

## Clinical and Etiological Profile of Unresolving Pneumonia Cases Attending Government Chest Hospital, Visakhapatnam

Dr. Vipparthi Surya kumari<sup>1</sup>, Dr. B.M.S. Pathrudu<sup>2</sup>, Dr. Raghumanda Sunil Kumar<sup>3</sup>,  
Dr. Gorantla Sambasiva Rao<sup>4</sup>, Dr. Sushmitha Jakka<sup>5</sup>, Dr. Sateesh Chandra Alavala<sup>6</sup>,  
Dr. Kona Muralidhara Reddy<sup>7</sup>

<sup>1,2,3</sup> Assistant professor in the Department Of Pulmonary Medicine, Government Hospital for chest and communicable diseases, Andhra Pradesh, India

<sup>4</sup> Professor & HOD in the Department Of Pulmonary Medicine, Government Hospital for chest and communicable diseases, Andhra Pradesh, India.

<sup>5,6</sup> Senior Resident in the Department Of Pulmonary Medicine, Government Hospital for chest and communicable diseases, Andhra Pradesh, India.

<sup>7</sup> DTCD 2<sup>nd</sup> Year Post Graduate student, Department Of Pulmonary Medicine, Government Hospital for chest and communicable diseases, Andhra Pradesh, India.

---

**Abstract:** Clinical and etiological profile of 30 cases of unresolving pneumonia attending GHCCD, Visakhapatnam was studied with special reference to demographic variables, etiology, symptomatology, location, bacteriology and outcome of medical management. The purpose of this study is to establish the etiological diagnosis of unresolving or slowly resolving pneumonia and to understand various modes of its presentation, clinical features, bacteriological and radiological features, complications and the clinical outcome of the study population.

**Keywords:** Etiological diagnosis, Outcome, Unresolving pneumonia.

---

### I. Introduction

Unresolving or slowly resolving pneumonia is not an infrequent clinical entity to the pulmonologists, and at the same time, can be a cause of concern in daily clinical practice. Pneumonia is defined as inflammation and consolidation of lung tissue due to an infectious agent. Bacterial pneumonia is caused by a variety of microorganisms with variable characteristics and antibiotic sensitivities. It presents a considerable challenge to the clinician. Unresolving or Non resolving pneumonia (NRP) is a commonly encountered problem and is a clinical diagnostic challenge for the treating physicians. The terms unresolving and slowly resolving pneumonia have been used interchangeably to refer to persistence of radiographic abnormalities beyond the expected time limit.[1] It is important to differentiate slowly resolving pneumonia from unresolving pneumonias because the causes of each of these two clinical entities are different. In general, slowly resolving pneumonias are due to antimicrobial or host defence factors and unresolving pneumonias are usually due to non infectious causes. Normal resolution of pneumonia is not easily defined. It can vary depending on the infecting organism and the host immune status. Patients typically note subjective improvement within 3-5 days of initiation of treatment.[2] In a study conducted by Kuru T et al., incorrect diagnosis, inadequate antibiotic therapy, impaired host defence, atypical organisms, resistant pathogens, non-infectious causes, tuberculosis, endobronchial lesions, etc. are the common causes of unresolving pneumonia.[3,4] Non infectious causes account for around 20% of cases of NRP in multicentric study.

The appropriate resolution rate for CAP depends to a great degree on age; comorbid factors, particularly the presence of an underlying disease; and factors such as alcohol abuse and social strata. The virulence of the infecting organism plays an important role in resolution rates, with Staphylococcus aureus, enteric gram negative pathogens and Legionella taking the longest to resolve, occasionally months; Mycoplasma resolving the fastest, at 2 to 4 weeks; and Chlamydia having an intermediate resolution rate.9,10 It is useful to determine if one is dealing with a slowly resolving process (i.e., <50% resolution in 1 month), the emergence of resistance, or treatment of the wrong pathogen or process. Physicians treating patients with CAP often are faced with dilemma of how to approach a patient with unresolving pneumonia. Amberson was the first person to describe the term "unresolved organising or protracted pneumonia" in 1943.34 There is lack of uniformity regarding the definition for unresolving pneumonia, but in many studies, the entity of "slow resolution" has been defined as failure of radiographic resolution by 50% in 2 weeks or failure of complete resolution by one month despite adequate antibiotic therapy.35 More recently, Fein and colleagues combined clinical and radiographic indices and defined unresolving pneumonia as "slow resolution of the radiographic infiltrates or clinical symptoms despite adequate antibiotic therapy".[5]

