OCCURRENCE AND OUTCOME OF OPPORTUNISTIC INFECTIONS AMONG HAART EXPERIENCED PATIENTS IN A TERTIARY CARE HOSPITAL OF KOLKATA

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ABSTRACT

BACKGROUND

There were about 21 lakh people living with HIV in India and number of new cases was 86,000 in 2015 as reported by UNAIDS in 2015. The scenario here is a bit different than the western population due to the differences in standard of living and access to ART. There is also insufficient knowledge regarding the burden and spectrum of opportunistic infections (OI) in HIV infected populations receiving HAART.

Our study was designed to estimate the prevalence and outcome of OIs in HIV patients on HAART therapy at a tertiary hospital in Kolkata in order to define the local priorities.

MATERIALS AND METHODS

100 patients of HIV on HAART for at least 1 year were taken up for a descriptive study with respect to the prevalence of OIs and their outcome. Clinical assessment and investigations were done as per the NACO guidelines. The data was analysed using multivariate and computerised statistical methods.

RESULT

The mean age of 100 patients in our study was 33.8 ± 1.10; 71% of the patients were male. Mean CD4 count was 239.9 ± 11.25. Most common presentation was fever (64%) and weight loss (35%). Tuberculosis was the most common opportunistic infection (55%) followed by candidiasis (51%), Pneumocystis carinii 16%, cryptosporidium diarrhoea 10%, cryptococcal meningitis 6%, cerebral toxoplasmosis 2%. 74 patients were successfully treated. 12 succumbed to death, of which 3 were of tubercular meningitis and pneumocystis carinii pneumonia and 2 were of cryptococcal meningitis, cerebral toxoplasmosis and bacterial pneumonia each. Mean CD4 count of those who survived was 263.17 ± 12.47 and those who succumbed was 133.25 ± 21.38. This was statistically significant showing that death occurred at a lower CD4 count.

CONCLUSION

Our descriptive study done at a tertiary care hospital of eastern India showed that the main burden of opportunistic infections in HAART experienced HIV patients still lies on tuberculosis followed by candidiasis. However, Pneumocystis carinii and tubercular meningitis are among the leading causes of mortality.

KEYWORDS

Opportunistic Infections, Antiretroviral Therapy, Highly Active.

HOW TO CITE THIS ARTICLE: Das I, Kargupta A, Roy K, et al. Occurrence and outcome of opportunistic infections among HAART experienced patients in a tertiary care hospital of Kolkata. J. Evolution Med. Dent. Sci. 2018;7(01):24-28, DOI: 10.14260/jemds/2018/7

BACKGROUND

According to the Joint United Nations Program on HIV/ AIDS (UNAIDS), an estimated 33.3 million individuals were infected with HIV by the end of 2009. Among these HIV infected individuals, more than 95% of the people living with HIV/ AIDS (PLHA) reside in low- and middle-income countries. In 2015, UNAIDS estimated that India had 2.1 million HIV-infected people.

'Financial or Other Competing Interest': None.
Submission 07-08-2017, Peer Review 27-11-2017,
Acceptance 18-12-2017, Published 01-01-2018.
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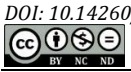
DOI: 10.14260/jemds/2018/7



The HIV-scenario in India is a bit different from western society as a result of the difference in socioeconomic and cultural environment, which are also important determinants in disease transmission. Opportunistic infections (OI) constitute a major cause of morbidity and mortality in PLHAs.[1,2] This is even more critical where the standard of living is generally poor and access to ART (anti-retroviral therapy) is still inadequate. In developing regions such as Sub-Saharan Africa and South-East Asia, OIs in the pre-ART era were tuberculosis, candidiasis, infective diarrhoea, meningitis, dermatitis and recurrent Herpes simplex infection.[3,4] Fortunately, following the widespread use of highly active anti-retroviral therapy (HAART) and implementation of guidelines for prevention of opportunistic infections, the incidence of secondary infection has declined dramatically.[5] However, there is insufficient knowledge about the burden and spectrum of OIs in HIV-infected populations receiving HAART in developing countries.

