International Journal of Advances in Medicine
Chockalingam P et al. Int J Adv Med. 2018 Feb;5(1):207-215
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: http://dx.doi.org/10.18203/2349-3933.ijam20180086

Original Research Article

Role of bronchoscopy in diagnosis of pulmonary infections in non-HIV immune compromised host

Palaniappan Chockalingam, Deepaselvi Meyyappan*

Institute of Thoracic Medicine, Madras Medical College, Tamil Nadu, India

Received: 06 January 2018
Accepted: 18 January 2018

***Correspondence:**
Dr. Deepaselvi Meyyappan,
E-mail: deepabibhuvi@gmail.com

ABSTRACT

Background: The occurrence of pulmonary infections is a common life threatening complication in immunocompromised patients, necessitating timely diagnosis and specific treatment. In our study bronchoscopic diagnostic techniques that include fiber optic bronchoscopy (FOB) and bronchoalveolar lavage (BAL) were applied in non-HIV immunocompromised conditions to determine the aetiology infectious microorganisms and comparing the clinical characteristics with bronchoscopic yield and to assess the influence of these methods on therapeutic outcome in this population.
Methods: This prospective observational study was conducted at Rajiv Gandhi Government General Hospital, Park Town, Chennai, for a period of 8 months from January 2016-August 2016. After meeting the requirements of eligibility criteria, the study included 65 immunocompromised patients consecutively who presented with pulmonary diseases. The primary outcome measure was the diagnostic yield of bronchoscopy among non-HIV immunocompromised patients. The secondary outcome measures were collecting the data including etiology of different microorganisms and non-infectious causes of pulmonary diseases among non- HIV immunocompromised patients, comparing the symptoms at the time of presentation, different radiological pattern with bronchoscopic yield and comparing the different subgroups of non-HIV immunocompromised patients with regards to presenting symptoms, radiological patterns, bronchoscopic yield, treatment modification, different spectrum of infections and complications.
Results: The mean age of the patients was 41.91 ranging from 15-74 years. Majority (n=36) patients showed chest symptoms alone. On bronchoscopy, 52 cases (80%) out of 65 showed positive results and negative result was noticed in 13 cases (20%). Among them bacterial infections were predominant with 24%. After BAL culture bacterial culture was positive in 23 (35%) patients and fungal culture was positive in 15 (23%) cases. After bronchoscopy, current treatment plan was changed in 37 patients and clinical improvement was seen in 26 cases i.e. yield of bronchoscopy was 71%. Minor complications were noticed in 16 cases after bronchoscopy.
Conclusion: Our study concludes, in clinically stable patients FOB was the preferred technique for finding the cause of lung infiltrates in non-HIV immunocompromised patients. Because our results signify that the yield of bronchoscopy was high (80%) despite empirical antimicrobial therapy.

Keywords: Bronchoscopy, Pulmonary infections, Non-HIV immune compromised patients

INTRODUCTION

The immune compromised host is defined as a person who has an alteration in phagocytes, the humoral or cellular immunity that increases the risk of infectious complication.[1] There is a growing group of individuals apart from acquired immunodeficiency syndrome (AIDS) who are now immune suppressed like, those receiving immune suppressants for solid organ transplants (SOT), bone marrow transplant (BMT), connective tissue

diseases (CTD) or treated with chemotherapeutic agents for cancer. Widespread use of "biological agents", which are generally antibodies targeting specific cell type or pathway of inflammation, has further expanded the susceptible population. Managing systemic infections are challenging in such patients among which pulmonary infection is very frequent. The development of pulmonary disease among such patients is considered as a serious problem. The differential diagnosis includes infectious and many non-infectious causes. Given the broad spectrum of potential infections and non-infectious causes, coupled with inherent toxicities of many therapies, a specific microbiological and cytopathological diagnosis should be considered essential to the management of pulmonary infections in non-HIV immune compromised host.[2]

Noninvasive test available can be done easily with less risk, but overall, they are of little diagnostic use and their yield is also low. So invasive strategies become essential for management of pulmonary diseases. Among the invasive test bronchoscopy and bronchoalveolar lavage (BAL) has proved to be the procedure with good yield and is well tolerated even in critically ill patients, with a low complication rate. It also leads to the most appropriate diagnosis. The sensitivity and specificity for diagnosing pulmonary infections is also good.[3,4] Early diagnosis and appropriate treatment reduces the mortality and increases survival benefits. Hence, early bronchoscopy if possible before starting antibiotic therapy remains crucial in the management of immune compromised host with pulmonary infections.

The study was conducted with the primary objective to study the diagnostic yield of bronchoscopy among non-HIV immunocompromised patients. The secondary objectives of the study was to collect data on etiology of different microorganisms and non-infectious causes of pulmonary diseases among non-HIV immunocompromised patients, comparing the symptoms at the time of presentation, different radiological pattern with bronchoscopic yield and comparing the different subgroups of non-HIV immunocompromised patients with regards to presenting symptoms, radiological patterns, bronchoscopic yield, treatment modification, different spectrum of infections and complications.

