

## Original Research Article

# Incidence of tuberculosis and opportunistic respiratory infections in cases of human immunodeficiency virus: a one-year study at a tertiary care hospital

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### ABSTRACT

**Background:** Evaluation of respiratory signs and symptoms among HIV patients is a challenging task for a number of reasons. A definitive diagnosis is highly recommended before starting management protocol. Objectives of this study was to primarily evaluate the incidence of pulmonary tuberculosis and opportunistic respiratory infections among the cases of HIV and to estimate the CD4 counts of all the patients and correlate with the respiratory infections among the cases.

**Methods:** The present study was a one-year study conducted at Narayana Medical College and all the cases of HIV presented with signs and symptoms of lower respiratory tract infections were included after obtaining consent. Relevant biochemical, microbiological investigations and CD4 counts of all the cases were done and noted. The data was entered in Microsoft excel spread sheet and analysed for any corrections. Mean, median and SD was calculated for all the continuous variables.

**Results:** A total of 127 cases with 87 males and females 40 females with a ratio of 2.2:1 were included. Mean age of the total cases in the study was  $46.12 \pm 8.3$  years and 29.92% were above 60 years. Hetero sexual exposure was the commonest cause and 59.84% of cases were diagnosed with bacterial pneumonia. Prevalence of tuberculosis among the cases of this study was 22.05%. The mean CD4 cell count with SD among the study was  $168.57 \pm 142.21$ .

**Conclusions:** 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.

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

### INTRODUCTION

HIV is one considered as one of the leading pandemics in 20<sup>th</sup> century. Globally the incidence has increased and has shown a decline because of the wide spread awareness and measures in control and prevention throughout the world. 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.<sup>1</sup>

Evaluation of respiratory signs and symptoms among HIV patients is a challenging task for a number of reasons. HIV associated pulmonary infections include

both opportunistic infections (OIs) and neoplasm's hence differentiation at right time and management is highly essential. Hence 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.<sup>2</sup> The CD4 cell count is an excellent indicator of an HIV-infected patient's risk of developing a specific OI or neoplasm, presumably because it reflects the stage of HIV disease and degree of immunocompromised of the HIV cases. The centers for disease control and prevention's adult and adolescent spectrum of HIV disease project has provided statistics on which conditions occur at or below certain CD4 cell count ranges as well as which conditions are more common within a particular CD4 cell count range.<sup>3</sup>

The objective of the present study is to primarily evaluate the incidence of pulmonary tuberculosis and opportunistic respiratory infections among the cases of HIV. The secondary objective was to estimate the CD4 counts of all the patients and correlate with the respiratory infections among the cases.

## METHODS

The present study was conducted at Narayana Medical College and Hospital a tertiary care hospital for a period of one year from June 2018 to May 2019 by department of General medicine association with department of Respiratory medicine. The study protocol was presented before the institutional ethical committee and was approved. 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.

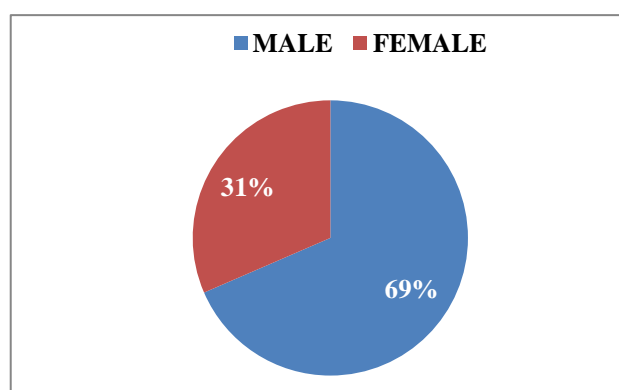
All the cases were subjected to relevant biochemical, microbiological examinations (sputum for staining (grams, Zn), special staining techniques for sputum examination in suspected cases of aspergillosis, PCP pneumonias etc. Radiological examination of chest including X-ray, CT and MRI were performed 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

