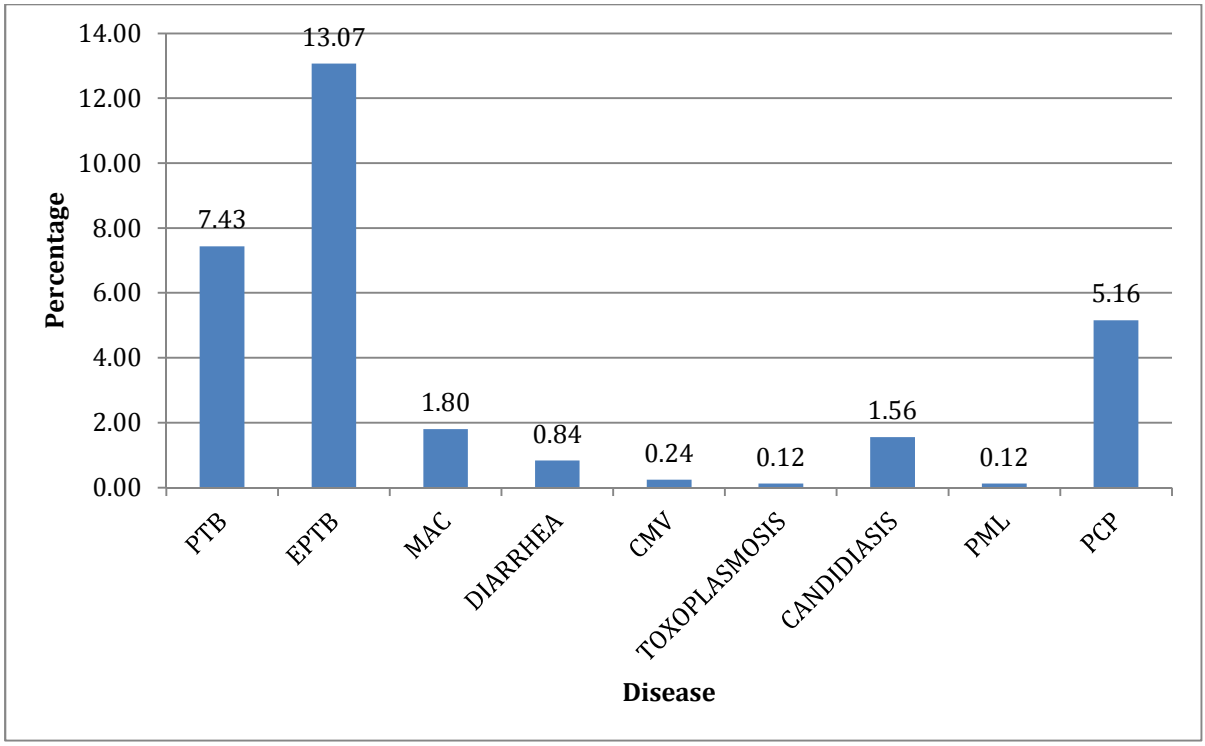
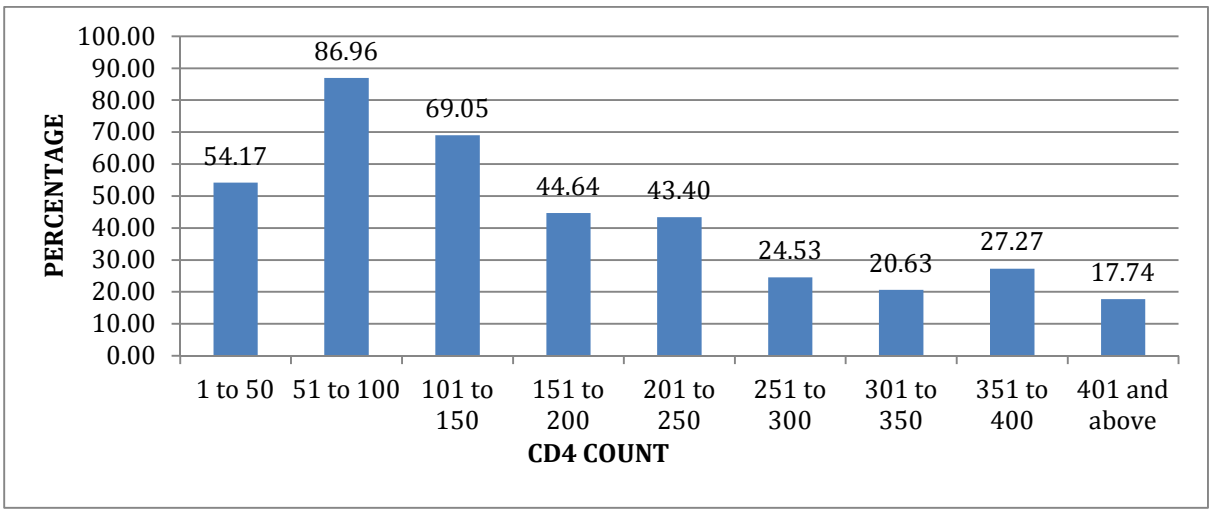