METHODS

The present study was a prospective observational study conducted at Rajiv Gandhi Government General Hospital, Park Town, Chennai, for a period of 8 months from January 2016 – August 2016. The study included immunocompromised patients consecutively who presented with pulmonary diseases. No controls were used in the study. A total of 592 patients referred from other departments like oncology, nephrology, rheumatology, hematology above the age of 12 years to Thoracic medicine department for evaluation of pulmonary diseases were screened for the study.

Eligibility criteria

Inclusion criteria

Patients having chest symptoms like cough, sputum, breathlessness, chest pain, hemoptysis with or without fever. Abnormal auscultatory findings like crackles, wheeze with or without symptoms and presence of pulmonary infiltrates in radiography were included in the study.

Exclusion criteria

All HIV positive patients, all sputum AFB smear positive pulmonary tuberculosis cases, patients having very poor general condition, very severe breathlessness, recent history of myocardial infarction and patients not fit for bronchoscopy and patients not willing to give informed written consent were excluded from the study.

Study procedure

After obtaining informed consent from all the participants complete history of the patients was collected in a predesigned proforma. General examination and a structured clinical examination of the respiratory system and other systems were done. Basic blood investigations were done in all patients like complete blood count, renal function test, bleeding time, clotting time, prothrombin time, activated partial thromboplastin time. Chest skiagram anteroposterior, lateral view, routinely plain computed tomography (CT CHEST) chest/contrast enhanced computed tomography chest (CECT-CHEST)/high resolution computed tomography chest (HRCT- CHEST) were done as required depending on the patient's diagnosis and clinical status. Careful pre-evaluation and cardiac fitness which includes an echo was done prior to fiber optic bronchoscopy (FOB) in all patients.

Sample size

Study protocol showing participants flow was given in Figure 1. After meeting the requirements of eligibility criteria, a total 65 patients completed the study. After completion of FOB, bronchoalveolar lavage (BAL) sample was sent for analysis according to internationally accepted guidelines to determine infectious etiology.[5]

Treatment modification and follow up

Patients were allowed to continue with same empirical treatment until the results of bronchoscopy were available. Appropriate Treatment modification was done based on the results. Patients diagnosed as tuberculosis were started on anti-tuberculous treatment (ATT).

For bacterial infections antimicrobials were changed as per culture sensitivity pattern if needed. For fungal infections antifungals were started in patients with proven and probable invasive fungal infections. Patients diagnosed with malignancy and lymphoma was referred

back to oncology department for restarting chemotherapeutic regimens. Patients were followed up until the signs of clinical improvement or discharge or death in hospital. Post discharge patients were enquired for clinical improvement during their follow up visits to the hospital or through telephone calls.

Statistical analysis

All statistical analysis was performed using the statistical package for social science (SPSS, version 17) for Microsoft windows. Descriptive statistics were presented as numbers and percentages. Chi-square test was used for comparison between two attributes. A two-sided p value <0.05 was considered statistically significant.

