<u>Original Research Article</u>

An Observational Assessment to Determine the Incidence of Pulmonary Tuberculosis and Opportunistic Respiratory Infections among the Cases of HIV

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Abstract

Aim: To primarily evaluate the incidence of pulmonary tuberculosis and opportunistic respiratory infections among the cases of HIV.

Material &Method: The present study was conducted at Darbhanga Medical College & Hospital, Darbhanga, Bihar, India, over a period of six months by department of General medicine. All the cases of HIV diagnosed earlier or at the time of attending the OPD of department presenting with the respiratory signs and symptoms and clinical evidence of respiratory tract infections were included in this study.

Results: A total of 100 cases fulfilling the inclusion criteria with 73 males and 27 females were included in the study. Male to female ratio in the study was 2:1. Of the 100 cases in the study, 75 cases were known cases of HIV and 25 cases were diagnosed during the hospital visit. Fever was the most common presenting symptom in 90% of cases with other signs and symptoms like cough (84%)**.** A total 51% of cases were diagnosed with bacterial pneumonia and the causative bacteria were isolated by culture and sensitivity.

Conclusion: Knowledge of the pattern of pulmonary complications in patients with HIV infection in relation to CD4 count will help clinicians develop faster diagnostic and therapeutic approach to patient management. There was strong correlation between CD4 counts and number of symptoms. The type of infections, bacterial or fungal and PJP were dependent on the CD4 counts of the HIV cases.

Keywords: Bacterial pneumonia, CD4 cell count, Human immunodeficiency virus, Tuberculosis

Introduction

Tuberculosis (TB) is the most common opportunistic disease in human immunodeficiency virus (HIV)-infected patients [1]. HIV-infected patients are at strikingly increased risk of TB [2]. The risk of death in HIV-infected patients with

TB is approximately three-to-seven times higher than in uninfected individuals [3] and two times higher than in HIV-infected patients without TB [4].

However, in low-income countries the incidence of cases is still alarming and appropriate control measures and strategies are essential. The total number of people living with HIV in India is estimated at 21.40 lakhs (15.90 lakhs-28.39 lakhs) in 2017 which is expected to rise by the end of 2020 to 25 lakhs. India has reported 69000 aids related deaths by the end of 2018 which is expected to increase by 10-12% by the end of 2020. Majority of the cause of all these deaths are opportunistic infections and malignancies acquired during the period. As most of the opportunistic infections are related to respiratory tract and associated tuberculosis with development of multi drug resistance is an additional grave factor for death. [5]

A definitive diagnosis is highly recommended before starting management protocol. In the current era of combination antiretroviral therapy, the frequency of HIV-associated OIs and neoplasms has decreased. In contrast, the frequency of non-infectious complications such as chronic obstructive pulmonary disease (COPD), pulmonary arterial hypertension (PAH), and lung cancer may be increasing. HIV infection appears to be an independent risk factor for COPD and PAH. [6]

Thus, this study aims to primarily evaluate the incidence of pulmonary tuberculosis and opportunistic respiratory infections among the cases of HIV.

Material & Method:

The present study was conducted at Darbhanga Medical College & Hospital, Darbhanga, Bihar,india.over a period of six months by department of General medicine. The study was conducted as per the guidelines of the committee and strict confidentiality of the cases was observed.

The study guidelines were clearly explained to all the participants and a written informed consent was obtained. The socio demographic data (age, sex, history etc.) was collected by a senior resident of the department by interview and noted in a separate predesigned questionnaire form.

All the cases of HIV diagnosed earlier or at the time of attending the OPD of department presenting with the respiratory signs and symptoms and clinical evidence of respiratory tract infections were included in this study. Detailed history (smoking, alcohol, history of exposure etc.) was collected from the cases and a through clinical examination was conducted by a senior resident of the department. The signs and symptoms were noted in a separate predesigned questionnaire form. History of HIV was obtained with regarding to duration of disease in old cases and whether on HAART, previous history of respiratory infections, past history of tuberculosis and any old history of pneumonia.

