*Journal of Rawalpindi Medical College (JRMC); 2019;23(1): 12-15*

**Original Article**

# Bacterial Isolates in Slow Resolving Pneumonias

**Abdul Rasheed Qureshi, Afzaal Ullah Khan, Muhammad Irfan, Aqeel Ahmed,Khalid Farooq Bhatti**
Department of Pulmonology , Gulab Devi Chest Hospital, Lahore

.

## Abstract

**Background : To study the pattern of bacterial isolates in slow resolving pneumonia (SRP) patients**

**Methods : In this prospective study patients (n=121) fulfilling the criteria of slow resolving pneumonia, having Age > 14 years and radiological evidence of consolidation were included in the study. Patients having Age > 65 < 14 years, not giving consent for Invasive investigation, nosocomial pneumonia, atypical pneumonia, fungal and mycobacterial infections were excluded. All patients were investigated with multiple view Chest X-ray, sputum smear for Gram staining, ZN-staining, cytology & culture sensitivity for pyogenic and fungal infections. Fiber-optic Bronchoscopy and BAL analysis was utilized. Contrast enhanced CT scan was employed for accurate definition of the lesion. Samples were sent for microbiological evaluation.**

**Result: Age group was 14-65 years with median age 53 years. One hundred and twenty one pyogenic bacterial isolates were obtained. Gram negative bacteria were 66.11% while gram positive bacteria were 30.57 % and mixed growth were seen in 3.30%.**

**Conclusion : Gram negative etiology predominates in SRP cases with pseudomonas at the top followed by klebsiella.**

**Key Words: Slow Resolving Pneumonia (SRP), Empiric Therapy, Bacterial isolates , Community Acquired Pneumonia (CAP).**

## Introduction

A slowly resolving pneumonia (SRP) is a real challenge in pulmonology practice.10-20% of patients admitted in a chest unit belong to this entity. Bacteriologic causes are unusual organisms, resistant pathogens, inadequate antibiotics, infectious complications, or incorrect diagnosis. Due to its high mortality, it is essential to recognize these patients and treat adequately to reduce the mortality._SRP is in reality a clinical dilemma, affecting 10-15% patients of the CAP. The majority of CAP patients respond rapidly to conventional antibiotic therapy without developing any complications.[1,2] Microbiological samples become negative quickly after antibiotic therapy & biomarkers such as C-reactive protein settle down.[3] A complete recovery requires several weeks or even months, but 10-15 % cases fail to respond to empirical treatment. [4-6] The mortality rate in such cases remains substantially increased 5-15% despite recent advances in clinical care. [1-3] Once slow-response is recognized, patients are subjected to a full re-evaluation process, including microbiological testing, X- Ray chest, consideration of further imaging, and the spectrum of antibiotics is increased if drug resistant pathogens are suspected. On detecting the micro-organism, a narrow spectrum is the drug of choice.

It is very difficult to categorize the patient as a case of SRP because this lacks uniformity in definition.[7]. Amberson was the first to describe this entity as protracted pneumonia in 1943.[8] Richard Interbauer, defined it as less than 50% clearance at two weeks or less than complete resolution at four weeks in immune-competent patients.[9] In 1975, it was defined by Hendin, as pulmonary consolidation persisting for more than 21 days. In 1991, Kirtland and Winterbauer defined slow resolving CAP by radiological criteria as < 50% clearance by two weeks or < complete clearance by 4 weeks in immuno-competent cases. Usually 10% CAP and 60% HAP show inadequate response to empirical antibiotics therapy. Fein and Feinsilver described it as delayed radiographic improvement .[10] Arancibia F et al stated that most common reasons are related to infections. Such delayed response depends upon the category of infecting organism and the immunity of the host.

Common causes are presence of unusual organisms, resistant bacteria, inappropriate antibiotics, super infections like fungal / mycobacterial disease, co-morbidities like drug abuse, HIV, DM, smoking etc. Defects in immune system, non compliance, incorrect diagnosis & diseases which masquerade pneumoni, like ILD, malignancy, pulmonary embolism and vasculitis can be other important causes .[11-13] These

cases appear as CAP but show abnormal behavior to the standard treatment and are associated with substantial increased mortality that is why it is essential to identify and manage these cases on priority to reduce the morbidity and mortality.