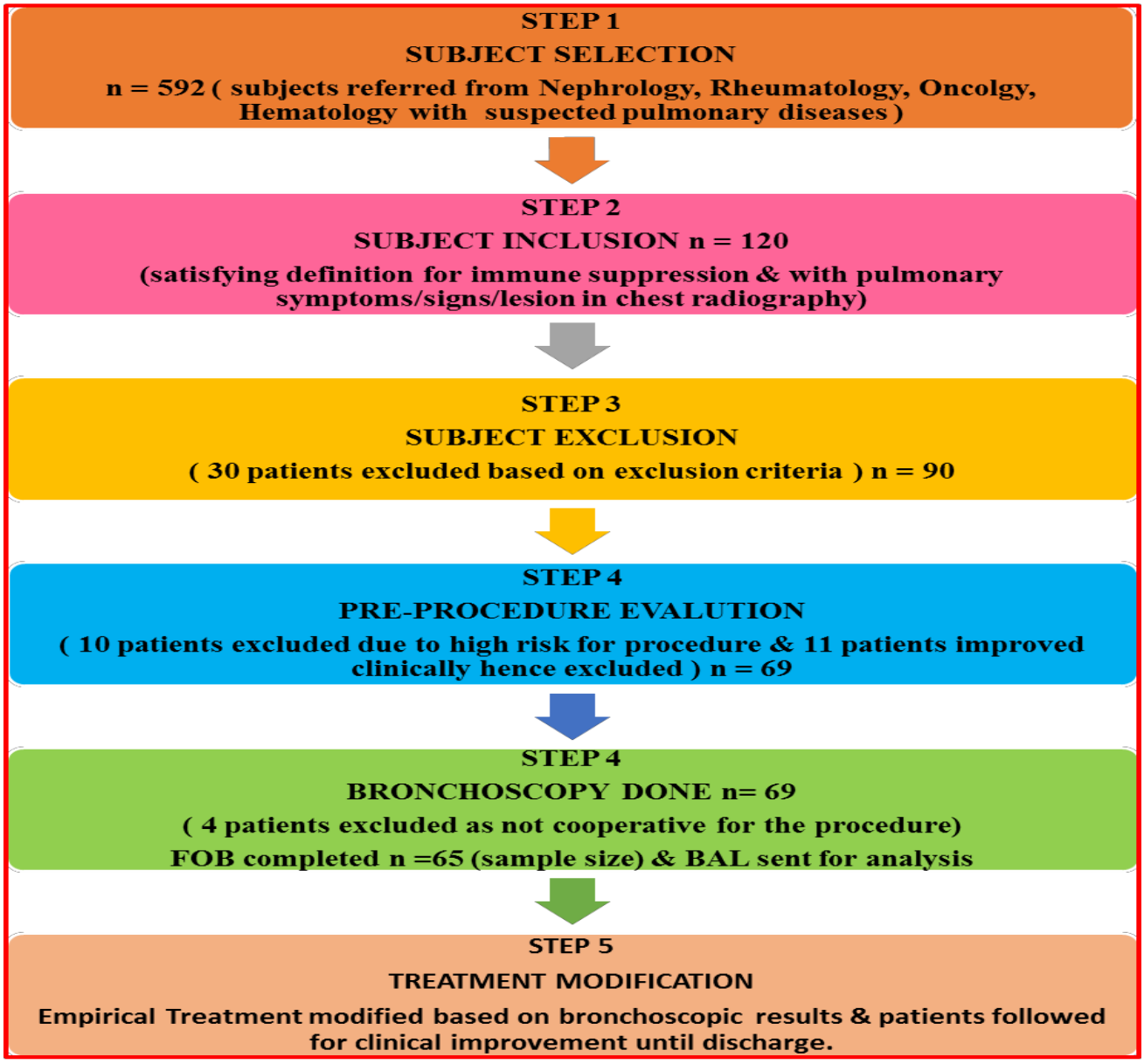

Figure 1: Study protocol.

RESULTS

A total of 592 patients were screened from the study. Of them 527 were excluded from the study and 65 patients were included in the study. Table 1 presents the demographic and clinical characteristics of the patients. The mean age of the patients was 41.91 ranging from 15-74 years. The patients were equally divided among two age groups <40 years & >40 years with 51% and 49% respectively. 36 were male and 29 were females. Based

on the disease pattern and nature of immunosuppression 65 patients were divided into 5 groups. Majority (n=36) patients showed chest symptoms alone. The radiological findings at the time of presentation were divided into groups based on the predominant pattern as assessed by the pulmonologist. Consolidation, GGO, cavity, tree in bud was considered together as alveolar pattern and reticular and nodular predominant forms were considered as non-alveolar pattern. Most of the patients (n=27) were affected with lower lobe infection.

Table 1: Demographic and clinical characteristics of the study participants.

Characteristics	Frequency (n=65)	(%)
Age		
<40 years	33	51
>40 years	32	49
Sex		
Male	36	55
Female	29	45
Grouping based on nature of immunosuppression		
Cancer chemotherapy group	11	17
Post renal transplant group	9	14
Chronic kidney disease group	16	25
Haematological malignancies	8	12
Connective tissue diseases	21	32
Symptoms		
Chest symptoms alone	36	55
Chest symptoms with fever	11	17
Hemoptysis	9	14
Fever alone	6	9
Asymptomatic	3	5
Radiological findings		
A) alveolar pattern	51	79
Consolidation	31	48
Ground glass opacities	9	14
Cavity	7	11
Tree in bud appearance	4	6
B) non-alveolar pattern	14	21
Reticular pattern	8	12
Nodular pattern	6	9
Lobe involvement		
Upper lobe	21	32
Middle lobe/lingula	17	26
Lower lobe	27	41

As indicated in Table 2, on bronchoscopy, 52 cases (80%) out of 65 showed positive results and negative result was noticed in 13 cases (20%). Out of the 52 cases positive bronchoscopic yield 42 (65%) were due to infectious etiology. Among them, bacterial infections were predominant with 24%, followed by mixed infections by 15%, tuberculosis 14% and fungal 12%. Remaining 10 (15%) were due to non-infectious causes. Most of them related to malignancies (n=6).

Table 2: Yield of bronchoscopy.

Bronchoscopic yield	Frequency (n=65)	(%)
Infectoius etiology	42	65
Bacterial alone	15	24
Tuberculosis alone	9	14
Fungal alone	8	12
Mixed	10	15
Non-infectious	10	15
Malignancy diagnosed by cytology/ HPE	6	9
Hogkins lymphoma-lymphomatous infiltration	1	1.5
Radiation fibrosis	1	1.5
Alveolar haemorrhage	1	1.5
Interstitial fibrosis	1	1.5
No diagnosis	13	20

Table 3 presents the spectrum of bacterial and fungal infections after BAL culture in study population. Out of 65 patients, bacterial culture was positive in 23 (35%) patients and fungal culture was positive in 15 (23%) cases.

