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Original Research Article

A STUDY ON THE SPECTRUM OF PULMONARY INFECTIONS IN HIV PATIENTS

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Abstract

Background: To the best of our knowledge, the spectrum of pulmonary infections in HIV-positive patients has not been studied among the people in Manipur, characterized not only by a high prevalence of HIV infection and injection drug use, but also by ethnic composition that is different from that of Mainland India. Hence, we planned to study the same along with patient characteristics and possible peculiarities of the respiratory infection specific to the HIV positive patient population of the state. The present study was done to study the spectrum of pulmonary infections in HIV-seropositive patients and also to study the correlation between pulmonary infections and CD-4 level. **Materials and Methods:** A hospital-based cross-sectional observational analytical study was done in the general wards and medical Intensive Care Unit (ICU) in the Department of Medicine, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Porompat, Imphal East, Manipur during the period of October 2022 toMarch 2024. The study population was 95 HIV seropositive patients, either ART-naïve or already on ART. The independent study variables were socio-demographic characteristics, mode of acquisition of HIV infection, smoking and alcohol use history and background medical characteristics like ART status at the time of admission with respiratory symptoms, baseline CD4 count on admission with respiratory symptoms, hypertension, diabetes mellitus, COPD etc. Outcome variables were radiological patterns and etiologies of respiratory infection. **Result and Conclusion:** Majority of the patients had cough (65; 68.4%) which was followed by fever (54; 56.8%). Maximum of the patient had consolidation (66.3%) followed by fibrosis (25.3%) and pleural effusion (18.9%). Majority of the patients had pulmonary tuberculosis (42.1%) followed by bacterial pulmonary infection (22.1%). Maximum number of infections were due to Mycobacterium tuberculosis (57.8%) followed by Klebsiella pneumonia (9.5%). The mean value of CD4 count was higher in patients under medication of ART than those patients who were not under medication. But the difference was not statistically significant. The mean value of CD4 count was lower in patients with fungal pneumonia in comparison to bacterial pneumonia and tuberculosis. The difference was found to be statistically significant.

INTRODUCTION

Opportunistic infections (OIs) are gaining its importance in patients with HIV and infection or AIDS as predominant cause of mortality in spite of widespread use of Anti-Retroviral Therapy (ART) and prophylaxis against these infections. Many infections share similar clinical representations and pose significant diagnostic challenges. The most common manifestation of opportunistic infections in respiratory system was pneumonia, of which Mycobacterium Tuberculosis (MTB) was the most frequent opportunistic causative pathogen followed by pneumocystis and pneumococcal infection.[1,2]

Adult HIV prevalence (15–49 age group) in India was estimated as 0.21%, and the estimated PLHIV burden in India was 24.01 lakhs in 2022.6 The "Golden Triangle," which comprises Myanmar, Thailand, and Laos, and the Yunnan Province of China, is known to be the world's most prominent source of illicit heroin and opium. Manipur lies closer to these regions and shares a long porous

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international border with Myanmar. Heroin has for long been illegally trans-shipped from Tamu, a Burmese town into the Moreh town of Manipur, and then on, via Asian Highway 2 (National Highway 102, earlier called National Highway 39), to the entire state of Manipur, the North-eastern states of India and the rest of India.[3] Manipur has 1.05%-estimated adult HIV prevalence among 15–49 years, which is much higher than the national average.[4]

To the best of our knowledge, the spectrum of pulmonary infections in HIV-positive patients has not been studied among the people in Manipur, characterized not only by a high prevalence of HIV infection and injection drug use, but also by ethnic composition that is different from that of Mainland India. Hence, we planned to study the same along with patient characteristics and possible peculiarities of the respiratory infection specific to the HIV positive patient population of the state. The study might help in the development of strategies such as formulation and effective implementation of evidence-based policy, reinforcement of health systems and emphasis on prevention, early detection, and treatment with the use of both conventional and innovative techniques.

Aims and Objectives

The present study was done to study the spectrum of pulmonary infections in HIV-seropositive patients and also to study the correlation between pulmonary infections and CD-4 level.

MATERIALS AND METHODS

A hospital-based cross-sectional observational analytical study was done in the general wards and medical Intensive Care Unit (ICU) in the Department of Medicine, Jawaharlal Nehru Institute of Medical Sciences (JNIMS), Porompat, Imphal East, Manipur during the period of October 2022 toMarch 2024. JNIMS is a tertiary care hospital receiving referrals from different health care centres across the state of Manipur and provides 24×7 emergency, critical care, outpatient and inpatient services.

