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TO STUDY THE CLINICAL, RADIOLOGICAL AND MICROBIAL PROFILE OF PULMONARY INFECTION IN IMMUNOCOMPROMISED PATIENTS

Medicine

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ABSTRACT

BACKGROUND The lung is one of the most frequently involved organs in complications of immunocompromised host. Among these, pulmonary infection is the most common complication. The chest radiograph is initial diagnostic tool for detection of suspected pulmonary infection in immunocompromised. However, chest radiograph findings are nonspecific in determining pathogens. The early use of Computed Tomography (CT) is helpful in detecting pulmonary lesions which may not be evident on routine chest radiographs. But there is overlap of CT finding in different infections. This study is therefore, designed to document the clinical, radiological & microbial profile of pulmonary infection in immunocompromised patients.

AIM To study the clinical, radiological and microbial profile of pulmonary infection in immunocompromised patients, and to study diagnostic yield of sputum examination, induced Sputum examination & bronchoscopic BAL examination.

METHODS The present prospective descriptive observational study was conducted in the Department of Chest Medicine at King Edward Memorial Hospital, Pune. It included immunocompromised patients with lower respiratory tract infection symptoms. A total number of 70 indoor & OPD patient with urban & rural background were included in the study. Among them 45 patients were HIV reactive group and 25 patients were having Non-HIV immunocompromised condition. All of them had pulmonary infection. The study was conducted over a period of 15 months.

RESULTS Incidence of pulmonary infection was higher in age 31-40 years (28.58%). There were 51 males and 19 females. Opportunistic infections were more common in males as compared to females. Majority of immunocompromised patients were HIV reactive (64.3%) followed by of Malignancy (15.7%). Focal non homogenous opacity (37.5%) was most common radiological finding followed by consolidation with air brochogram (25%). Pulmonary Tuberculosis (40.5%) was most common opportunistic infection in immunocompromised patients followed by bacterial (30.38 %) and fungal infections (17.72%). Sputum (40.98), induced sputum examination (19.29), and Bronchoscopy with BAL (91.42%) had good diagnostic yield in diagnosis of pulmonary infection in immunocompromised patients.

CONCLUSION Induced sputum had less diagnostic yield in immunocompromised patients and also it is time consuming.Early bronchoscopy with BAL remains crucial to establish the diagnosis in immunocompromised patients with pulmonary infection when the cause is infectious in nature.

KEYWORDS

Pulmonary Infection, Immunocompromised Patients, Induced Sputum, Bronchoscopy with BAL

INTRODUCTION

"Immunocompromised host" defined as a condition in which individual is susceptible to life-threatening infection as a result of a primary or acquired abnormality of the immune system. Most patients of immunodeficiency are acquired but some people are born with defects in their immune system (primary immunodeficiency). With medical advances, the population of immunocompromised host has expanded enormously, reflecting the increased use of immunosuppressive agents for the treatment of malignancies, collagen vascular diseases, autoimmune disorders & for the prevention of rejection in solid organ transplant recipients. Also, HIV/AIDS pandemic has resulted in the existence of many immunocompromised patients.

The lung is one of the most frequently involved organs in complications of immunocompromised host. Among these, pulmonary infection is the most common complication and accounts for about 75% of pulmonary complications with high morbidity and mortality. Bacterial, fungal, viral & mycobacterial pathogen may infect immunocompromised patient[3].

The chest radiograph is initial diagnostic tool for detection of suspected pulmonary infection in immunocompromised. It help in detection of pattern of the abnormality and its rate of progression on serial images in the diagnosis. However, chest radiograph findings are nonspecific in determining pathogens.The early use of Computed tomography (CT) is helpful in detecting pulmonary lesions which may not be evident on routine chest radiographs. But there is overlap of CT finding in different infections[3]. Because, several infections can present with similar clinical & radiological features in immunocompromised patients, the cause of pulmonary infection is challenging in this setting. The specific aetiology should be sought and for this sputum examination, induced sputum examination, bronchoscopy with bronchoalveolar lavage (BAL) studies & trans bronchial biopsies (TBLB), CT guided lung FNAC and trucut biopsies in appropriate individuals are the investigational procedures in diagnosis, to start early therapeutic interventions and to decrease morbidity & mortality.This study is therefore, designed to document the clinical, radiological & microbial profile of pulmonary infection in immunocompromised patients.