Table 3: Spectrum of bacterial and fungal infections.

Isolates of BAL culture	Frequency (n=65)	(%)
Bacterial culture		
Bacterial alone + (bacterial + other organisms (TB/fungal))	15+8	35
Streptococcus pneumonia	1	1.5
Klebsiella pneumoniae	5	7.5
Pseudomonas aeruginosa	7	10.5
Acinetobacter	3	4.5
MRSA	5	7.5
Enterococci	2	3
E. coli	1	1.5
Negative for bacterial culture	42	65
Fungal culture		
Fungal alone isolated + (Fungal + other organisms)	8+7	23
Candida albicans	2	3
Candida tropicalis	1	1.5
Candida parasilopsis	1	1.5
Penicillium marneffi	1	1.5
Aspergillus niger	4	6
Aspergillus fumigatus	3	4.5
Aspergillus flavus	2	3
Aspergillus versicolor	1	1.5
Negative for fungal culture	50	77

Table 4: Complications of bronchoscopy.

Complications	Frequency (n=65)	(%)
Transient hypoxemia	10	15
Minor bleeding	5	8
Pneumothorax	1	1
No complications	49	76

Out of 65 immunocompromised patients, after bronchoscopy and BAL culture TB was noticed in 15 patients (24%). Of them tuberculosis alone was detected in 9 patients and in remaining 6, TB was detected with other organisms (Table 4).

On bronchoscopy, 49 (76%) cases did not show any complications and in remaining 16 (24%) minor complications were present (Table 5).

Table 5: Treatment modification.

Treatment plan	Frequency (n=65)	(%)
ATT started	15	23
Antibiotics	8	12
Antifungals	9	14
Chemotherapy	5	8
No change	28	43

After bronchoscopy, current treatment plan was changed in 37 patients. ATT was started in 15 cases, antibiotics in 8 cases, antifungals in 9 cases and chemotherapy in 5 cases (Table 5). Of them, 26 patients (71%) improved clinically, 4 patients died due to other comorbidities, 4 patients lost to follow up and in remaining 3 cases the condition was not improved (Table 6).

Table 6: Clinical improvement on follow up.

Condition on follow up	Frequency (n=37)	(%)
Improved clinically	26	71
Died due to comorbidities	4	11
Lost follow up	4	11
Not improved	3	8

Table 7 presents the comparison of clinical characteristics with yield of bronchoscopy. Out of 65, symptoms were noticed in 52 patients. Positive yield of bronchoscopy in patients with fever alone as presenting symptom gave a yield of 91%, followed by chest symptoms with fever with 78% patients. Yield was negative in asymptomatic patients. Yield of bronchoscopy was 100% positive in group of patients with cavities determined by radiology. The upper lobe disease had a better yield of 95% compared to middle and the lower lobe involvement.

Based on bronchoscopy, current treatment was modified in (n=37, 57%) patients. For them yield of bronchoscopy was positive in 71% cases.

Table 7: Comparison of clinical characteristics with yield of bronchoscopy.

Characteristics	Yield on bronchoscopy		
	Positive N=52 (%)	**Negative N=13 (%)**	**Total N=65 (100%)**
Symptoms			
Chest symptoms with fever	10 (91)	1 (9)	11
Chest symptoms alone	28 (78)	8 (22)	36
Haemoptysis	8 (89)	1 (11)	9
Fever alone	6 (100)	0 (0)	6
Asymptomatic	0 (0)	3 (100)	3
Radiological presentation			
Consolidation	27 (87)	4 (13)	31
Ground glass pattern	7 (78)	2 (22)	9
Tree in bud pattern	3 (75)	1 (25)	4
Cavity	7 (100)	0 (0)	7
Reticular/nodular pattern	8 (57%)	6 (43)	14
Lobe involvement			
Upper lobe	20 (95%)	1 (5)	21
Middle lobe	12 (70%)	5 (30)	17
Lower lobe	20 (74%)	7 (26)	27
Treatment modified			
Yes	37 (57)	0 (0)	37 (57)
No	15 (23)	13 (20)	28 (43)

Analysis of different subgroups of immunocompromised patients was given in Table 5. Group-1 is the cancer patients receiving chemotherapy contributes to 17% (n=11) of total population. Of them 1 (1.5%) had lung cancer. had oesophageal cancer, 1 (1.5%) had stomach cancer, 5 (8%) had cancer to pharynx and 2 (3%) had breast cancer. 55% of patients presented predominantly with chest symptoms. 18% had acute/short duration of symptoms (<3 weeks) remaining 72% had symptoms for more than >3 weeks. When compared to other groups cancer group had longer duration of symptoms possibly because of more non- infectious nature of pulmonary disease (p=0.001). Nodular involvement in this group was 36% compared to only 4% in other groups. This was statistically significant with P value 0.008. Focal involvement was seen in 82% as against diffuse involvement (2 or more lobes) seen only in 18%. In cancer only 36% of pulmonary lesions were infective remaining 64% non- infectious cause. In other groups, non-infectious cause contributed to only 6%. This was statistically significant with chi-square P value 0.000. Overall, only 36% patients clinically improved when compared to other groups with 80% clinical improvement with a change in treatment. This was statistically significant with P value 0.003. Minor bleeding episodes in this group is 27% compared to other groups with 4%, which is statistically significant with P value 0.031.