Figure - 2: Prevalence of OI related to CD4 count.



Conclusion

In conclusion, the prevalence and spectrums of OIs varied contingent on sex, age, CD4 levels and treatment with ART. Tuberculosis, candidiasis, PCP, CMV infection and MAC emerged as the most common OIs. In-hospital mortality rate was considerable due to severe OIs, malignancies and cost constraints. It would help to increase the awareness of physicians to come up with right diagnoses and implement empirical treatment sooner and plan good management strategies, especially in resource constrained regions in China.

References

1. Joint United Nations programme on HIV/AIDS: Epidemiological fact sheets on HIV/AIDS and sexually transmitted infections 2002 update: India. World Health Organisation, Geneva; 2002.
2. Chacko S, John TJ, Babu PG, Jacob M, Kaur A, Mathai D. Clinical profile of AIDS in India: A review of 61 cases. J Assoc Physicians India, 1995; 43: 535-538.
3. Ramalingam S, Kannangai R, Zachariah A, Mathai D, Abraham C. CD4 counts of normal and HIV-infected south Indian adults: Do we need a new staging system? Natl Med J India, 2001; 14: 335-339.
4. Creese A, Royd K, Alban A, Guinness L. Cost-effectiveness of HIV/AIDS interventions in Africa: A systematic review of the evidence. Lancet, 2002; 359: 1635-1642.
5. Core epidemiology From UNAIDS. Available from http://www.unaids.org/sites/default/files/media_asset/20150714_epi_core_en.pdf
6. National Aids Control Program. Available from http://www.naco.gov.in/NACO/
7. Sharma SK, Kadhiravan T, Banga A, Goyal T, Bhatia I. Spectrum of clinical disease in a series of 135 hospitalised HIV-infected patients from north India. BMC Infect Dis, 2004; 4: 52.
8. Naba MR, Kanafani ZA, Awar GN, Kanj SS. Profile of opportunistic infections in HIV-infected patients at a tertiary care center in Lebanon. J Infect Public Health, 2010; 3: 130-133.
9. Srirangaraj S, Venkatesha D. Opportunistic infections in relation to antiretroviral status among AIDS patients from south India. Indian. J Med Microbiol., 2011; 29: 395-400.
10. Severe P, Leger P, Charles M, Noel F, Bonhomme G. Antiretroviral therapy in a thousand patients with AIDS in Haiti. N Engl J Med., 2005; 353: 2325-2334.
11. Chakraborty N, Mukherjee A, Santra S, Sarkar RN, Banerjee D. Current trends of opportunistic infections among HIV-seropositive patients from Eastern India. J Infect Dis., 2008; 61: 49-53.
12. Saha K, Firdaus R, Santra P, Pal J, Roy A. Recent pattern of Co-infection amongst HIV seropositive individuals in tertiary care hospital, Kolkata. Virol J., 2011; 8: 116.