Pulmonary infiltrates that do not change substantially over time include those due to radiation pneumonitis, oxygen toxicity, bronchiolitis obliterans with organizing pneumonia, drug induced pneumonitis, idiopathic pulmonary fibrosis and malignancies.[6] Malignancies, particularly bronchoalveolar carcinoma, may present with post obstructive pneumonias. In addition, lymphangitic spread of carcinomas may present as diffuse pulmonary infiltrates that do not resolve over time. Lymphomas, particularly Hodgkin's lymphoma, with extension from the mediastinum into the parenchyma of the lungs may also present as an unresolving pneumonia. Slowly resolving pneumonias that are non infectious may be due to slowly resolving pulmonary infarct, chronic congestive heart failure, SLE pneumonitis, phantom tumour due to localized collections of fluid in the lung fissures and various granulomatous diseases, particularly sarcoidosis.[7,8]

## **II. Patients And Methods**

Thirtyconsecutive cases of unresolving pneumonia of both genders, attending the department of pulmonary medicine in Government hospitalfor chest and communicable diseases (GHCCD), Visakhapatnam were selected by adhering to the inclusion and exclusion criteria.

The inclusion and exclusion criteria used for this study were,

### **2.1. Inclusion criteria:**

- a) Patients presenting with at least two clinical symptoms suggestive of lower respiratory infection like fever with chills and rigors, cough with or without expectoration, pleuritic chest pain and breathlessness with radiological evidence of consolidation and
- b) Persistence of clinical symptoms and signs (cough, sputum production, with or without fever more than 100°F), failure of resolution of the radiographic features by 50% in 2 weeks or completely in 4 weeks on serial chest X-rays (indicated in at least 2 consecutive chest X-rays) in spite of antibiotic therapy for a minimum period of 10 days.
- c) Age >13 years.

### **2.2. Exclusion criteria:**

- a) Age <13years
- b) Known cases of lung cancer
- c) Known cases of sputum positive tuberculosis
- d) Patients with HIV

The initial consideration in a patient with unresolving pneumonia involves re-evaluation of possible host-related or pathogen related factors. Older age, comorbid systemic diseases, and alcoholism are some of the risk factors for longer resolution. Baseline Chest X-ray was taken and patients were started on empirical broad spectrum antibiotics based on Infectious Diseases Society of America (IDSA) guidelines (changed later according to culture & sensitivity results). Repeat Chest X-ray was taken after 2 weeks of treatment. Those patients showing <50% resolution after 2 weeks of antibiotics were included in the study and investigated with Mantoux, sputum gram stain, sputum culture and sensitivity, sputum for AFB stain, 24 hours sputum for AFB, sputum for mycobacterial culture, HIV ELISA, FOB etc. CT scan, FNAC/ biopsy was done in indicated cases. In one case of suspected pulmonary thromboembolism CT pulmonary angiogram was done. Diagnosed cases after these investigations - malignancy, BOOP etc. were managed accordingly. Patients who have no other diagnosis even after these investigations, chest X-ray lesion suggestive of tuberculosis and Mantoux>10mm were started on empirical ATT. All patients were followed up clinically & radiologically and clinical outcome was assessed based on extent of clinical and radiological improvement.

## **III. Results**

The present study is undertaken to establish the etiological diagnosis of unresolving pneumonia and to understand various modes of its presentation, clinical features, bacteriological and radiological features, complications and the clinical outcome of the study population.

- 1) This prospective study was carried out at GHCCD, Visakhapatnam. A total of 30 patients of age > 13 years with unresolving pneumonia were included in the study.
- 2) The age group of the patients ranged from 14 – 73 years with a mean age of  $48.3 \pm 17.65$  years. 5 patients who were more than 60 years of age had malignancy as a cause of unresolving pneumonia. Therefore malignancy should be considered as an important differential in evaluating a non resolving infiltrates in elderly patients. Age also had an important implication in outcome of the present study, as 75% of the deaths had occurred in patients of age more than 60 years.