Table 8: Analysis of different subgroups of immunocompromised patients with clinical charcteristics.

Characteristics	Group 1 (n=11) %	Group 2 (n=9) %	Group 3 (n=16) %	Group 4 (n=8) %	Group 5 (n=21)%
Symptoms					
Chest symptoms with or without fever	6 (55)	6 (67)	10 (62.5)	4 (50)	4 (19)
Haemoptysis	-	-	4 (25)	-	-
Duration of symptoms					
<3 weeks	2 (18)	8 (89)	10 (62.5)	3 (37.5)	11 (52)
3-8 weeks	4 (36)	1 (11)	6 (37)	2 (25)	7 (33)
>8 weeks	5 (46)	-	-	1 (12.5)	2 (10)
Asymptomatic	-	-	-	2 (25)	1 (5)
Radiological presentation					
Consolidation	5 (46)	6 (67)	12 (75)	2 (25)	6 (29)
Cavity	2 (18)	2 (22)	3 (19)	2 (25)	3 (14)
Nodular	4 (36)	-	-	2 (25)	-
Reticular	-	-	-	1 (12.5)	7 (33)
Tree lobe	-	-	-	-	2 (10)
GGO	-	-	-	1 (12.5)	3 (14)
Lobe involvement					
Lower lobe	4 (36.4)	5 (55)	8 (50)	1 (12.5)	9 (42.9)
Upper lobe	3 (27.3)	3 (33)	4 (25)	5 (62.5)	6 (28.6)
Middle lobe	4 (36.4)	1 (12)	4 (25)	2 (25)	6 (28.6)
Etiology					
TB	1 (9)	1 (11)	2 (12)	1 (12.5)	4 (19)
Bacterial	1 (9)	1 (11)	3 (19)	1 (12.5)	5 (24)
Fungal	2 (18)	1 (11)	2 (13)	3 (38)	
Mixed	-	2 (22)	4 (25)	-	4 (19)
Malignancy	6 (54)	-	-	1 (12.5)	
Radiation fibrosis	1 (9)	-	-	-	1 (5)
No diagnosis		1 (11)	5 (31)	2 (25)	6 (28)
Treatment modification					
ATT	1 (9)	1 (11)	5 (30)	1 (12.5)	7 (33)
Antibiotic	-	3 (33)	2 (12.5)	-	3 (14)
Antifungal	2 (18)	2 (22)	2 (12.5)	2 (25)	1 (5)
Second line chemotherapy	3 (27)	-	-	1 (12.5)	1 (5)
Clinical improvement	4 (36)	7 (78)	6 (75)	4 (50)	17 (81)
Yield on bronchoscopy	11 (100)	8 (88.8)	11 (69)	6 (75)	15 (71)
Organisms isolated					
Streptococcus pneumonia	-	1 (11)	5 (31)	1 (12.5)	7 (33)
Klebsiella pneumoniae	-	1 (11)	2 (12.5)	1 (12.5)	-
Pseudomonas aeruginosa	1 (9)	2 (22)	1 (6.25)	-	3 (14.2)
Acinetobacter	-	2 (22)	1 (6.25)	-	
MRSA	-	1 (11)		-	3 (14.2)
Enterococci	-	-	1 (6.25)	-	1 (4.7)
E. coli	-	-	-	-	1 (4.7)
Pseudomonas aeruginosa+ MRSA	-	-	-	-	1 (4.7)
Candida albicans	-	1 (11)	1 (6.25)	1 (12.5)	-
Candida tropicalis	-	-	-	-	-
Candida parasilopsis	-	1 (11)	-	-	-
Penicillium marneffi	-	-	1 (6.25)	-	-
Aspergillus niger	1 (9)	1 (11)	1 (6.25)	1 (12.5)	-
Aspergillus fumigatus	1 (9)	-	-	1 (12.5)	1 (4.7)
Aspergillus flavus	-	-	1 (12.5)	-	-
Aspergillus versicolor	-	-	-	-	1 (4.7)
Complications					
Bleeding	3 (27)	-	-	1 (5)	-
Transient hypoxemia	-	5 (55)	5 (31)	-	-
Pneumothorax	-	-	-	-	1 (5)
Others	-	-	1 (6)	-	-

Group-2 is the post renal transplant patients receiving immunosuppresive drugs. This group contributing to 13.8% (n=9) of the total population. 67% patients had fever with or without chest symptoms at time of presentation compared to 20% in other groups. Out of 9 patients, 8 had a positive yield (89%) contributing 17% of overall positive yield. This was statistically significant with P value 0.003. Bacterial infections were more common in this group, 67% compared to other groups. Spectrum of bacterial infections was more common in this group even after more than 6 months after transplant. Transient hypoxemia was frequently observed (55% vs. 9% in the rest). Statistical significance was P value 0.004.