## Patients and Methods

This prospective study was conducted over a period of 32 months, in the male ward of department of pulmonology, Gulab Devi Chest Hospital Lahore from January,2014 to August, 2016.Adult-male patients (n=121) of CAP, having age ≥ 14 years, with radiological signs of consolidation on chest x-ray, not showing adequate radiological improvement after 04-weeks of antibiotics therapy, were included in the study. Exclusion Criteria was patients with age < 14 years, atypical pneumonia, hospital acquired pneumonia, known cases of mycobacterial disease, anaerobic infections, negative sputum bacteriology, bronchiectasis, cavitary lesions, empyema, pleural effusion and fungal infections. Hematological and non hematological malignancy & congenital lung disorders and those not willing for participation in the study or invasive investigations were also excluded. Routine investigations like complete blood count, blood sugar, urea,creatinin & LFTs were done. All patients were re-investigated with multiple view Chest X-ray, sputum smear for Gram staining, ZN-staining, cytology & Culture sensitivity for pyogenic and fungal infections. Fiber-optic Bronchoscopy and BAL analysis was utilized. Contrast enhanced CT scan was employed for accurate definition of the lesion. FNAC/biopsy were used for sampling after an informed-consent, in pertinent cases. Samples were sent for microbiological evaluation. Data was collected, tabulated, analyzed and conclusions were drawn by statistical interpretation.

## Results

During 32-months period in 121 cases, pyogenic bacterial isolates were obtained. Age group was 14—65 years with median age 53 years. Patients aged 50 years and more constituted 66.3% of the study population. Cough (94.1%) was the commonest presenting feature (Table 1) . Smoking (71.90%) was the commonest risk factor (Table 2). Total 121 pyogenic bacterial isolates were obtained. 37 patients showed gram positive, 80-cases gram-negative while 04 cases had mixed bacterial pathogens (Table 3). Gram negative bacteria were 66.11% while gram positive bacteria were 30.57 % and mixed growth were seen in 3.30%. Strep Pneumoniae (78.3%) was commonest in gram positive and Pseudomonas (65.0%) was commonest in gram negative(Table 3).Lung abscess was the commonest complication (Tale 4)

**Table 1: Clinical Features** (n=121)

| Clinical feature | Number | Percentage |
|---|---|---|
| Cough | 114 | 94.21 |
| Fever | 107 | 88.42 |
| Expectoration | 96 | 79.33 |
| Weight Loss | 95 | 78.51 |
| Dyspnoea | 87 | 71.90 |
| Smoking | 87 | 71.90 |
| Hemoptysis | 38 | 31.40 |
| Clubbing | 11 | 9.09 |

**Table 2: Frequency of Risk Factors in 121 patients**

| Risk factor | Number | Percentage |
|---|---|---|
| Cigarette smoking | 87 | 71.90 |
| Diabetes Mellitus | 44 | 39.66 |
| Drug Abusers | 18 | 14.87 |
| HIV Positive cases | 03 | 2.47 |

**Table 3: Frequency of Bacterial Isolates**

| Total Isolates n = 121 | Observed cases | Percentage |
|---|---|---|
| Gram positive isolates | | |
| Strep. Pneumonie | 29 | 78.37% |
| Staph. Aureus | 05 | 13.51% |
| Strep. Pyogenes | 03 | 8.10% |
| Total | = 37 | *30.57% |
| Gram negative isolates | | |
| Pseudomonas | 52 | 65.0% |
| Klebsiella | 14 | 17.50% |
| Gram negative rods | 09 | 11.25% |
| Coliform bacteria | 05 | 6.25% |
| Total | = 80 | *66.11% |
| Mixed growth isolates | | |
| Pseudomonas + Staph. | 01 | 25 |
| Pseudomonas + Strep. Pyogenes. | 01 | 25 |
| Pseudomonas + Klebsiella. | 02 | 50 |
| Total | = 04 | *3.30% |

*Percentage is calculated for 121patients.

**Table 4: Slow Resolving Pneumonia Patients-Complications** (n=121)

| Complications | Observed Cases | Percentage |
|---|---|---|
| Pl. Effusion | 27 | 22.31 |
| Lung Abscess | 13 | 10.74 |
| Empyema | 07 | 5.78 |
| Pneumothorax | 01 | 0.82 |

## Discussion

In study period 1728 CAP patients were admitted.Out of these 249 showed slow resolution. 83 cases were diagnosed as tuberculosis, 45 cases were of

malignancy and 121 cases (7.0% of 1728) were with pyogenic etiology. All patients gave history of illness of more than 04 weeks. Because our study was conducted in a male department, all included patients were adult male. A few studies have reported that male gender may be at greater risk of slow resolving pneumonia.[14]

In our study, the median age was 53 years and 66.3% patients were with age 50 years and above. Elderly age itself is a recognized factor for slow resolution. Blasi F et al demonstrated the old age itself as a significant factor for slow resolution. Jayaprakash et al showed 84.6% of patients, above 40 years old and Chaudhuri et al reported 80% cases above 40 years of age, with slow resolution.[14-1]. Gram-negative bacteria predominated in elderly while majority of the young patients, showed infection by gram positive pathogens.