AIM

- To study the clinical, radiological and microbial profile of pulmonary infection in immunocompromised patients.
- To study diagnostic yield of sputum examination, induced Sputum examination & bronchoscopic BAL examination.

METHODS

The present prospective descriptive observational study was conducted in the Department of Chest Medicine at King Edward Memorial Hospital, Pune. It included immunocompromised patients with lower respiratory tract infection symptoms. A total number of 70 indoor & OPD patient with urban & rural background were included in the study. Among them 45 patients were HIV reactive group and 25 patients were having Non-HIV immunocompromised condition. All of them had pulmonary infection. The study was conducted over a period of 15 months (From September 2014 to November 2015).

INCLUSION CRITERIA

Patients included in this study were those who present with lower respiratory tract infection symptoms like cough,sputum production, breathlessness, and fever with underlying disease like:

- HIV/ AIDS
- Malignancy on chemotherapy and radiotherapy
- Solid organ transplant
- Hematopoietic cell transplants
- Individuals on immunosuppressive therapy

EXCLUSIONCRITERIA

- Immunocompromised patients without respiratory symptoms
- Patient not willing to give consent

- Pediatric age group less than 12 years of age
- Uncooperative patient

Procedure

A detailed history was taken and clinical examination was done. Aassessment of oxygenation (usually by pulse oximetry) was done.History of presence of human immunodeficiency virus (HIV) infection, history/treatment of TB, malignancy, solid organ transplant history, use of immunosuppressive & corticosteroid medicine was documented. Investigations were performed to find out the cause of pulmonary infection.

Specimen obtained for microbiological evaluation were:

- Sputum
- Induced Sputum
- Bronchial washing or BAL

Table 1: Staining Procedures used in for the Study

Staining Method	Pathogens
Gram stain	Bacteria
Ziehl Neelsen stain (20% acid fast)	Mycobacteria
10% KOH mount	Fungi
Saline mount	Fungi, parasites
Modified Ziehl Neelsen stain (1% acid fast)	Nocardia
Methenamine silver stain	P.jiroveci.
India Ink preparation	Encapsulated yeasts
Giemsa stain	P.jiroveci.

Data Collection and Statistical Analysis

All the data pertaining to detailed history including medication history, clinical examination & investigations were collected as per study proforma. Data analysis was performed by using SPSS (Statistical Package for Social Sciences version 19.0).In this observational study we described the quantitative data by Mean/SD/Range /Median and qualitative data expressed in frequency and percentage.A 'p' value was calculated using Fisher's exact test of significance for categorical variables. The p-values less than 0.05 are considered to be statistically significant.

RESULTS

In this study, incidence of pulmonary infection was higher in age 31-40 years (28.58%) followed by in age group more than 50 years (22.86%). There were 51 males and 19 females, giving a male to female ratio of 2.6:1. Opportunistic infections were more common in males as compared to females. Majority of immunocompromised patients were HIV reactive (64.3%) followed by of Malignancy (15.7%). Results showed 80% HIV reactive patients were on HAART and among all the patients, only 14 % of patients had past history of previous Tuberculosis infection.