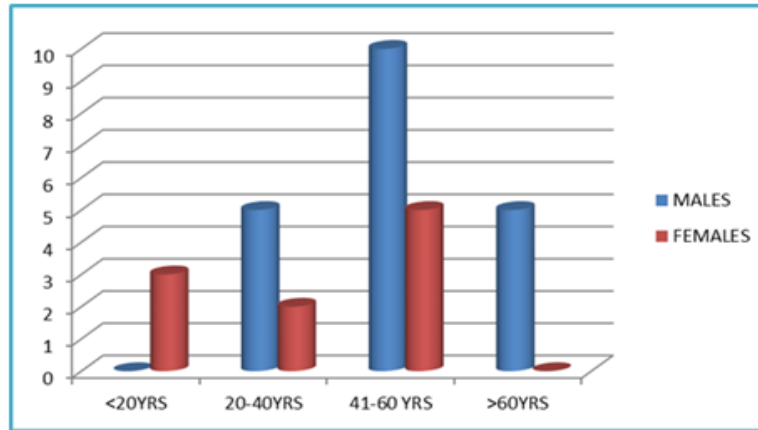


Figure 1 showing age and sex distribution.

- 3) The incidence of unresolving pneumonia was more common in men (68.3%), when compared to women (33.3%).
- 4) The mean duration of illness was  $9.02 \pm 5.12$  weeks with 50% of cases having symptoms for more than 8 weeks. This can be attributed to chronic nature of illness in most of the cases.
- 5) Smoking was the most common risk factor associated with unresolving pneumonia (66.6%).
- 6) The most common presenting symptoms were cough (100%) followed by breathlessness (70%), fever (56.6%), chest pain (30%), hemoptysis (10%).

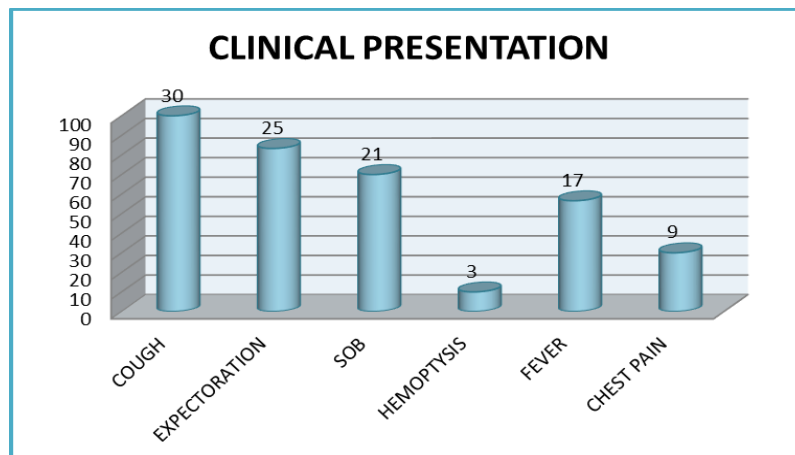


Figure 2 showing clinical presentation of unresolving pneumonia

- 7) Diabetes (23.3%) was the most common co-morbidity associated with unresolving pneumonia in the study followed by, COPD (20%), and Hypertension (16.6%).

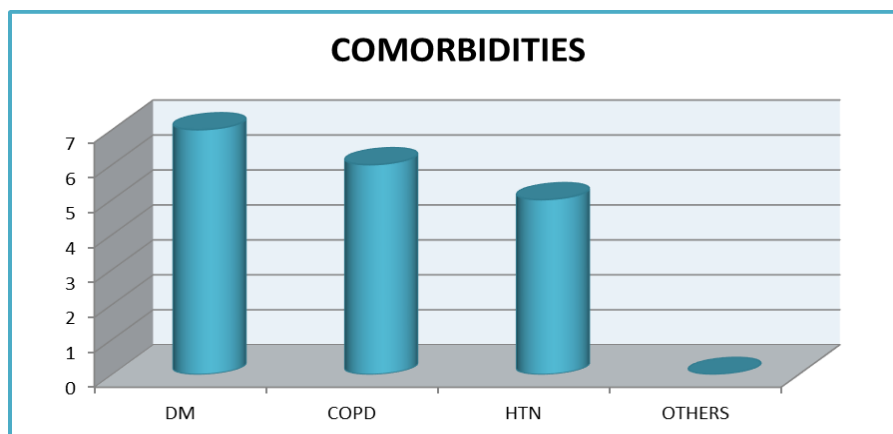


Figure 3 showing comorbidities and associated diseases.

8) Pallor was present in 33.3% of cases, clubbing in 16.66%, pedal oedema in 6% and peripheral lymph node enlargement in 6% of cases. The increased incidence of anaemia in the present study was probably due to co existing COPD, alcoholism or an underlying disease. All the cases having peripheral lymph node enlargement were of malignant etiology and FNAC showed metastatic deposits of squamous cell carcinoma. Therefore, presence of a peripheral lymph node in a case of unresolving pneumonia can be a clue towards underlying malignancy.