Group-3 is the chronic kidney disease patients on maintanence haemodialysis. This group contributing to 25% (n=16) of the total population studied. Presence of fever was lesser in this group similar to cancer groups. All patients had an alveolar pattern in radiology like when compared to 71% in other groups which was statistically significant with P value 0.016. There were no non-infective causes like in the renal transplant group. Out of mixed infections 3 were due to tuberculosis. (Tuberculosis + Bacteria-1, Tuberculosis + Fungal -2, Bacterial + Fungal -1). The predominant complication was transient hypoxemia, which required oxygen therapy during and after procedure in 31% (n=5).

Group-4 is the patients with haematological malignancies. This group contributed about 12% (n=8) of the total population. Chest symptoms were main presenting symptoms with 50%, followed by 25% with fever and remaining 25% were asymptomatic. The noninfectious case was a Lymphomatous infiltration in a patient with Hodgkin's Lymphoma presenting with right upper lobe consolidation, which was proven by Trans Bronchial lung biopsy.

Group-5 is the connective tissue disease (CTD) patients on corticosteroids/immunosuppressive drugs/biological agents. This group constituted around 32% (n=21) of the total studied population. Only 19% had fever with or without chest symptoms at time of presentation as compared to 81% who did not have fever, possibly because of high level of immune suppression induced by drugs. The most common radiological pattern in this group is the reticular pattern due to the presence of underlying interstitial lung disease. Diffuse disease is more common in this group than other groups (48% vs. 18%). This was statistically significant P value 0.013. Overall complications in this were less when compared to other groups.

DISCUSSION

The present study included sixty-five non-HIV immunocompromised patients with pulmonary diseases. The main goal of our study was to evaluate the diagnostic utility of early bronchoscopy in non-HIV immunocompromised patients and the therapeutic utility in terms of treatment modification and clinical improvement as the result of bronchoscopic intervention.

This is the first kind of study done in of non-HIV immunocompromised population at our tertiary care hospital. The purpose of doing the study was because of lack of studies done in our Indian population on bronchoscopic evaluation of pulmonary diseases especially in non-HIV immunocompromised patients. Studies are only available in different subgroups like hematological malignancies, CKD, renal transplant recipients etc. With better chemotherapeutic drug availability for management of malignancies, well-functioning organ transplant programs, increased use of potent immunosuppresive drugs and newer biological agents for managing connective tissue diseases, more people are made immunocompromised for therapeutic reasons for management of their primary diseases. Ultimately more and more patients are developing pulmonary diseases and the number of referrals is being increased to the pulmonology department for their management.

Most of these patients are already been treated empirically with multiple potent antimicrobial drugs before being referred to our Pulmonary medicine department. There is also increasing demand from other departments to start empirical antituberculosis treatment once patient does not improve with empirical antimicrobial therapy. Even some of the non-infectious causes like pulmonary edema, alveolar hemorrhage, and malignancy are misdiagnosed and treated as infectious empirically. Because of this empirical treatment approach, there is increased economic burden, toxicity of antimicrobial therapy, increased incidence of multidrug resistant organisms and delay in starting proper treatment. This study highlights the role of early bronchoscopy in immunocompromised patients with pulmonary diseases that are not improving with empirical treatment with regards to its diagnostic yield, safety and change in empirical treatment. Patients were also followed up to look for clinical improvement.

The mean age of the patients was 41.91 ranging from 15–74 years. The bronchoscopic yield was almost similar in both age groups with 81% in <40 years and 78% in >40 years. There was no statistical difference in yield, symptomatology, radiology or infections in both groups. Out of 65 patients included in study, 36 were male and 29 were females. Similar observations were also made by Jain et al in his study on 104 immunocompromised patients with lung infiltrates.[6]

Chest symptoms alone were the most common presentation with 55%, followed by chest symptoms along with fever in 17% patients. 5% of patients were asymptomatic. Presence of fever gave a higher overall yield of 95%. In asymptomatic patients, yield was zero. The statistical significance in chi-square P value was 0.004. Brownback et al, observed similar findings where

the diagnostic yield was significantly improved in the presence of fever.[7]

52% of patients presented with acute symptoms <3 weeks, followed by 31% with symptoms 3-8 weeks duration and 12% with >8 weeks duration. 5% were asymptomatic. Cancer chemotherapy group had longer duration of symptoms (72% with symptoms >3 weeks duration) at the time of presentation. Post renal transplant (89%) and CKD patients (69%) more often had shorter duration of symptoms (<3 weeks). The statistical significance was P value <0.05. The reason for more acute presentation in renal transplant and CKD group is because the pulmonary diseases were more of infectious etiology especially bacterial. In cancer group the disease process was mainly malignant infiltration hence fever was absent, and they presented more gradually.