All the cases were subjected to relevant biochemical, microbiological examinations (sputum for staining (grams, Zn), special staining techniques for sputum examination in suspected cases of aspergillosis, PCP pneumonias etc. Radiological examination of chest including X-ray, CT and MRI were performed in cases based on necessity. Special investigations like CD4 count in newly diagnosed cases, S. LDH, body fluid examination (pleural fluid etc.) were done under special conditions. HIV status was confirmed by ELISA test with two different antigens. Absolute CD4 counts were obtained through hematology analyzer and flow cytometry in which reagent BD multi-test CD3/CD4/CD8/CD45 was employed. All the patients were screened for Hepatitis B surface antigen and VDRL as routine protocol. All the cases were treated accordingly for HIV and respiratory

infections. Prophylaxis for all respiratory opportunistic infections was administered in indicated cases in the study.

Statistical analysis:

The data was entered in Microsoft excel spread sheet and analyzed for any corrections. Mean, median and SD was calculated for all the continuous variables.

Results:

A total of 100 cases fulfilling the inclusion criteria with 73 males and 27 females were included in the study. Male to female ratio in the study was 2:1 (Figure 1).

Of the 100 cases in the study, 75 cases were known cases of HIV and 25 cases were diagnosed during the hospital visit. Majority of the cases were in the age group of >61 years with 31% followed in order by 51-60 years (28%), 41-50 years (21%), 20-30 years (12%) and 31-40 years (8%) (Figure 2).

History of sexual exposure was the commonest cause of the disease (83%) following with needle prick in 6%, blood transfusion in 1% and in 10% of cases the cause was unknown. Among the risk factors for acquisition of lower respiratory tract infection, smoking was reported in 42%, alcohol consumption in 18%, old history of pneumonia was reported in 15%, tuberculosis in 14% and treatment for other respiratory disorders in 11% of the cases (Table 1).

Table 2 depicts that fever was the most common presenting symptom in 90% of cases with other signs and symptoms like cough (84%), dyspnoea (44%), weight loss (51%), chronic diarrhea (30%), oral candidiasis (14%) and skin manifestations (22%). Lymphadenopathy was observed in 48% of cases. The findings of CD4 counts among the cases in the present study. 37% of the cases had CD4 counts within the range of 350-200 cells/μl, 23% of cases with range of 350-500 cells/μl, 22.05% in range of >500 cells/μl and only 19% with CD4 counts <200 cells/μl. The number of symptoms increased the CD4 count was reduced and there was a statistically significant correlation between number of symptoms and CD4 counts.

A total 51% of cases were diagnosed with bacterial pneumonia and the causative bacteria were isolated by culture and sensitivity. *Klebsiella pneumoniae* was the commonest causative agent of bacterial pneumonia (35%) followed in order by others like *Streptococcus pneumoniae* (32%), *Acinetobacter sp* (15%), *Pseudomonas aeruginosa* (12%) and *Escherichia coli* (8%). Prevalence of tuberculosis among the cases of this study was 19% with Mycobacterium tuberculosis being identified by Zn staining and confirmed by BACTEC. Only 3% cases were of atypical mycobacteria identified as mycobacterium avium intracellular (MAC). (Table 3).
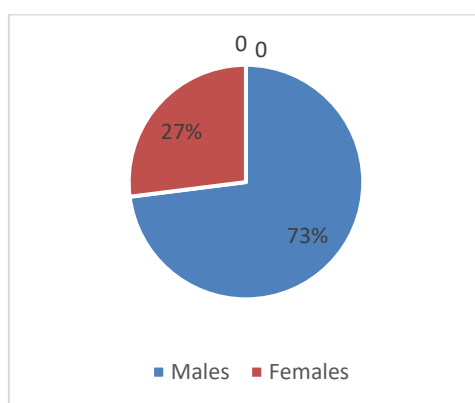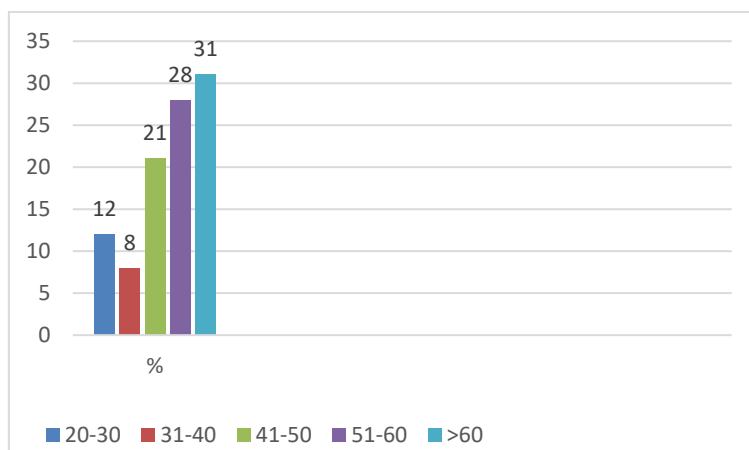

Figure 1: Gender distribution of cases in the study.