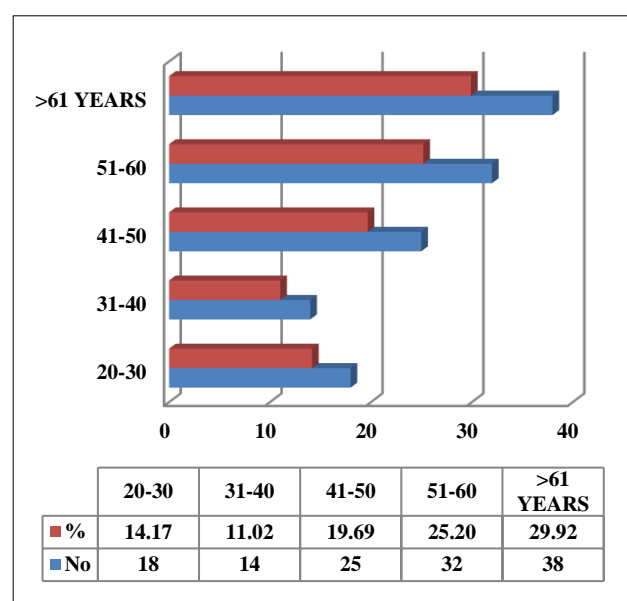
The present prospective study was conducted for a period of one year by department of general medicine and respiratory medicine. All the cases presenting to the OPD of general medicine and respiratory medicine with signs and symptoms of lower respiratory tract infections and diagnosed with HIV (both known and newly diagnosed) were included in the present study. A total of 127 cases fulfilling the inclusion criteria with 87 males (68.5%) and 40 females (31.5%) were included in the study. Male to female ratio in the study was 2.2:1 (Figure 1).



**Figure 1: Gender distribution of cases in the study.**

Of the 127 cases in the study, 94 cases were known cases of HIV (74%) and 33 cases were diagnosed during the hospital visit (26%). Majority of the cases were in the age group of >61 years with 29.92% followed in order by 51-60 years (25.2%), 41-50 years (19.69%), 20-30 years

(14.17%) and 31-40 years (11.02%) (Figure 2). Mean age of the total cases in the study was  $46.12 \pm 8.3$  years and males were  $54.21 \pm 5.9$  years and female's  $48.40 \pm 5.9$  years.



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

Hetero sexual exposure was the commonest cause of the disease (85.83%) following with needle prick in 3.15%, blood transfusion in 1.57% and in 9.45% of cases the cause was unknown. Among the risk factors for acquisition of lower respiratory tract infection, smoking was reported in 64.57%, alcohol consumption in 44.09%, old history of pneumonia was reported in 15.75%, tuberculosis in 14.17% and treatment for other respiratory disorders in 25.2% of the cases (Table 1).

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

Cause of disease	No.	%
History of sexual exposure	109	85.83%
Needle prick	4	3.15%
Blood transfusion	2	1.57%
Unknown	12	9.45%
<b>Risk factors for RTI</b>		
Smoking	82	64.57%
Alcohol	56	44.09%
Old H/O of pneumonia	20	15.75%
Old H/O of tuberculosis	18	14.17%
Other respiratory disorders	32	25.20%

Fever was the most common presenting symptom in 80.31% of cases with other signs and symptoms like cough (77.17%), dyspnoea (58.27%), weight loss (53.54%), chronic diarrhea (33.07%), oral candidiasis (16.54%) and skin manifestations (21.26%). Lymphadenopathy was observed in 46.46% of cases with maximum cases (38/59) with cervical lymphadenopathy

and inguinal in 12 cases and generalized lymphadenopathy in 9 cases. Table 2 summarizes the findings of CD4 counts among the cases in the present study. 33.07% of the cases had CD4 counts within the range of 350-200 cells/ $\mu$ l, 25.20% of cases with range of 350-500 cells/ $\mu$ l, 22.05% in range of >500 cells/ $\mu$ l and only 19.69% with CD4 counts <200 cells/ $\mu$ l. The mean CD4 cell count with SD among the study was  $168.57 \pm 142.21$ . In this study authors observed that as the number of symptoms increased the CD4 count was reduced and there was a statistically significant correlation between number of symptoms and CD4 counts.

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

Presenting signs and symptoms	No.	%
Cough	98	77.17%
Dyspnoea	74	58.27%
Fever	102	80.31%
weight loss	68	53.54%
Diarrhoea	42	33.07%
Oral candidiasis	21	16.54%
Skin manifestations	27	21.26%
Lymphadenopathy	59	46.46%
<b>CD4 counts</b>		
> 500 cells/ $\mu$ l	28	22.05%
500 -350 cells/ $\mu$ l	32	25.20%
350-200 cells/ $\mu$ l	42	33.07%
<200 cells/ $\mu$ l	25	19.69%