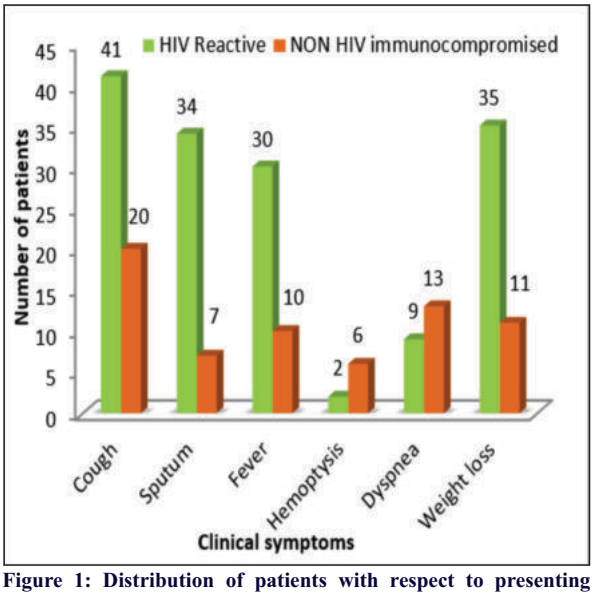

Figure 1: Distribution of patients with respect to presenting complaints

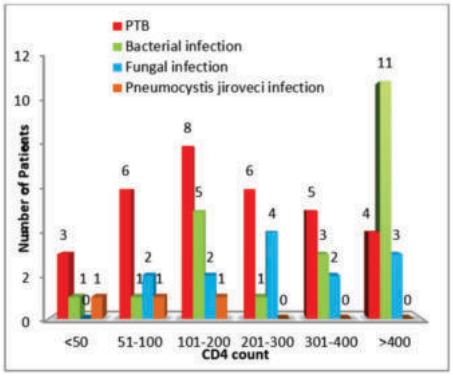

Figure 2: Distribution of CD4 count with respect to various pulmonary infections

Cough (87.14%) was most common presenting complaints, and 58.66% of all opportunistic infections seen with CD4 counts less and equal to 300 cells per cumm. Further, disseminated infections (80%) was more commonly seen with immunocompromised patients with CD4 counts < 300 per cumm.

Table 2: Spectrum of Chest Radiology finding

Chest X-Ray Findings	HIV Reactive	Non-HIV Immunocompromised	Total	Percentage
Normal	3	2	5	6.25
Non homogenous Opacity	21	9	30	37.5
Consolidation	10	10	20	25
Miliary TB	2	1	3	3.75
Cavity	3	2	5	6.25
Ground Glass Opacity	1	1	2	2.5
Pleural Effusion	4	1	5	6.25
Non-Specific Findings	5	5	10	12.5

As per table 2, focal non homogenous opacity (37.5%) was most common radiological finding followed by consolidation with air brochogram (25%). Normal chest radiograph also seen in 6.25 % patients. Further, as per Fisher's Exact Test, HIV reactive patients having CD4 count less than 200 cells per cumm, had predominant lower lobe involvement on chest radiography.

Table 3: Distribution of opportunistic Pulmonary infection in Immunocompromised Patients

Diagnosis	HIV Reactive	Non-HIV Immunocompromised	Total	Percentage (%)
Pulmonary tuberculosis	24	8	32	40.5
Bacterial infection	12	12	24	30.38
Fungal infection	7	7	14	17.72
Viral pneumonia	3	3	6	7.60
Pneumocystis jiroveci infection	3	0	3	3.80
Total	49	30	79	100

Table 3 shows that Pulmonary Tuberculosis (40.5%) was most common opportunistic infection in immunocompromised patients followed by bacterial (30.38 %) and fungal infections (17.72%). Further, figure 3 below shows that total 79 opportunistic pulmonary infections were seen in 70 patients.

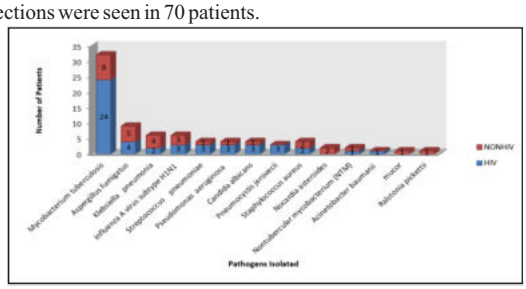

Figure 3: Distribution of spectrum of pathogens

9 patients (11.39%) had polymicrobial infection. Pulmonary Tuberculosis (40.50%) was most common opportunistic infection followed Aspergillus fumigatus (11.40%), Klebsiella pneumoniae &Influenza A virus subtype H1N1 (7.60%) in immunocompromised patients. In addition, nine patients (11.39%) had polymicrobial infection. Fisher's Exact Test showed no association between incidence of drug resistant tuberculosis in HIV and non-HIV immunocompromised. Further, MDR Pulmonary TB infection was observed in 6 patients (18.75 %) of total Pulmonary tuberculosis patients.