9) The haematological findings showed mean Hb  $10.6 \pm 2.34$  g/dl, mean total leucocyte count  $9145 \pm 2496.7$  with neutrophilic predominance. Mean RBS mean serum bilirubin was  $0.42 \pm 0.18$  mg/dl.

10) Lobar pneumonia was seen in 80% of cases, bronchopneumonia in 20% of cases.

11) Right sided lesions accounted for 60% of cases, left side 36.6% and bilateral involvement was seen in 3.3% cases.

12) On analysis of the data, **tuberculosis (33.33%)** was the most common cause of unresolving pneumonia in the present study. Sputum negative pulmonary tuberculosis presenting as consolidation was treated as bacterial pneumonia because they lacked the typical chest X-ray lesions of tuberculosis, especially cavitation. The diagnosis of tuberculosis was made after excluding all other causes of non resolution, careful interpretation of chest X-ray, Mantoux test, sputum cultures, lung FNAC and CT examination. Out of 10 cases of tuberculosis, the diagnosis was established by mycobacterial culture in Lowenstein Jensen medium in 4 cases (40%), FNAC/Biopsy of the consolidation in 4 cases (40%), CT findings like tree in bud opacities with cavitations in 1 case (10%), and one (10%) by 24 hours sputum smear examination which was positive for acid fast bacilli.

**Malignancy** was the next common cause (30.33%) of non-resolution. FOB was done in all the cases and bronchial washings were taken. FOB guided biopsy could establish diagnosis of malignancy in 2 cases whereas transthoracic needle aspiration (both CT and USG guided) established the diagnosis in 5 cases and in the remaining 2 cases; it was by lymph node FNAC. None of the cases were diagnosed by pleural fluid cytological examination. A total of 9 malignant cases were diagnosed of which 4 (44.4%) were squamous cell carcinomas, 4 (44.4%) were adenocarcinomas and 1 (11.1%) was synovial cell carcinoma.

ETIOLOGY	NUMBER (n=30)
<b>Tuberculosis</b>	10 (33.3%)
<b>Malignancy</b>	9 (30.3%)
<b>Bacterial pneumonias unresponsive to empirical antibiotics</b>	5 (16.6%)
<b>Occult bronchiectasis</b>	2 (6.6%)
<b>COP</b>	1 (3%)
<b>Pulmonary infarction</b>	1 (3%)
<b>Undiagnosed</b>	2 (6.6%)

**Table 1** showing etiology of unresolving pneumonia.

13) In cases with bacterial pneumonias unresponsive to empirical antibiotics, the commonest organism isolated in the present study was Klebsiella (57.14%) followed by pseudomonas (28.5%) and E.coli (14.2%).

14) Complications were seen in 23.3% cases. Lung Abscess formation (10%) was the most common complication followed by pleural effusion (6%), respiratory failure requiring NIV (3%), ARDS and sepsis with renal failure in another 3% cases.

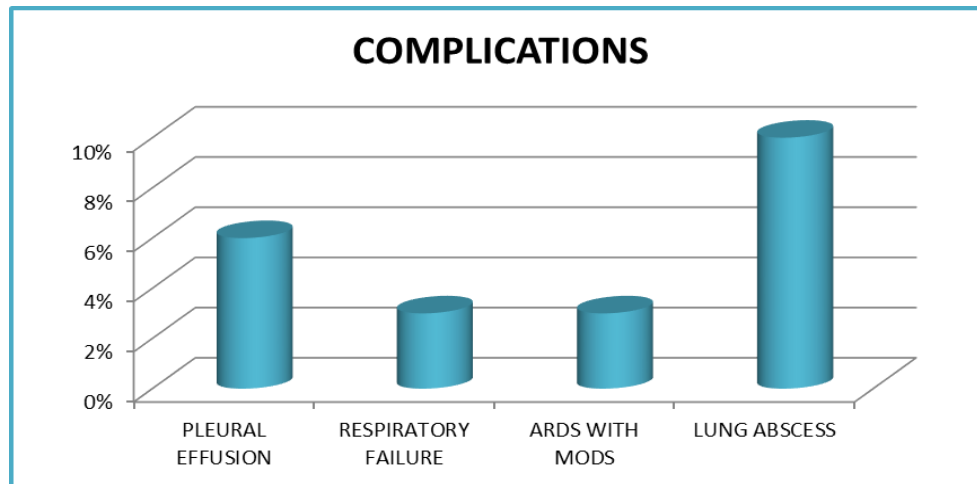


Figure 4 showing complications.