An evidence-based assessment of the prevalent OIs in PLHAs in the era of HAART is necessary in order to define local priorities in HIV/ AIDS care and form a targeted expenditure on prophylaxis and treatment of HIV-related comorbidities. Our study was devised keeping in mind to study the occurrence of OIs in HAART experienced HIV persons at a tertiary care hospital in eastern India and to study the outcome of opportunistic infections in these patients and correlation with CD4 counts.

Medical College and Hospital, Kolkata, has been at the forefront of the fight against HIV since 1993. The APEX Referral Centre for HIV/ AIDS, run by the Department of Medicine, conducts thrice weekly Outpatient Clinics for PLHAs, catering to the largest number of HIV patients from West Bengal, Bihar, Jharkhand, Orissa and North Eastern states. A large number of HIV patients are referred to the said clinic from various Departments and Outpatient Clinics of Medical College, Kolkata. HIV patients are also referred to the said clinic from other peripheral government hospitals and clinics as well as private practitioners for proper evaluation and linkage to comprehensive HIV care. In addition, patients who have been diagnosed as HIV positive subsequent to their admission to the Inpatient Department of Medicine as well as other departments in Medical College also receive HIV care.

Thus, Medical College, Kolkata stands at a unique position to present information related to the occurrence of opportunistic infections in HAART experienced HIV persons and to study the outcome of opportunistic infections in these patients and correlation with CD4 counts considering the vast number of HIV positive patients treated by the APEX Referral Centre. There has been no large published data on this topic from eastern India. The objective of our study was to document the occurrence of opportunistic infections in HAART experienced HIV patients and their outcome and correlation with CD4 count at this large teaching hospital.

Aims

This study was done to determine the changing trend of OIs among HAART experienced patients, their outcome and the impact of ART on the occurrence of OI and improvement in quality of life in HIV patients.

The Objectives are as under

1. To document the type of opportunistic infections in HAART experienced HIV subjects at a tertiary care hospital of eastern India.
2. To record the outcomes of opportunistic infections in these patients.
3. To correlate the spectrum and outcomes of opportunistic infections with CD4 counts (if any).

MATERIALS AND METHODS

Study Area

1. Apex Clinic for HIV patients at Medical College, Kolkata.
2. General Medicine outpatient department.
3. Inpatients of Medicine ward, Medical College, Kolkata.

Study Population

Patients receiving ART at least for one year and attending Apex clinic, Medicine OPD at Medical College Kolkata or are admitted in IPD at Medical College Kolkata.

Study Period

Jan 2014 to July 2015.

Sample Size

Approximately, 100 HIV patients were taken into this study conveniently.

Inclusion Criteria

1. HIV infected patients documented at any ICTC centre who are on HAART for at least 1 year.
2. Patients from both sexes.

Exclusion Criteria

1. Those with concomitant illness unrelated to HIV.
2. Those with poor adherence to ART (< 95% as per ART centre record).
3. Those with more than 1 HAART interruption in last 1 year (not taken medicines for more than 15 days at a stretch).

Study Design

It is a descriptive study. All cases have been followed up for one year.

Parameters Studied

1. Diagnosis of OIs has been made from signs and symptoms driven test as per NACO guidelines.
2. Outcome of OIs among HAART experienced patients has been recorded from clinical case records (from OPD tickets and BHTs).
3. The occurrence and outcome of OIs have been correlated with CD4 count estimation.