The study population was HIV seropositive patients, either ART-naïve or already on ART, admitted in Medicine ward and ICU of JNIMS during the study period with the following inclusion and exclusion criteria. The inclusion criteria consisted of patients older than 18 years, HIV seropositivity by Enzyme Linked Immune-Sorbent Assay (ELISA) or by any other methods either before or during admission and having respiratory complaints of recent onset. Those who were pregnant or refused to participate in the study were excluded.

Based on the proportion of pulmonary infection of 56% as found out from a previous study by Shilpa et al,[1] a significance level of 95% and an absolute allowable error of 10%, a sample size of 95 was calculated. The required sample size was obtained by recruiting patients consecutively.

The independent study variables were socio-demographic characteristics, mode of acquisition of HIV infection, smoking and alcohol use history and background medical characteristics like ART status at the time of admission with respiratory symptoms, baseline CD4 count on admission with respiratory symptoms, hypertension, diabetes mellitus, COPD etc. Outcome variables were radiological patterns and etiologies of respiratory infection as evident from gram stain, bacterial culture, fungal stain (KOH mount or special stains like Gomori methenamine silver stain, etc.), fungal culture, acid-fast bacillus (AFB) stain, Cartridge-Based Nucleic Acid Amplification Test (CBNAAT) for MTB, mycobacterium culture (Mycobacterium Growth Indicator Tube: MGIT) performed on respiratory clinical specimens like sputum, broncho-alveolar lavage fluid, pleural fluid or other acceptable alternatives like fine needle aspirates from lymph nodes (peripheral or mediastinal).

A predesigned structured proforma was used for collecting data required for the purpose of the research work. The proforma had sections on socio-demography, clinical history, clinical examination and investigations as deemed appropriate. No effort was made by the research team to guide or direct the management of individual study participants. However, informed consent was obtained.

The collected data were entered and analyzed in SPSS (IBM) version 26. Summarizations of data like age, sex, occupation, education level, smoking and tobacco use, CD4 count, etc. were carried out by using descriptive statistics such as mean, standard deviation and percentages. Independent t-test was used to test the association between CD 4 count and ART status of the patient. To determine the association between mean value of CD4 count and clinical profile of the patient, ANOVA test was used. P-value of less than 0.05 was taken as statistically significant.

Ethical approval was obtained from the Research Ethics Board, JNIMS, Imphal before the beginning of the study. Written informed consent was taken from each participant. Study participants were managed by respective treating units as per national guidelines and local institutional protocols without any interference by the research team in terms of treatment or investigation decisions. A unique code number was given to each study participant, and no names were taken to maintain confidentiality. The information collected for the study was utilized only for the purpose and not disclosed to anyone outside the research team.

RESULTS

Data could be collected from 95 study participants. There was no refusal. Males (64%) outnumbered females. The mean age (SD) was found to be 46.82 (10.58) years. One-third (31.6%) of them belonged to the age-group of 31-40 years which was followed by the age-group of 41-50 years (26.3%). Majority of them (84.2%) were married. More than half of them were daily-waged laborers (50; 50.2%) by

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occupation. A maximum of the patients had education level of 12th class (35.8%) followed by 10th class (27.4%). Few patients were illiterate (18.9%). Nearly two-thirds (67; 70.5%) of them were already on ART.

Majority of the patients had cough (65; 68.4%) which was followed by fever (54; 56.8%). Loss of appetite, generalized weakness, altered sensation and shortness of breath were the other symptoms they had.

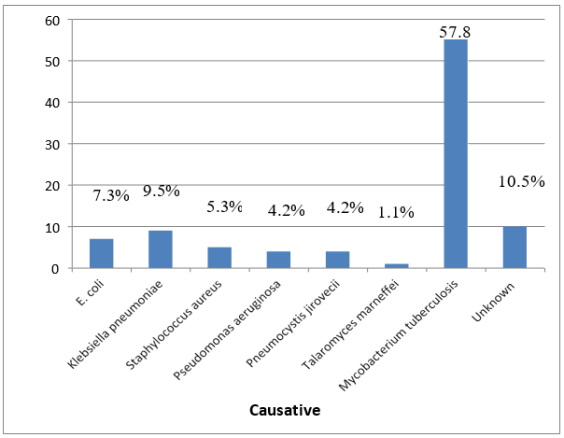

Figure 1: Distribution of the patients by causative agents (N=95)

Most of the patients were currently using oral tobacco (93.7%) and 20% of the patients were current alcohol users. Only 8.4% of the patients were IDU. Current smokers constituted 23.2% of the patients. A maximum of the patients had heterosexual route (66%) as the mode of acquisition of HIV infection followed by IDU (18%) and homosexual route (7%). Only 9% had unknown sources of infection.