Consolidation was the predominant pattern seen in 48%, followed by GGO with 14%, reticular pattern 12%, cavity 11%, nodular 9% and tree in bud 6%. Cavitary disease had a maximum yield of 100%, followed by consolidation with 87%. Reticular pattern had the lowest yield of 57%. Yield was better in an alveolar pattern of involvement in radiography. Brownback et al and Danes et al, in their study also had similar findings, unilateral and alveolar pattern in radiography had a better diagnostic yield.[7,8]

Lower lobe involvement was most common with 41% followed by upper lobe with 32% and middle lobe/lingula with 26%. Focal involvement (single lobe) was more common with 78%. Yield was better in upper lobe involvement and focal involvement with 95% and 85% respectively.

The overall yield of bronchoscopy in our study was 80% with no diagnosis obtained in remaining 20%. 65% were due to infectious causes and 15% were due to non-infectious etiology. Similar studies done in immunocompromised patients have shown wide variations in overall yield ranging from 50-80%. But in most of the studies yield has been high for an infectious etiology ranging from 60-80% similar to our study.[8-11] A similar study done in the Indian population of Menon et al.[12] He studied 16 renal transplants, 14 dialysis, 8 HIV positive patients, and the clinical utility of BAL in diagnosis of pulmonary infections. The overall yield was 76% of all the three groups put together. BAL cytology had a better yield when compared to culture.

Our study results showed that in our tertiary care hospital among the immunocompromised patients bacterial infections were the predominant cause of pulmonary infections (35% overall, 23% by bacterial alone and 12% of bacterial+other organisms). Among the bacterial isolates *Pseudomonas* was the most common, followed by equally by *Klebsiella* and MRSA. This pattern is similar to the microbiological spectrum of hospital acquired pneumonia where gram negative organisms and MRSA are more common. These results are in accordance with several other published studies.[13,14]

Tuberculosis was the second most common infectious cause (24% overall, TB alone 14% and TB + other organisms 10%). In spite of excluding sputum AFB positive cases from the study, still the incidence of tuberculosis is quite high in our study. This highlights the importance of thoroughly searching for pulmonary tuberculosis among non-HIV immune compromised patients with pulmonary disease in high prevalence countries even if the sputum AFB smear is negative. Chan et al in his study conducted in Hong Kong among 62 non-HIV immunocompromised patients found a similar result with tuberculosis being the second most common infection with a 19% incidence.[15]

Aspergillus species was the most common fungi isolated from respiratory tract of non-HIV immunocompromised patients in our study. Among *Aspergillus* species *niger* was the most common, followed by *fumigatus*. Similar studies done in Non-HIV immunocompromised patients show that among fungal infections *Aspergillus* is most common similar to our study.[8,13,14]

In our study, 15% of pulmonary infiltrates were due to non-infectious causes. Among them most common cause (9%) was malignancy diagnosed by cytology or endobronchial biopsy and the remaining (6%) were due to radiation fibrosis, alveolar hemorrhage, interstitial pneumonia and lymphomatous infiltration of the lung in a case of secondary pulmonary lymphoma.

Complications of bronchoscopy in our study were only minor except one case of pneumothorax which required ICD insertion. The overall complication rate was 24%. Transient hypoxemia during and within the first hour of bronchoscopy, which required supplemental oxygen occurred in 15%, followed by mild to moderate bleeding episodes during biopsy procedures occurred in 8%. Bleeding controlled by wedging the bronchoscope at the site of bleeding and cold saline instillation. Pneumothorax occurred in 1%. Previous studies have shown the complication rate among non-HIV immunocompromised patients ranging from 13%-21%.[6,13] In general population, studies have shown the complication rate ranging widely from 5%-32%, with serious complication in 1.1% and mortality of 0.02%. There was no procedure related mortality in our study. Hence the proper pre procedural evaluation, patient selection and monitoring and care during/post procedure is necessary.

In our study empirical treatment was modified to the most appropriate treatment in 57% of patients based on bronchoscopic results which was statistically significant with P value 0.000 Studies have shown similar results like our study where treatment modification based on bronchoscopic yield has ranged from 38%-51%.[12,16-18] The treatment modification rate was higher in our study

compared to other studies. Among patients in whom treatment was modified, those in whom antibiotic were changed as per culture sensitivity pattern showed maximum clinical improvement with 90%, followed by those in whom anti tuberculosis treatment was started showed 70% improvement and those in whom antifungals were started 60% clinical improvement. Those patients in whom malignancy was diagnosed and second line chemotherapeutic agents restarted only 20% showed clinical improvement probably because of their advanced nature of the disease. The overall clinical improvement with treatment modification was around 70%.

