

Evaluation of diagnostic outcomes of non-resolving pneumonia by fiberoptic bronchoscopy

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Abstract:

Background: Non-resolving pneumonia (NRP) is a cause of concern among treating physicians due to its diagnostic dilemma. Bronchoalveolar lavage (BAL) is an important tool in diagnosing non resolving pneumonia. This study was undertaken to evaluate non resolving pneumonia by fiberoptic bronchoscopy and BAL to find the etiological diagnosis.

Methodology: A prospective observational study was done at a tertiary care centre, Rajarajeswari Medical College and Hospital Bangalore over the period of one and a half year. Total 64 cases of non-resolving pneumonia were included and patients were evaluated thoroughly by history, clinical examination, radiological tests like chest X-ray and CT-chest, laboratory investigations like white blood cell count, sputum culture and bronchoscopic BAL culture were obtained in all patients.

Results: 64 patients enrolled in the study out of which 46 (71.87%) male and 18(28.125%) female, mean age of the patients was 52.6 ±11.2. unilateral lung involvement was in 48(75%) of the patients and right lung was most commonly involved in 39(60.93%) patients. The bronchoscopic findings of mucosal inflammation and purulent secretion were most common findings in 36(56.25%). Bacterial culture was positive in 52(81.25%) in BAL analysis, among that Klebsiellae pneumoniae was most common organism in 23(35.93%). BAL AFB smear was positive in 7(10.93%) and 9(14.06%) positive for CBNAAT test.

Conclusions: NRP is difficult to treat and diagnostic dilemma for physicians. Bronchoscopic interventions like BAL show significant results in etiological diagnosis of non-resolving pneumonia. Timely intervention of FOB BAL helps in treating patients of non-resolving pneumonia.

Keywords: Fiberoptic bronchoscopy; Non resolving pneumonia.

Introduction:

Pneumonia is a common clinical condition requiring admission and treatment with antibiotics. Patients usually respond rapidly with good clinical outcomes. The dilemma arises when patients with pneumonia have delayed resolution or persistence of radiographic infiltrates despite treatment with a course of antibiotics ranging from ten to fourteen days [1].

Slowly resolving or non-resolving pneumonia is defined as clearance of radiographic infiltrates of up to 50% in two weeks or incomplete resolution within four weeks [2].

Mortality of patients with non-resolving pneumonia remains a concern as delay in establishing a diagnosis leads to increase in mortality rates [3]. Non resolving pneumonias have been attributed to be caused by impaired host defences, resistant microorganisms, tuberculosis, malignancies, inadequate antibiotic therapy, non-infectious causes and in patients greater than 50 years of age [4,5].

Due to diagnostic dilemma and difficulty in treating of non-responding pneumonia early interventions to find the etiological diagnosis like CT chest and bronchoscopic evaluation by bronchoalveolar lavage BAL is required to aid in the treatment. As mentioned in many studies bronchoscopic evaluation by bronchoalveolar lavage and bronchial brushing or bronchial biopsy can successfully diagnose the etiological cause in 90% of patients [6].

The aim of the present study was to determine the aetiological diagnosis in cases of non-resolving pneumonia with timely intervention by fiberoptic bronchoscopy (FOB) and BAL, biopsy and to assess the yield of FOB in establishing the etiological diagnosis to aid in the treatment.

Materials and Methods:

The study was a prospective observational study done in the department of respiratory medicine in a tertiary care centre over the period of one year six months from October 2016 to march 2018 after obtaining approval from the ethical committee of the institution.

64 patients of non-resolving pneumonia were selected for the study and analysed based on inclusion and exclusion criteria.

Inclusion Criteria

1. Patients having clinico-radiological evidence of pneumonia and meeting the criteria of non-resolving pneumonia as per the study, that is persistent clinical symptoms and signs such as cough with sputum production fever above 100°F, delayed radiographic clearance of less than 50% within 2 weeks and less than complete resolution within 4 weeks on serial series of chest radiography on at least two consecutive chest x-ray with AFB smear being negative for 2 consecutive days [2].

2. Patients above 18 years of age

Exclusion Criteria

1. Poor general condition
2. Patients who are sputum positive tuberculosis
3. Patients having pre-existing diagnosis of lung malignancies
4. Patients diagnosed with HIV
5. Uncooperative patients and patients who did not give consent for the study.