Majority of the patient had consolidation (66.3%) followed by fibrosis (25.3%) and pleural effusion (18.9%). Miliary mottling was seen in one patient only [Table 1].

Majority of the patients had pulmonary tuberculosis (42.1%) followed by bacterial pulmonary infection (22.1%) and tubercular pleural effusion (15.2%). Only 5.3% of the patients had fungal infection. 10.5% of the patients had undetermined etiology [Table 2].

Maximum number of infections were due to Mycobacterium tuberculosis (57.8%) followed by Klebsiella pneumonia (9.5%). Escherichia coli (E. coli), Staphylococcus aureus and Pseudomonas aeruginosa were also seen in 7.3%, 5.3% and 4.2% of the patients, respectively. Talaromyces marneffei and Pneumocystis jirovecii were also seen in 1.1% and 4.2% of the patients respectively [Figure 1].

The mean value of CD4 count was higher in patients under medication of ART than those patients who were not under medication. But the difference was not statistically significant. The mean value of CD4 count was lower in patients with fungal pneumonia in comparison to bacterial pneumonia and tuberculosis. The difference was found to be statistically significant [Table 3].

Bacterial infection was more or less equally distributed across the spectrum of CD 4 cell count. There was no statistically significant association between CD4 count and bacterial infection. All patients with fungal infections had their CD4 cell count less than 100 per mm3. And there was a statistically significant association between fungal infection and low CD4 count of less than 100 per mm3. Maximum of the patients with tubercular infection had CD4 count within the range of 100 to 200 per mm3 of blood. And there was a significant association between tubercular infection and low CD4 count of within 100 to 200 per mm3 [Table 4].

Table 1: Distribution of patients by Imaging findings.

Sl. No.	Imaging findings	No. of patients	Percentage (%)
1	Consolidation	63	66.3
2	Pleural effusion	18	18.9
3	Calcified lesion	12	12.6
4	Fibrosis	24	25.3
5	Mediastinal lymphadenopathy	11	11.6
6	Miliary mottling	1	1.1
7	Diffuse ground glass opacities	5	5.3

Table 2: Etiology of pulmonary infection (N=95)

Sl. No.	Etiology	No. of patients	Percentages (%)
1.	Bacterial pneumonia	21	22.1
2.	Pulmonary tuberculosis	40	42.1
3.	Fungal pneumonia	5	5.3
4.	Tubercular pleural effusion	15	15.2
5.	Bacterial pleural effusion	4	4.2
6.	Unknown	10	10.5

Table 3: Mean CD4 count and profile of patients (N=95)

Sl. No.	Variable	Mean value of CD4 count	Standard Deviation	P value
1	Under ART Yes No	 177.85 144.14	 151.24 66.86	0.261
2	Clinical profile Bacterial pneumonia	 170.81	 136.20	0.024

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	Tuberculosis	167.30	101.70	
	Extra Pulmonary TB	113.47	38.78	
	Fungal pneumonia	46.20	18.41	
	Bacterial pleural effusion	230.00	9.12	

Table 4: Association between etiology and CD4 count (N=95)

CD4 count per mm3, n (%)					
Sl. No.	**Type etiology**	**< 100**	**100-200**	**> 200**	**P value**
1	Bacterial etiology				0.172
	Yes	8 (32.0)	9 (36.0)	8 (32.0)	
	No	22 (31.4)	37 (52.9)	11 (15.7)	
2	Fungal etiology				0.005
	Yes	5 (100)	-	-	
	No	25 (27.8)	46 (51.1)	19 (21.1)	
3	Tubercular etiology				0.019
	Yes	15 (27.3)	33 (60.0)	7 (12.7)	
	No	15 (37.5)	13 (32.5)	12 (30.0)	

DISCUSSION

A total of 95 HIV infected patients were included in this study. Among them males accounted for 64% of the population. Shilpa et al, Garchar S et al, Rooku KC et al, Singh RP et al, Mehta AA et al and Nissapatorn V et al,[1,2,5-8] also reported male predominance. This may be related with exposure to smoking which is more commonly practiced by males than females and among HIV infected population; male smokers were more likely to develop early airway dysfunction and manifestations than female smokers.