15) There was good clinical and radiological improvement in 50% cases, poor clinical response and radiological response in 20% cases, non compliance to treatment in 6% cases, deaths occurred in 13.3% and 10% of cases were lost to follow up.

#### IV. Outcome

After 3 months of follow up, 9 of the 10 tuberculosis cases had a good response to antituberculosis therapy, the remaining one case was lost to follow up. Of the 9 malignancy cases, 3 had poor response to chemotherapy, probably due to advanced stage at presentation, 3 of them died, 2 cases refused for chemotherapy (non compliant to treatment) and 1 was lost to follow up. 3 of the 5 bacterial pneumonias which were unresponsive to empirical antibiotics also had a good response clinically and radiologically after modification of antibiotics, one case did not respond even after modification of therapy which may be due to development of complications and the remaining one case succumbed to severe sepsis and MODS and had succumbed to death. The COP case responded well to steroids. One of the 2 undiagnosed cases had good response to empirical ATT and the other was lost to follow up. The single case of pulmonary infarction had good improvement after initiation of anticoagulant therapy. There was poor response to therapy in both the cases of occult bronchiectasis. To sum up there was good clinical and radiological improvement in 50% of cases, poor clinical response and radiological response in 20% of cases, non compliance to treatment in 6% of cases, deaths in 13.3% of cases and 10% of cases were lost to follow up. 75% of the deaths had occurred in patients of age more than 60 years. All the 4 patients who died were smokers and alcoholics. Therefore, advanced age, presence of risk factors like smoking, alcoholism, co-morbidities like diabetes, COPD, hypertension had implications in the outcome of the study population and was associated with increased mortality.

Unresolving pneumonia is often an area of clinical dilemma. Tuberculosis was the commonest etiology in the present study; malignancy and other non infectious causes like BOOP, pulmonary infarction etc are the other important etiologies to be looked for. The most common clinical error made in approaching these patients is to treat the patient with different antibiotics over an extended period of time. The response should not be extended to polypharmacy since antibiotic related causes of failure in treating problems resulting in unresolving pneumonia are one the least common reasons for this clinical presentation. Unresolving or slowly resolving pneumonia should prompt the clinician to intensify diagnostic efforts to arrive at an etiologic diagnosis. FOB, FNAC and CT are extremely useful investigations for establishing diagnosis in cases with unresolving pneumonias. Thorough investigation for an alternative diagnosis should be done in every patient presenting with unresolving chest infiltrate. A systematic approach should be used in managing these cases.

#### V. Conclusion

Patients aged 40 years and above are at risk for non resolving pneumonia. Comorbidities like COPD, diabetes, alcoholism and immunosuppression are significant factors causing nonresolution. Tuberculosis was the commonest cause of non resolving pneumonia in our setting. This possibility has to be kept in mind during evaluation, since it is a curable cause. Malignancy was the next common cause of unresolving pneumonia, so a high index of suspicion is needed. Invasive procedures were needed more frequently to reach a diagnosis. We have to consider unusual or resistant pathogens and non infectious etiologies while evaluating a case of unresolving pneumonia. This study stresses the need for a systematic approach to manage non resolving pneumonia properly.

### **References**

- [1]. Fein AM, Feinsilver SH: The approach to non-resolving pneumonia in the elderly. *Semin Respir Infect* 1993; 8:59-72.
- [2]. Lehtomaki K. Clinical diagnosis of pneumococcal adenoviral mycoplasmal and mixed pneumonias in young men. *Eur Respir J* 1988; 1:324-9.
- [3]. Kuru T, Lynch JP III. Non-resolving or slowly resolving pneumonia. *Clin Chest Med* 1999; 20:623-51.
- [4]. Fayez K, Tamim H, Walid K, Shadi L. Nonresolving pneumonia. *Am J Ther* 2011; 18:e177-9.
- [5]. Menéndez R, Torres A. Treatment failure in community-acquired pneumonia. *Chest* 2007; 32:1348-55.
- [6]. Epler, G.R. Bronchiolitis obliterans organizing pneumonia. Definition and clinical features *Chest* 1992; 102(suppl.1):107-23.
- [7]. Johnson, A.J.L. Slowly resolving and nonresolving pneumonia: Questions to ask when response is delayed. *Postgrad Med* 2000; 108:115-22.
- [8]. Cunha, B.A. Community-acquired pneumonia in HIV patients. *Clin Infect Dis* 1999; 28:410-11.