Materials and Methods:

All patients meeting inclusion and exclusion criteria were enrolled in the study. A detailed history of the patients were asked based on symptoms such as cough, fever, shortness of breath, chest pain, wheeze and past history of respiratory disease was asked to all patients and comorbid conditions was asked and noted in all patients. All the patients were examined thoroughly by general physical examination parameters such as clubbing cyanosis, icterus, lymphadenopathy, pedal oedema and respiratory system examinations parameters such as inspection, palpation, percussion and auscultation was done and findings was tabulated for analysis. Based on history and clinical findings, patients were subjected for blood investigations such as complete blood count, ESR, CRP. Relevant parameters were noted and tabulated for evaluation. Sputum examination was done for Gram stain, culture and sensitivity and AFB staining was done on two consecutive day's one sample before food and another sample after food.

All patients were examined radiologically by chest X-ray and CT chest and noted for relevant findings. Chest x-ray findings were categorised as unilateral involvement, bilateral involvement, right or left lung involvement. CT chest was noted for findings such as consolidation, cavities, mass lesions, lymphadenopathy, effusion and collapse.

Under all aseptic precautions fiberoptic bronchoscopy was done and bronchoalveolar lavage was taken and in relevant patients endobronchial biopsy

and bronchial brushing was done and histopathological examination was done and findings noted for study. Bronchoalveolar lavage was sent for analysis for Gram stain, culture and sensitivity and AFB staining and CBNAAT test, post bronchoscopy sputum analysis for AFB staining was done for all the patients.

Statistical Analysis: Statistical analysis was done using SPSS version 10.0 software for MS-windows. A descriptive analysis was done frequencies of parameters were expressed by mean, standard deviations, percentages and P value was calculated using Fisher's exact test and P value was considered significant if it was <0.05.

Results:

This study was done on 64 patients of non-resolving pneumonia in which 46(71.87) patients were male and 18(28.125%) were female 18(28.125%). The mean age of the patients were 52.6 with a standard deviation of about 11.2. Among 64 patients 36(56.25%) were smokers and 28(43.75%) were non-smokers. History of alcohol abuse was present in 7(10.93%) and 57(89.06%) had no history of alcohol abuse.

History of pre-existing lung disease was present in 7(10.93%) patients and among these patients, history of tuberculosis was present in 5(7.81%) patients and bronchiectasis was in 3(4.68%) and history of asthma and COPD patients was in 12(18.75%) and 8(12.5%) patients respectively.

Diabetes mellitus was the most common comorbid condition in our study patients which was present in 36(56.25%) patients followed by Hypertension which was present in 21(32.81%) of patients. There were three patients (4.68%) who had history of IHD none of the patients had recent history of IHD. There were 6(9.37%) patients who had other systemic diseases like benign prostatic hypertrophy, pancreatitis, liver disease and hypothyroidism. The details of demographic data and other characteristic and history of patients is depicted in Table 1.

Table 1: Patient demographic details and other characteristics

Total no patients (n= 64)	Number (%)	
Age	Mean \pm SD 52.6 \pm 11.2	
Sex	Male	46(71.87)
	Female	18(28.125)
Smoking status	Smoker	36(56.25)
	Non smoker	28(43.75)
History of alcohol abuse	Present	7(10.93)
	Absent	57(89.06)
History of lung disease	Tuberculosis	5(7.81)
	Bronchiectasis	3(4.68)
	Asthma	12(18.75)
	COPD	8(12.5)

Co morbidities		
	DM	36(56.25)
	HTN	21(32.81)
	IHD	3(4.68)
	Other Systemic disease	6(9.37)

In clinical features most common symptom was cough which was present in 57(89.06%) patients, followed by fever 48(75%), breathlessness 52(81.25%), chest pain 19(29.68%), haemoptysis 10(15.625%), wheeze 21(32.81%). There were 12(18.75%) who had history of weight loss.

On general physical examination mean respiratory rate of the patient was 22.4 ± 6.2 and mean temperature was 109.6 ± 1.6 and laboratory investigations showed mean of WBC count 9200 ± 3600 . On respiratory system examination 62(96.87%) had positive respiratory findings such as crepitation, bronchial breath sound, rhonchi. The details of clinical features depicted in Table 2 and 3.