Study Tools

1. History taking and a standard questionnaire for assessment of symptoms in HIV patients.
2. Clinical examination including haematology, biochemistry, serology, culture and relevant imaging studies in a case to case basis for diagnosis of OIs. Depending on the patient's clinical features specimens were collected which included blood, sputum (two sputum specimens, first spot, early morning), cerebrospinal fluid, lymph node aspirate, oral swab, stool and urine. Occurrence of different types of opportunistic infections in HAART experienced group was the purpose of the study. All sputum samples were used to make separate smears and stained by Ziehl-Neelsen staining method for diagnosis of tuberculosis. Diagnosis of tuberculosis was made as per Revised National Tuberculosis Control Programme (RNTCP) guidelines.[6] Giemsa stain was done for detection of Pneumocystis jirovecii in suspected patients. Stool specimens were collected as per WHO standard procedures and examined microscopically. Saline wet Lugol's iodine mount was used for detection of ova, trophozoites, larvae and cysts of intestinal parasite. Smears of stool specimens were subjected to modified acid-fast staining for Cryptosporidium parvum, Isospora belli and Cyclospora. Also gram-staining and bacteriological culture of stool specimens was done following the WHO standard procedures to mainly identify Salmonella and Shigella.[7] Diagnosis of

cryptococcal meningitis was established by India-ink preparation and by culture on Sabouraud's dextrose agar. Specimens were also inoculated on different media like MacConkey's agar, blood agar and chocolate agar for isolation of various pathogens. For the diagnosis of candidiasis, oral swab was cultured on Sabouraud's dextrose agar. Identification of microorganisms was done following the standard protocol.[8]

3. CD4 count facility at the ART Centre of Medical College and Hospital for immunological parameter.
4. Medical records of the patients to determine the duration of HAART therapy, adherence and other relevant and necessary information.

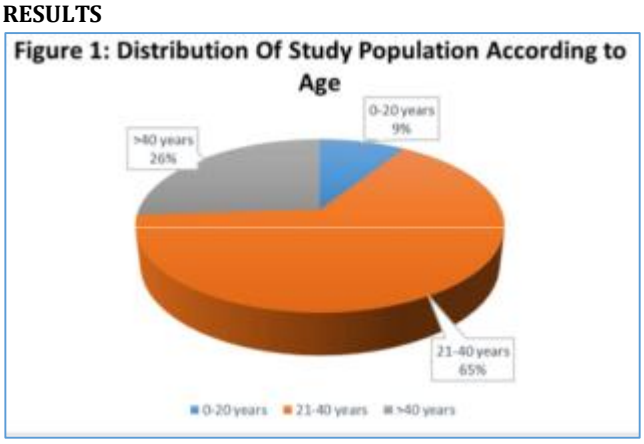
Study Techniques

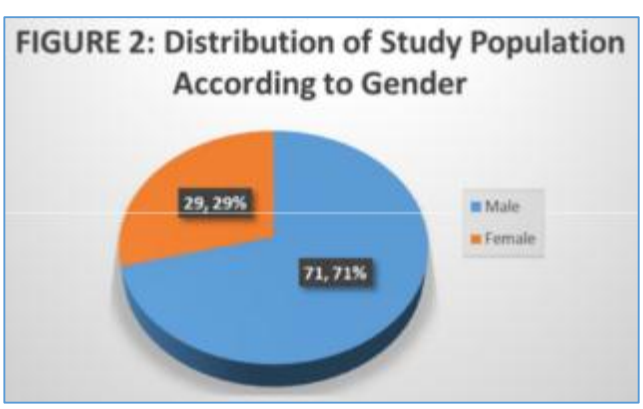
This hospital-based descriptive study required detailed history taking, clinical examination and relevant investigations for diagnosis of OIs among HAART experienced patients and their outcome.

Data Analysis

All the data have been tabulated into a master chart and analysed using standardised statistical techniques for calculating the mean values, standard deviation and standard errors. ANOVA with post-hoc test is used. Computerised statistical program SPSS V 20 software was used to determine significant difference between the groups of patients having single OI, two OIs and three OIs. Comparative outcome in relation to CD4 count between the deaths and successfully treated HAART patients was determined with T-test. A p-value of < 0.05 was significant, < 0.001 highly significant and > 0.05 was not significant.