In this study, maximum numbers of patients were in the age group 31-40 years with 31.6% followed by 41-50 years (26.3%) and minimum in 18-30 years group with 7.4%. The mean age of the study population in the current study was 46.82 ± 10.58 years. Previous studies done by Rooku KC et al, Singh RP et al, Mehta AA et al and Jaryal A et al,[1,5,6,9] reported the most commonly affected age group in their study was 31-40 years and mean age of the patients was 34.94 year (range 22-56 years). Thus, most of the studies demonstrated most of their study population to be young adults in the range of 25 to 45 years, which is in line with our study's finding.

In the current study, majority of the study population were married (84.2%) and most of the patients were daily wage labourers (52.6%) followed by businessmen in 20 % and only 4.2% were servicemen. Similarly, maximum number of the patients were educated and only few patients were illiterate (18.9%) in the present study. These findings are comparable with findings made by Garchar S et al, Shilpa et al, Mehta AA et al and Giri PA et al.[1,2,7,10]

Majority of the patients were currently using oral tobacco (93.7%) and 20% of the patients were current alcohol user. Only 8.4% of the patients were IDU. Smoking was currently done by 23.2% of the patients. Rooku KC et al,[5] also reported 35% of their study population to be smoker and 24% to be alcohol user.

In the present study, the most common symptoms were cough (68.4%) followed by fever (56.8%) and shortness of breath (52.6%). Loss of appetite, general weakness and altered sensorium were seen in 31.6%, 17.9% and 18.9% of the patients respectively. Shilpa et al,[1] reported loss of appetite to be the commonest symptom. Singh RP et al,[6] reported fever to be the most common symptom (70%). Mehta AA et al,[7] reported the most common presenting complaints were cough (96%). Jaryal A et al,[9] also reported fever in 100% of their patients, cough in 57.4%, loss of appetite in 68.9%, weight loss in 55.1%, diarrhoea in 36.7% and neurological manifestation in 25.2% which is also similar to this study finding. Thus, most of the studies reported cough and fever to be the commonest presenting symptoms in their studies, which is in line with this study finding.

The common routes of infection were heterosexual route and IDU followed by homosexual route in 7% of the study population. Garchar S et al,[2] reported maximum of their study population had heterosexual (94%) route of infection followed by blood transfusion (3%). Singh RP et al,[6] reported heterosexual sex was the most common route of transmission. Mehta AA et al,[7] reported the commonest mode of acquiring the infection was through heterosexual contact (68%). Nissapatorn V et al,[8] reported the most frequent route of transmission were heterosexual. Thus most of the studies have reported sexual route as the commonest route of transmission. Also in the current study the commonest route of transmission is heterosexual route (66%) which is followed by intravenous drug use (13%).

In this study, Chest X ray was done in all the patients, and it showed abnormality in 90% of patients. CT scan was done in 25% of the patients. Five patients showed features of extensive ground glass appearance with septal thickening and multiple lung cyst suggestive of pneumocystic jirovecii pneumonia (PJP), one case showed widespread small nodules (miliary pattern) throughout the lung field. Maximum of the patient had consolidation with 66.3% on imaging followed by fibrosis (25.3%) and pleural effusion (18.9%). Miliary mottling was seen in only one patient. Shilpa et al2 reported consolidation was the most frequent presentation accounting for 75% of the total respiratory cases in their study population.

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Study conducted by Swaminathan S, et al,[12] showed that HIV seropositive patients with pulmonary TB were having normal chest radiographs in 14.2% cases, miliary TB in 10% cases, pleural effusion in 16.6%, cavitations in 17.8%, while maximum number of cases (65%) showed infiltrates. Similarly, the study conducted by Perlman DC et al,[12] also showed infiltrates in maximum (43.75%) of cases of HIV positive pulmonary tuberculosis. Mehta AA et al,[7] reported on chest radiography pulmonary infiltrates/opacities in 64% of their study population followed by pleural effusion in 18%, mediastinal lymphadenopathy in 16%, cavitation in 10% and military in another 10% of their study population which is more or less similar to this study's finding. Jaryal A et al,[9] found pulmonary infiltrates, pleural effusion, cavity, military lesions and fibrosis on chest radiography among their study population. Zuber A et al, Baril L et al and Sircar AR et al reported similar radiological findings consisting of multi-lobar consolidation, bilateral involvement with either patchy bronchopneumonia or alveolo-interstitial infiltrates.[13-15] Thus, the maximum of the studies reported infiltrates or consolidation/ opacities as the commonest radiography finding which is in line with this study finding. The spectrum of pulmonary manifestations of HIV disease globally varies due to differences in current availability of effective ART programs and regular intake of ART. The current study also includes patients not under ART. In resource limited settings, AIDS-related infectious complications such as Pneumocystis carinii pneumonia and pulmonary tuberculosis are still predominant.