Table 2: Clinical features symptoms:

	N (%)
Cough	57(89.06)
Fever	48(75)
Breathlessness	52(81.25)
Chest pain	19(29.68)
Haemoptysis	10(15.625)
Wheeze	21(32.81)
Loss of weight	12(18.75)
Positive respiratory findings	62(96.87)

Table 3: Clinical examination and laboratory test

	Mean \pm SD
Respiratory rate	22.4 ± 6.2
Temperature	109.6 ± 1.6
White blood cell count	9200 ± 3600

On radiological test chest X-ray, unilateral lung involvement was most common in 48(75%) and among that Right lung was most commonly involved 39(60.93%). on CT scan chest test all patients had consolidation with air-bronchogram in 64(100%) patients and 8(12.5%) had cavitary lesions. 3(4.68%) of the patients had mass lesion and 14(21.87%) patients had lymphadenopathy and 8(12.5%) had pleural effusion and 2(3.12%) had lobar collapse. The details Radiological examination was depicted in Table 4.

Table 4: Radiological findings

	Number (%)
Chest x-ray	
Unilateral	48(75)
bilateral	16(25)
Right	39(60.93)

Left	25(39.06)
CT Chest	
consolidation	64(100)
cavities	8(12.5)
Mass lesion	3(4.68)
lymphadenopathy	14(21.87)
Effusion	8(12.5)
Collapse	2(3.12)

Fiberoptic bronchoscopy was performed in all enrolled patients and the findings of bronchoscopy is depicted in Table 5 which shows mucosal inflammation and purulent secretion as most common findings in 14(21.87%) followed by endobronchial mass lesion in 14(21.87%) and mucus plugs were seen in 4(2.56%) none of the patients had external compression of bronchus. In patients having endobronchial mass lesion endobronchial biopsy/ bronchial brushing sample was taken for histopathological examination. 9(14.06%) patients were positive for malignancy and 2(3.12%) had granulomatous lesion.

Table 5: Fiber optic bronchoscopy and histopathological examination (HPE)

	N (%)
Endobronchial Mass lesion	14(21.87)
External Compression of bronchus	0
Mucous Plugs	4(2.56)
Mucosal inflammation and purulent secretions	36(56.25)
Normal	10(15.62)
Endobronchial biopsy/ Bronchial brushing positive for malignancy	9(14.06)
Granulomatous lesion in HPE	2(3.12)

All the patients underwent bronchoscopy, bronchoalveolar lavage was taken and examined for bacterial culture and sensitivity, AFB staining, and CBNAAT test. 52(81.25%) patients had bacterial culture positive for various organism and among bacterial culture *Klebsiella pneumoniae* was the most common aetiology followed by *Streptococcus pneumoniae* which was positive in 19(29.68%) and *Staphylococcus* was positive in 7(10.93%) and *E-coli* was positive in 3(4.68%) patients. 12(18.75%) shows no growth in bacterial culture examination of BAL. KOH smear was positive in 5(7.81%) patients. AFB smear was positive in 7(10.93%) and CBNAAT was

positive in 9(14.06%) the details of which is depicted in Table 6.

Table 6: BAL fluid analysis for infectious aetiology

	BAL
Bacterial	52(81.25)
Klebsiella pneumoniae	23(35.93)
Streptococcus pneumoniae	19(29.68)
Staphylococcus aureus	7(10.93)
Escherichia Coli	3(4.68)
NO Growth	12(18.75)
KOH Smear positive	5(7.81)
Acid fast bacilli smear Positive	7(10.93)
CBNAAT positive	9(14.06)

Discussion:

Our study was a prospective observational study done on 64 patients of non-resolving pneumonia who were enrolled in the study based on inclusion and exclusion criteria and yield of fiberoptic bronchoscopy. BAL was assessed and the result of which showed high yield of bronchoscopy BAL culture which was positive in 52(81.25%) which is in accordance with studies published. A study conducted by Weyers et al., which concluded fiberoptic bronchoscopy and BAL, brush biopsy and transbronchial biopsy can give the etiological diagnosis in up to 90% of the non-resolving pneumonia patients [6].

In our study mean age of the patients were 52.6 ±11.2 in which majority were male 46(71.87%) and 18(28.125%) were female. A study conducted by Fein et al., showed that in patients above 50 years age only 30% of patients had radiological resolution at four weeks [7]. In a study conducted by El Solh et al., concluded that age is main factor in resolution of pneumonia and stated that, chest x-ray resolution was found to be 35.1% by three weeks and 60% by six weeks in patients above the age of 70 years [8].