RESULTS





CD4 Count	HAART Experienced Group
<200	43
200-350	40
>350	17
Total	**100**

Table 1. Distribution of the Study Population according to the CD4 Count

Clinical Presentations	Number of Patients/ Percentage
Fever	64/ 64%
SOB/ Cough	31/ 31%
Diarrhoea	31/ 31%
Weight Loss	35/ 35%
Altered Sensorium	14/ 14%
Dysphagia	15/ 15%
Lymphadenopathy	12/ 12%
Dermatologic Manifestations	5/ 5%
Genital Ulcer	5/ 5%

Table 2. Clinical Presentations in HAART Experienced HIV Patients

Sl. No.	OI	No. of Patients/ 100	Mean CD4 Count	SE
1	Herpes	14	145.21	16.46
2	TB	55	210.38	11.89
3	Candidiasis	51	176.16	9.97
4	Cryptococcal Meningitis	6	77.67	6.41
5	PCP	16	119.94	11.41
6	BAC Pneumonia	8	270.25	33.49
7	Cryptosporidiosis	10	119.2	20.83
8	Toxoplasma	2	64.5	8.5

Table 3. Correlation of Individual Opportunistic Infections with CD4 Count

DISCUSSION

Total Study Population

100 HIV positive patients on HAART and presenting with one or more clinical features suggestive of opportunistic infections such as fever, diarrhoea, cough, altered sensorium, lymphadenopathy and dysphagia were taken into the study and investigated for various pathogens including opportunistic ones after they fulfilled the laid down inclusion and exclusion criteria.

Age Distribution of Study Population

The majority of our patients belonged to the 21 - 40 years' age group (9% in Group A, 65% in Group B and 26% in Group C) (Figure 1). The mean age of our study population was 33.85 ± 1.10 years (65% of the population). This is also observed in other studies from India and aboard. Findings of our study are similar to findings of SK Sharma et al 2004 and J Chakravarty et al 2006.[9]

The mean age among the male patients of our study population was 34.42 ± 11.236 years and among female patients was 32.45 ± 10.789 years and there was no statistically significant difference between the two groups (P value 0.422 at 95% level of significance).

Gender Distribution of Study Population

The genders were not equally distributed in our study (males 71% and females 29%) having a male-to-female ratio of 2.45 (Figure 2).

Distribution of Study Population according to CD4 Count

Mean CD4 count in the study population of HAART experienced group were 239.9 ± 11.250 cells/ µL. In the study population, 17 patients had CD4 count > 350 cells/ µL, 40 patients had CD4 count between 200 - 350 cells/ µL, 43 patients had CD4 between < 200 cells/ µL (Table 1). Mean CD4 count among the male patients of our study population was 237.39 ± 13.501 cells/ µL and in female patients of our study population was 243.03 ± 20.629 cells/ µL. There were no statistically significant differences between these two groups (P value- 0.729, at 95% level of significance).

Clinical Presentations in HAART Experienced HIV Patients

Most of the patients presented with more than one symptoms. Fever and weight loss were the most common presentations. Fever was present in 64 patients (64%) and weight loss was present in 35 patients (35%). Among the others, shortness of breath (SOB)/ Cough were present in 31 (31%) patients, diarrhoea was present in 31 (31%) patients, altered sensorium in 14 (14%) patients, dysphagia in 15 (15%) patients and lymph node swelling and dermatologic manifestations were present in 12 (12%) and 5 (5%) patients respectively and genital ulcer was present in 5 (5%) patients (Table 2). These findings are similar with studies of SK Sharma et al 2004 and Gupta V et al 2007, where fever was the chief complaint in 70.4% and 51% patients respectively followed by weight loss in 65.2% and 43% patients respectively.[10,11]