Table 4: Distribution ofDiagnostic Modalities that Yielded Final Diagnosis

Method	Positive yeild in number of patients	Diagnosticyeild
Sputum Examination	25/61	40.98%
Induced Sputum Examination	11/57	19.29%
BAL	32/35	91.42%
TBLB	1/2	50%
CT guided Biopsy	1/1	100%
RT PCR(In Patient of H1N1)	6/8	75%
Post mortem Biopsy	1/1	100%
Total	77	

Sputum (40.98) and induced sputum examination (19.29) had good diagnostic yield in diagnosis of pulmonary infection in immunocompromised patients. Bronchoscopy was performed on 35 patients. Bronchoscopic findings revealed that inflamed bronchial mucosa was most common finding. Secretion was seen in many patients mostly mucoid in nature and few patients associated with mucopurulent secretion; and Whitish lesion were seen on mucosa suggestive of Candida. Bronchoscopy with BAL had good diagnostic yield (91.42%) in diagnosis of opportunistic infection in immunocompromised patients. Thus, Bronchoscopy with BAL should always be performed especially when sputum and induced sputum was non-contributory for microbiological diagnosis.

Six patients throat swab were positive for H1N1 influenza A infection from National Institute of Virology, Pune. H1N1 infection also seen in immunocompromised patients as Maharashtra state specially Pune had the highest number of H1N1 bronchopneumonia patient with high mortality (83.33%). Five out of six patients with H1N1 Infection died despite of good ICU care and medical management.

DISCUSSION

In this study, the mean age of the immunocompromised patients was 40 years, and in a similar study, JA Crocket et al, studied 86 immunocompromised patients with a mean age of 45 years. Also, most of the HIV positive patients belonged to the age group of 31 to 40 years of age with mean age of the patients was 37.92 years. This is the age of maximum outdoor involvement and sexually active age. This reflects the route of transmission of the HIV virus in these individuals. Similar demographic profile with young male predominance has been observed by other studies[5]. Most of Non-HIV Patients shows high incidence in age group above 50 years (52%) which mainly constitute malignancy patients. In study by Shreevaidya et al in 2011 reported that majority of malignancy patients with pulmonary infections belonged to age group 51-60 years of age (47.7%) followed by 41-50 years of age (15.9%). Thus, this study correlates with the above report in parameters of age distribution. In our study male gender predominated in study population. Similar observation made in study by JA Crocket et al,[7] out of total 86 patients 68 (79.07 %) were males and 18 (20.93%) females.

In this study, cough (87.14%) is the most common symptom but not always associated with expectoration, here lies the value of induced sputum and bronchoscopy. Significant relationship was observed with TB symptoms like cough, fever and weight loss and pulmonary tuberculosis patients. Similar results noted in other study from India.Patel et al studied 50 patients with HIV -TB infection and reported most common symptom was cough in 47 (94%) patients. Further, the study shows that 71.87% of pulmonary tuberculosis (n=23) infection with HIV reactive patients had CD4 count less than 300 cells per cumm. Mean CD4 count in HIV patient with Pulmonary TB coinfection was 200.7 cells per cumm. In studies conducted in India, reported that TB is unique in that it can occur over a wide range of CD4 count, although it is more frequent at CD4 counts less than 300 cells per cumm.Jaryal et al reported all the patients with disseminated tuberculosis had CD4 count below 200/cumm in HIV reactive patients. Chest radiology finding in our study showed that unilateral non-homogenous opacities (37.5%) most common finding followed by consolidation (25%). FB Demirkazık et al studies 57 immunocompromised patients with haematological malignancy reported consolidations most common finding with bacterial infection. Chest X ray shows 20 patients with unilateral involvement (7 upper lobe and 13 lower lobe), 3 with bilateral involvement (2 miliary TB). Of 7 patients with upper lobe opacity, 5 had CD4 count more than 200 cell per cumm. Out of 13 patients with lower lobe involvement 12 had CD4 count less than 200 cells per cumm. In study by Mahesha Padyana et al in 200 HIV patients found that Non homogenous opacities (Infiltration) (39%) followed by consolidation (30%), cavity (11%), and lymphadenopathy (9%) seen with CD4 less than 200 cells per cumm. Also reported that infiltration (37.5%) followed by cavity (25%) and miliary (25%) is more common in HIV reactive patients with CD4 above 200cells per cumm.