Figure 2: Age wise distribution of cases in the study.

Table 1: Cause of disease and risk factors for RTI among the cases in the study

Cause of disease	N
History of sexual exposure	83
Needle prick	6
Blood transfusion	1
Unknown	10
Risk factors for RTI	
Smoking	42
Alcohol	18
Old H/O of pneumonia	15
Old H/O of tuberculosis	14
Other respiratory disorders	11

Table 2: Signs and symptoms and CD4 counts of cases in the study

Presenting signs and symptoms	No.
Cough	84
Dyspnoea	44
Fever	90
weight loss	51
Diarrhoea	30
Oral candidiasis	14
Skin manifestations	22
Lymphadenopathy	48
CD4 counts	
> 500 cells/µl	21
500 -350 cells/µl	23
350-200 cells/µl	37
<200 cells/µl	19

Table 3: Pulmonary diagnosis and causative organisms of bacterial pneumonia

Pulmonary diagnosis	No.
Bacterial pneumonia	51
Fungal pneumonia	11
Tuberculosis	19

Pneumocystis pneumonia	5
Atypical mycobacterial tuberculosis	3
Bacterial pneumonia	
Causative organism	
Streptococcus pneumoniae	32
Klebsiella pneumoniae	35
Acinetobacter sp	15
Escherichia coli	8
Pseudomonas aeruginosa	12

Discussion:

This study identified that patients who developed opportunistic infections were more likely to develop TB after ART initiation (AOR: 3.728 95% CI: 2.058, 6.753) which is similar to a retrospective cohort study conducted at Debre-Markos referral Hospital and a case-control study conducted at Addis Ababa [7-9]. This may be explained by the occurrence of opportunistic infection indicates a decreased immune function of the patient. As supported by different studies, the occurrence of OIs not only determines the development of TB among HIV patients but also increases mortality among TB/HIV co-infected patients [10].

The findings of Murray JF et al who reported 64% of cases with respiratory tract infections in age group >60 years with male preponderance.4 Male dominance was observed in this study with 68.5% cases which is correlating with the findings of global statistics with an incidence of 59% and in India with an incidence of 64.2%. Mean age of the total cases in the study was 46.12±8.3 years which is contrary to the findings of Chakravarty J et al with mean age of 54 years.5 Few studies from the west reported that mean age of female of HIV cases is more than male which is due to causes of exposure, racial differences and other co-associated factors. [11]

Comprehensive HIV prevention, care, and treatment guideline recommended the provision of adherence counselling for people living with HIV at the time of initiation and throughout the course of treatment. The guideline recommended combining viral load monitoring with other approaches for strict assessment of adherence to ART, which is the major cause of drug-resistant and treatment failure. [12]

However, most of the studies reported wide varieties of respiratory symptoms and the signs and symptoms were variable depending upon the study age, place of study and co morbid respiratory conditions and whether patient was on anti-retroviral therapy or not. Many studies reported that respiratory infections were less on cases receiving ART. The data of this study was comparable with findings of the Crothers K et al who reported hilar lymphadenopathy also as a finding among the cases by performing CT of the chest. [13] As stated in many reports, *Klebsiella pneumoniae* was the commonest bacterial pathogen in causing pneumonia among the cases of HIV and among the cases, CD4 counts were between 350-200 cells/µl as observed in the findings of Shah H et al.12 However few studies from the west reported *S. pneumoniae* as the most common agent of pneumonia in HIV individuals. [14, 15]

Conclusion:

Knowledge of the pattern of pulmonary complications in patients with HIV infection in relation to CD4 count will help clinicians develop faster diagnostic and therapeutic approach to patient management. There was strong correlation between CD4 counts and number of symptoms. The type of infections,

bacterial or fungal and PJP were dependent on the CD4 counts of the HIV cases.

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