CONCLUSION

The results of the study conclude that bronchoscopy was a useful tool among non-HIV immunocompromised patients with pulmonary diseases with good diagnostic yield and therapeutic utility despite empirical antimicrobial therapy. For clinically stable patients early bronchoscopy before starting empirical treatment can be the preferred approach. Patients, who are clinically unstable or not fit for procedure, early empirical treatment is advised, followed by bronchoscopy once the general conditions improve or if the patient does not respond to empirical therapy. Hence, when encountered with a non-HIV immune compromised patient with pulmonary disease, early bronchoscopy must be preferred, as the benefits outweigh the risk.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Pizzo PA. Fever in Immunocompromised Patients. N Engl J Med. 1999;341:893-900.
2. Grippi MA, Elias JA, Fishman JA, Kotloff RM, Pack AI, Senior RM, et al. Fishmans textbook of pulmonary medicine. 5th edition. Mc Graw Hill Education;2015:4006.
3. Meyer KC, Raghu G, Baughman RP, Brown KK, Costabel U, du Bois RM, et al. American Thoracic Society Committee on BAL in Interstitial Lung Disease. An official American Thoracic Society clinical practice guideline: the clinical utility of bronchoalveolar lavage cellular analysis in interstitial lung disease. Am J Respir Crit Care Med. 2012;185:1004-14.
4. Efrati O, Sadeh-Gornik U, Modan-Moses D, Barak A, Szeinberg A, Vardi A, et al. Flexible bronchoscopy and bronchoalveolar lavage in pediatric patients with lung disease. Pediatr Crit Care Med. 2009;10(1):80-4.
5. Technical recommendations and guidelines for bronchoalveolar lavage (BAL). Report of the European Society of Pneumology Task Group. Eur Respir J. 1989;2:561-85.
6. Prasoon Jain, Sunder Sandur, Yvonne Meli, Alejandro C. Arroliga, James K. Stoller, Atul C. Mehta. Role of flexible bronchoscopy in immunocompromised patients with lung infiltrates. Chest. 2004;125(2):712-22.
7. Kyle R. Brownback Association of bronchoalveolar lavage with computer tomogram and symptoms in immunocompromised patients. Annuals Thoracic Med. 2013;8(3):153-9.
8. Danés C, González-Martín J, Pumarola T, Rañó A, Benito N. Pulmonary in filtrates in immunosuppressed patients: analysis of a diagnostic protocol. J Clin Microbiol. 2002;40(6):213440.
9. Kahn FW. Analysis of Bronchoalveolar Lavage Specimens from Immunocompromised Patients with a Protocol Applicable in the microbiology laboratory. J Clin Microbiol. 1988;26(6):1150-5.
10. Baughman RP. Use of bronchoscopy in the diagnosis of infection in the immune-compromised host. Thorax. 1994;49:3-7.
11. Vélez L, Correa LT, Maya MA, Mejía P, Ortega J, Bedoya V, et al. Diagnostic accuracy of bronchoalveolar lavage samples in immunosuppressed patients with suspected pneumonia: Analysis of a protocol. Respir Med. 2007;101:2160-7.
12. Menon LR, Divate S, Acharya VN, Mahashur AA, Natrajan G, Almeida AF. Utility of bronchoalveolar lavage in the diagnosis of pulmonary infections in immunosuppressed patients. J Assoc Physicians India. 2002;50:1110-4.
13. Shorr AF, Susla GM. Pulmonary Infiltrates in the Non-HIVInfected Immunocompromised Patient, Etiologies, Diagnostic Strategies, and Outcomes. Chest. 2004;125(1):260-71.
14. Rañó A, Agustí C, Benito N, Rovira M, Angrill J. Prognostic factors of non-HIV immunocompromised patients with pulmonary infiltrates. Chest. 2002;122(1):253-61.
15. Chan JC, So SY, Lam WK, Mary SM. High incidence of pulmonary tuberculosis in the non-HIV infected immunocompromised patients in Hong Kong. Chest. 1989;96(4):835-9.
16. Du Rand IA, Blaikley J, Booton R, Chaudhuri N, Gupta V, Khalid S, et al. British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults, 2013. Thorax 2013;68:1-i44.
17. Hsu AA, Allen DM, Yeo CT, Ang BS, Ong YY . Bronchoscopy in immunocompromised host with pulmonary infiltrates. Ann Acad Med Singapore. 1996;25(6):797-803.
18. Hummel M, Rudert S, Hof H, Hehlmann R, Buchheidt D. Diagnostic yield of bronchoscopy with bronchoalveolar lavage in febrile patients with hematologic malignancies and pulmonary infiltrates. Ann Hematol. 2008;87(4):291-7.

Cite this article as: Chockalingam P, Meyyappan D. Role of bronchoscopy in diagnosis of pulmonary infections in non-HIV immune compromised host. Int J Adv Med 2018;5:207-15.