In this study, among the respiratory pathogens, Mycobacterium tuberculosis constituted the maximum number (40.50%) followed by other bacterial infections (30.38%) and fungi (17.72%). The high incidence of AFB in our study was unexpected but not surprising. Mycobacterium tuberculosis is endemic in India thus, is the commonest opportunistic infection in India.A study conducted in 2007 by Lazaro Veleza et al on 101 immunosuppressed patients at Colombia, reported that mycobacteria TB (26.7%) is most common cause of pulmonary infection followed by bacteria (18.8%) and Pneumocystis jirovecii (17.8%). Predominant aetiology varied according to immunosuppression.

In this study, sputum examination including staining and culture yielded diagnosis in 25 out of 61 patients with yield of 40.98%. Most of patients presented in advanced stage with extensive nature of disease that had resulted in good diagnostic yield from simple sputum examinations. In study by Rano et al,sputum analysis was performed in 96 patients but only 88 samples were accepted for microbial analysis, 27 of which (22 spontaneous, five induced) resulted in a positive culture (31%). When only the group of infectious aetiology was considered, this percentage increased to 46%. Induced sputum was performed in 57 patients out of which 11 patients (19.29%) yielded the final bacteriological diagnosis. Rosemeri Maurici Da Silva et al studied roles of induced sputum for the diagnosis of lung disease in HIV-positive patients shown that sputum induction presented 57.5% sensitivity, 42.9% specificity, 87.1% predictive positive value, 13% predictive negative value and 55.6% overall accuracy. Thus, induced sputum had less diagnostic yield in Non-HIV immunocompromised patients and also it is time consuming. Though in suspected patient of Pulmonary tuberculosis in HIV reactive patients it could have good diagnostic yield. The reason low sensitivity of induced sputum result may be paucibacillary nature of disease. Some studies have reported that sputum smears are frequently negative for AFB in patients with advanced HIV disease[8].

Bronchoscopy with BAL was performed in 35 patients, out of which 32 patients had yield of 91.42% final diagnosis. Diagnostic yield of Bronchoscopy with BAL was 100% for nosocomial causes of pneumonia in one prospective review of hospitalized renal transplant recipients.The overall yield of diagnostic FOB is variable, ranging from 30 to 73% in SOT recipients, with the highest yield for infection during the first 6 months after transplantation[10].In study by S Shawgi et al in haematological malignancy reported that BAL fluid examination and culture grew microbial isolates in 21 of 25patients (84%). Because of the importance of obtaining a diagnosis, BAL should always be performed especially when sputum and induced sputum is non-contributory for microbiological diagnosis. Although the diagnostic yield of surgical biopsy is high, associated mortality limits its use as a first-line diagnostic modality in transplant patients.

CONCLUSION

Pulmonary infections remain a vexing problem in the care of the immunosuppressed patient like HIV-AIDS, chemotherapy, transplant recipients and patients on immunosuppressive drug therapy. The differential diagnosis of pulmonary infections in this setting is broad. It is important to search for both infectious and non-infectious aetiologies. No one pattern of symptoms or radiographic findings conclusively points to a diagnostic possibility. Low CD4 count less than 300 cells per cumm suggests decreased immune status and higher chances of opportunistic infections and high mortality.Mycobacterium Tuberculosis is the commonest opportunistic infection in immunocompromised patients in the tertiary care hospital, Pune. HIV AIDS with advanced immunosuppression more often have extra-pulmonary and disseminated TB and also risk factor for development

of drug resistant tuberculosis. Atypical radiological presentations of pulmonary tuberculosis are more common as CD4 count goes below 200 cells per cumm. High index of suspicion kept for diagnosis of tuberculosis in such patients.Induced sputum had less diagnostic yield in immunocompromised patients and also it is time consuming.Early bronchoscopy with BAL remains crucial to establish the diagnosis in immunocompromised patients with pulmonary infection when the cause is infectious in nature. Overall Bronchoscopy is minimally invasive and safe procedure in experienced hands.Influenza A infection H1N1 type (swine Flu) had highest mortality in immunocompromised patients.

Limitations of the Study

1. The sample size was small and there was limited prospective follow up. Statistical analyses therefore have limited power.
2. Among infectious causes viral aetiology was not diagnosed except H1N1 swine flu infection due to unavailability of its diagnostic facility.
3. As there was no diagnostic facility for paediatric population less than 12 years and almost every patient was treated based upon empirical and clinical background. So paediatric population less than 12 years of age not included in the study.

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