Correlation of Individual Opportunistic Infections with CD4 Count

There were a total of 58 episodes of opportunistic infections in the HAART experienced group. A diagnosis of tuberculosis was made in 55% patients and a diagnosis of candidiasis was also made in 51% patients. The other different diagnoses are as follows- cryptococcal meningitis in 6% patients, cryptosporidium diarrhoea in 10% patients and pneumocystis jirovecii pneumonia in 16% patients and cerebral toxoplasmosis in 2% patients. Among the 55 patients of the HAART experienced group who were diagnosed with tuberculosis, 24 patients had pulmonary tuberculosis, 8 patients had tuberculous meningitis, 13 patients had pleural effusion and 10 patients had tuberculous lymphadenopathy. Tuberculosis was the commonest observed opportunistic infection in our study and matches with findings by other authors.[12,13,14,15] This is because tuberculosis is endemic in India and patients with HIV and TB rapidly downgrade with high mortality and multidrug resistance. In case of candidal infection, our study findings are comparable with incidence of candidiasis observed in studies by others.[16,17,18] Oral candidiasis was the commonest mucocutaneous opportunistic infection observed in our study. Mean CD4 count of patients with different types of opportunistic infections were calculated. It was seen that while patients with TB had a mean CD4 count of 210.40 ± 11.88, patients with Pneumocystis jirovecii pneumonia had a CD4 count of 119.93 ± 11.40. The mean CD4 count of different opportunistic infections are shown in Table 3.

There was a statistically significant difference between the groups of patients having single OI, two OIs and three OIs respectively, as determined by One-Way ANOVA (F (2, 86) = 4.237, P= 0.018. A Tukey post-hoc test revealed that the CD4 level was lower in patients who were having two OIs (176.71 ± 13.830, P= .185) and three (119.17 ± 19.532, P= 0.030) than the patients having single OI (210.38 ± 11.886). There were statistically significant differences between the single OI and triple OIs group (P= .030).

Hospital Outcome of the Patients

Out of the total 100 patients admitted with one or more opportunistic infections, 74 patients were successfully treated/ followed up for this episode of infection. But unfortunately, 12 patients succumbed to their infection and 14 were lost for follow-up. The cause-specific mortality is given in the table below. The key-findings of this study revealed that:

1. Lost in follow-up cases were= 14 nos.
2. Total followed-up patients 100 - 14= 86 nos.
3. Total fatality= 12 nos.
4. Mortality percentage amongst those followed up= 12/86= 13.95%.
5. Cause of Fatality • PCP: 3/12(25%)
   - TBM: 3/12 (25%)
   - Cryptococcal Meningitis: 2/12 (16.67%)
   - Cerebral Toxoplasmosis: 2/12 (16.67%)
   - Bacterial Pneumonia: 2/12 (16.67%)

Correlation of CD4 Count with Hospital Outcome

Out of the 100 patients in our study population, the episode of opportunistic infection in 74 patients were treated successfully. Unfortunately, 12 patients could not be saved and succumbed to their opportunistic infections. The mean CD4 count in the patients who were successfully treated were 263.17 ± 12.47, whereas the mean CD4 count in those patients who could not be saved were 133.25 ± 21.38. The difference between these mean CD4 count was calculated by using the T-test of the two independent samples assuming unequal variances (in Excel 2013 using Real Statistics Resource Pack). 'T statistics' value was 4.86 and 'p value' one tail was 0.000078 (P < 0.01) at 95% confidence level, which was highly significant indicating increased chances of mortality at lower CD4 counts.

CONCLUSION

Our study done at a tertiary care hospital of eastern India showed that the main burden of opportunistic infections in HAART experienced HIV patients still lies on tuberculosis followed by candidiasis. However, Pneumocystis carinii and tubercular meningitis are among the leading causes of mortality.

ACKNOWLEDGEMENTS

First of all, we would like to thank the patients who willingly gave consent to be included in our study. We are extremely grateful to Dr. Prasenjit Saha and all the staffs of ART centre and the Departments of Radiology, Pathology, Biochemistry and Community Medicine of Medical College, Kolkata, for their immense support, co-operation and suggestions to carry out the necessary investigations and calculations without which the study would not have been possible.

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