In our study majority were male 46(71.87%) and 18(28.125%) were female this was in concordance with the study conducted by Angele et al. and Schroer et al., they concluded that females are less likely to develop complications and this difference is male and female may be due biological response to and patterns of health care delivery [9,10].

In our study among 64 patients 36(56.25%) were smokers and 28(43.75%) were non-smokers. History of alcohol abuse was present in 7(10.93%) and 57(89.06%) had no history of alcohol abuse. In many studies smoking and history of alcohol abuse was directly correlated with occurrence of pneumonia and incidence of pneumonia were more common among smokers [11,12].

Diabetes mellitus was the most common co morbid condition in our study patients which was present in 36(56.25%) patients followed by Hypertension which

was present in 21(32.81%) of patients. Avijgan et al., concluded that diabetes mellitus was strongly associated with delayed response in the treatment of pneumonia, Begamy et al., also concluded that Klebsiella pneumoniae was most common in diabetes patients [13,14].

In our study cough was the most commonest symptoms in 57(89.06%) patients, followed by fever 48(75%), breathlessness 52(81.25%), chest pain 19(29.68%), haemoptysis 10(15.625%), wheeze 21(32.81%). A study conducted by Kirtland et al. concluded their study that coughs is the most common symptom in non-resolving pneumonia patients followed by chest pain, breathlessness, fever and hemoptysis [15].

Our study concluded that on doing chest X-ray, unilateral lung involvement was most common in 48(75%) and among that Right lung was most commonly involved 39(60.93%). In a study conducted by S.H Silver et al emphasised that for evaluating severity of illness radiography is an important tool in respect to multilobar involvement and bilaterality. our study concluded that right lung was most commonly involved than left which is in concordance with study conducted by Boyed et al., in which right lung was at more risk of slow resolution than left and his study also noted a predilection of chronic infiltrative disease for right upper lobe [17].

Our study concluded that the yield of fiberoptic bronchoscopy is very high in 52(81.25%) out of 64 patients which is in accordance with various studies done. As mentioned in many studies bronchoscopic evaluation by bronchoalveolar lavage and bronchial brushing or bronchial biopsy can successfully diagnose the etiological cause in 90% of patients [6]. In another study conducted by silver et al, Concluded that 86% of cases were successfully etiologically diagnosed for in particular infectious aetiology by fiberoptic bronchoscopy [17]. Balamugesh et al., also concluded that fiberoptic bronchoscopy is a very useful tool in assessment of non-resolving pneumonia [18].

In this study Klebsiella pneumoniae was the most common aetiology followed by Streptococcus pneumoniae which was positive in 19(29.68%) and staphylococcus was positive in 7(10.93%) and E-coli was positive in 3(4.68%) this is in accordance with the study in which it was concluded that non responding pneumonia was more common in patients in which initial empirical antibiotic was not covered for organisms like Kebsiella pneumoniae and Staphylococcus and Ecoli.20 In other studies conducted by Lin et al., Motayo et al., Arancibia et al., concluded that Klebsiellae pneumonia was most common infectious etiological diagnosis in non-resolving pneumonia.

Our study also concluded that 14(21.87%) patients had endobronchial mass lesions and on doing histopathological examination 9(14.06%) were positive

for malignant aetiology and BAL AFB was positive in 7(10.93%) and BAL CBNAAT was positive in 9(14.06) which showed that infectious aetiology is more common than non-infectious aetiology and among infectious aetiology pyogenic infections are more common than non pyogenic infections. These results were in accordance with studies done by Arancibia et al. the study was conducted on 444 CAP patients in which 30 patients had non resolving pneumonia in that infectious ecology was most common cause.

Conclusions:

Non resolving pneumonia is difficult to treat and diagnostic dilemma for treating physicians. We conclude that early interventions like bronchoalveolar lavage is useful tool in diagnosing the etiological cause, considering with our finding that infectious cause is the most common cause in particular to Klebsiellae pneumonia which was not responding to initial empirical therapy and was not diagnosed by routine sputum culture and sensitivity and can be diagnosed by early intervention of bronchoscopy and bronchoalveolar lavage.

Conflicts of Interest: None declared

Acknowledgements: None

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