**Table 3: Pulmonary diagnosis and causative organisms of bacterial pneumonia.**

Pulmonary diagnosis	No.	%
Bacterial pneumonia	76	59.84
Fungal pneumonia	16	12.60
Tuberculosis	28	22.05
Pneumocystis pneumonia	5	3.94
Atypical mycobacterial tuberculosis	2	1.57
<b>Bacterial pneumonia</b>		
<b>Causative organism</b>		
<i>Streptococcus pneumoniae</i>	24	31.58
<i>Klebsiella pneumoniae</i>	28	36.84
<i>Acinetobacter sp</i>	10	13.16
<i>Escherichia coli</i>	6	7.89
<i>Pseudomonas aeruginosa</i>	8	10.53

A total 59.84% 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 (36.84%) followed in order by others like *Streptococcus pneumoniae* (31.58%), *Acinetobacter sp* (13.16%), *Pseudomonas aeruginosa* (10.53%) and *Escherichia coli* (7.89%). Prevalence of tuberculosis among the cases of this study was 22.05% with *Mycobacterium tuberculosis*

being identified by Zn staining and confirmed by BACTEC. Only two cases (1.57%) were of atypical mycobacteria identified as mycobacterium avium intracellular (MAC). Seven cases had both tuberculous and bacterial pneumoniae and five cases had tuberculous and fungal pneumoniae in common. Sixteen cases (12.6%) were identified with fungal pneumonia and the commonest isolate being *Aspergillus sp.* Two cases had *Candidial pneumoniae* in addition to *Klebsiella pneumoniae*. Among the cases in the study only five cases (3.94%) had pneumocystis jiroveci pneumonia (PJP) in association with bacterial pneumonia. Pneumocystis was identified by performing GMS staining of the sputum or BAL in highly suspected cases (Table 3).

## DISCUSSION

HIV is associated with multi system involvement primarily affecting the immune system with dominant involvement of CD4 and CD8 lymphocytes. Involvement of the respiratory system is found in all the age groups and all the stages of the disease. However, the manifestations are protean and depend upon the age, associated risk factors and co morbidities and the CD4 cell counts of the affected individual. Few studies have reported that 70% of HIV infected persons have at least one episode of respiratory illness during their course of their disease.

Majority of the individuals in the study were >60 years as contrary to the national statistics stating that 31-40 years as the most common age group of HIV cases. This can be explained by the reason that in the study cases presented with respiratory tract infections which is more common in >60 years group. Findings in this study were on par with the findings of Murray JF et al who reported 64% of cases with respiratory tract infections in age group >60 years with male preponderance.<sup>4</sup> 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.<sup>5</sup> 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.

Heterosexual route was the commonest cause of the disease as stated globally and nationally but the incidence in this study was 85% which is quite high when compared with the findings in the study of Swaminathan S who reported only 76% as the cause of the disease in his study, which may be due to difference in the study group selected and geographical distribution.<sup>6</sup> In this study, the cause of disease was unknown in 9% of the cases which is similar to the findings of Swaminathan S et al.<sup>6</sup>

In this study fever and cough was the major common symptoms because the study group involved patients with RTI and other co associated symptoms were dyspnoea, weight loss, chronic diarrhea and lymphadenopathy. 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.<sup>7</sup>

In this study authors observed that the mean CD4 cell count with SD was 168.57±142.21 and CD4 counts were significantly inversely correlated with the number of symptoms and the number of opportunistic infections. Findings of this study were on par with the reports of Havlir DV who reported similar like relations of this study.<sup>8</sup> Prevalence of tuberculosis among the cases of this study was 22.05% with mycobacterium tuberculosis and 1.57% were atypical mycobacteria (MAC), findings of this study were in accordance with the reports of Kirk O et al.<sup>9</sup>

*Aspergillus pneumonia* was the commonest opportunistic fungal infection in this study with a prevalence of 12% which is comparable with findings of Miller WT et al who reported the prevalence of 15% in his study, however since the advances in diagnosis and therapeutic regimens the incidence is still on a raise.<sup>10</sup> *Pneumocystis jiroveci pneumonia* was identified in 3.94% of cases in association with bacterial pneumonia. In all the cases of PJP, CD4 counts were <50 cells/μl which is quite similar with findings of Selwyn PA et al.<sup>11</sup>

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.<sup>12</sup> However few studies from the west reported *S. pneumoniae* as the most common agent of pneumonia in HIV individuals.

## CONCLUSION

To conclude, in this study 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. Previous studies have also reported that higher prevalence of diseases and opportunistic infections and tuberculosis are associated with lower CD4 counts. 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.

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