Majority the patients in this study had pulmonary tuberculosis (42.1%) followed by bacterial pulmonary infection (22.1%) and tubercular pleural effusion (15.8%). Only 5.3% and 4.2% of the patients had fungal infection and bacterial pleural effusion, respectively. In the present study 10.5% of the patients had undetermined etiology. Extra pulmonary tuberculosis was seen in 13 patients. Out of these cases, six cases were with tubercular meningitis and 5 cases were with abdominal tuberculosis and one with disseminated tuberculosis. Oral candidiasis was also seen in 17 cases while cryptococcal meningitis was seen in 7 cases and diarrhoea was found in 10 cases in the present study.

In this study, maximum number of the infections were due to Mycobacterium tuberculosis (57.8%), followed by Klebsiella pneumoniae (9.5%). Bronchoscopy was done in 18 patients, out of which 09 patients were diagnosed as cases of PTB, 04 as cases with PJP, two each with E. coli and Klebsiella pneumonia, and one case was positive for both E. coli and Talaromyces marneffei. Shilpa et al,[1] reported Mycobacterium tuberculosis to be the most frequent opportunistic pathogen accounting for 59.52% of cases and pneumocystis in 35.72% of all the respiratory infections. Garchar S, et al,[2] also reported tuberculosis to be the most common opportunistic pulmonary infection among their HIV infected study population. Singh RP et al,[7] reported tuberculosis to be the common cause followed by bacterial pneumonia in 28.6% and fungal pneumonia in 2.8%. Mehta AA et al,[7] reported Tuberculosis (72%) to be the most common respiratory infection followed by bacterial pneumonia as the second most common infection (22%).

In the present study the mean value of CD4 count was higher in patients under medication of ART than those patients who were not under medication. But the difference was not statistically significant. On further analysis the mean value of CD4 count was significantly lesser in patients with fungal pneumonia (46.20 ± 18.41 cells/mm3) in comparison to bacterial pneumonia (170.81 ± 136.20 cells/mm3) and tuberculosis (167.30 ± 101.70 cells/mm3). All the fungal infected patients had their CD4 cell count less than 100 cells per mm3 and maximum number of the patients with tubercular infection had CD4 count within the range of 100 to 200 cells per mm3 of blood. And there was a significant association between tubercular infection and low CD4 count of within 100 to 200 per mm3. But there was no association between bacterial infection and CD4 count. Shilpa et al,[5] reported the mean CD4 count to be 190 cells/mm3 for candidiasis, 217.72 cells/mm3 for tuberculosis and 212 cells/mm3 for cryptosporidiosis. Vajpayee M, et al,[16] reported a different observation, that median CD4 count for candidiasis was 189/mm3, tuberculosis was 189.15 cells/mm3. Rooku KC, et al,[5] reported a significant association between lower CD4 count and the infections by bacteria and fungi. The lower the CD4 count, the higher the rate of colonization by bacteria and fungi. Thus CD4 counts were lower among HIV patients with pulmonary manifestation which is in line with this study finding. Further this study showed that patients with extrapulmonary tuberculosis and fungal infections have lower CD4 count in comparison to bacterial and pulmonary tuberculosis. This was also supported by a study conducted by Ogba OM, et al,[17] where they found fungal pleural infections having significantly lower CD4 count in comparison to other non-fungal pleural infection among HIV infected study population.

CONCLUSION

Pulmonary infection is common among HIV-seropositive population, especially among the males in the productive age group. Cough, fever and shortness of breath are the commonest symptoms. Hence, caregivers need to be vigilant of these symptoms in the HIV-seropositive population. Pulmonary tuberculosis is the most common pulmonary infection followed by bacterial pulmonary infection. Among bacterial infections (other than mycobacterium), Klebsiella pneumonia was the commonest followed by Escherichia coli and Staphylococcus aureus. And among fungal pathogens, Pneumocystis jirovecii was the

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commonest in this study conducted at a tertiary care hospital in Manipur, unlike the findings of studies conducted elsewhere. Most of the infections were commonly seen in low CD4 count < 200 cells/mm3. Lower CD4 count was seen in fungal infection than other pulmonary infections. Overall, the conclusions drawn from the study advocate for improved healthcare strategies, including regular screening for opportunistic infections, timely initiation of antiretroviral therapy (ART) and targeted interventions to reduce the burden of TB and other OIs in HIV-positive populations.

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