The most common symptoms in our study were cough (94.21%) followed by fever (88.42%), expectoration (79.33%), Weight loss (78.51%), Dyspnoea(71.90%) and hemoptysis (31.40%) while Kirtland *et al*. reported cough as commonest symptoms (92%) followed by chest pain (38%), breathlessness (38%), fever (36%), and haemoptysis (28%). Chaudhuri et al showed cough 100%, followed by fever 96.6%, hemoptysis 53.5%, chest pain 38.5% and shortness of breath in 33.3%.

Our study showed, 95 cases (78.51%) with significant weight loss and low BMI levels. Low body weights are associated with lower complement levels and down immune system. Devendra Prasad Singh has reported malnutrition, general debility and poor social support in the elderly, a contributing factor for slow resolution. Cigarette Smoking was the most common risk factor (71.90 %) in our study. Jayaprakash et al also reported smoking as the most common co-morbidity.[16]. Other co-morbidities were DM (39.66%), 14.87% drug abuse and 2.47% HIV infections, cutting down the immune system, responsible for slow resolution. We had 09 cases of alcohol consumers, 06 opium addicts and 03 cases were of heroin addicts. Drug abuse is a documented factor for slow resolution.[18-19]

Avijgan has reported DM as a major association in delayed resolution.[20]. Klebsiella pneumoniae was the most common etiology in diabetics in our study, also reported by literature. Begamy also reported increased occurrence of Klebsiella infection in diabetic patients.[21] So in the presence of DM, we should expect Klebsiella infection and be ready to face slow resolution.

In our study, 76(62.80%) cases showed right sided involvement which is comparable to the results reported by Boyd DH.[22]. Although we excluded the cases of pleural effusions and cavitary lung lesions at the time of inclusion, 27 cases (22.31%) developed minimal pleural effusion,13 cases (10.74%) lung abscess and 07 cases (5.78%) of empyema were identified by contrast enhanced CT, during the course of investigation. One case of pneumothorax was also found. These complications are undisputedly a recognized factor for delayed resolution, as reported by several researchers.[23-28]

This study showed 37 cases (30.57%) with gram-positive etiology. 29 cases (78.37%) with pneumococci, 05 cases (13.51%) of Staph aureus, while 3 cases (8.10%) were with Strep. pyogenes etiology. Our study shows the pneumococcal predominance in gram positive spectrum which is the normal bacteriologic behavior towards CAP in immuno-competent patients but when there is an immune deficiency and associated co-morbidities, these bacteria exhibit an abnormal behavior – slow resolution. Similarly, Staph. aureus and Strep. pyogenes are already well-known for slow resolution by nature.[25, 29-32]

## Conclusions

1.Slow Resolving Pneumonia is a practical challenge in daily pulmonology practice. After identification, these cases must be dealt by considering bacteriology, host factors and infective complications.

2.The antibiotic cover, in slow resolving pneumonias, must include against pseudomonas and Klebsiella in addition to conventional gram-positive cover, so as to enhance resolution and reduce the morbidity and mortality.

## References


1. Akram AR. An evaluation of clinical stability criteria to predict hospital course in community-acquired pneumonia. Clin Microbiol Infect. 2013;19(12):1174-80.
2. Aliberti S. Incidence, etiology, timing, and risk factors for clinical failure in hospitalized patients with community-acquired pneumonia. Chest. 2008;134(5):955-62.
3. Menéndez R, Sabtin S. Stability in community-acquired pneumonia: one step forward with markers? Thorax. 2009;64(11):987-92.
4. Lamping DL, Schroter S, Marquis P, Marrel A. The community-acquired pneumonia symptom questionnaire. Chest. 2002;122(3):920-9.
5. El Moussaoui R[1], Opmeer BC, de Borgie CA Long-term symptom recovery and health-related quality of life in patients with community-acquired pneumonia. Chest. 2006;130(4):1165-72
6. Menéndez R, Torres A, Zalacaín R, Aspa J. Risk factors of treatment failure in community acquired pneumonia. Thorax. 2004;59(11):960-65.

7. Simon Finch, James D. Chalmers, Brief Clinical Review: Non-Responding Pneumonia : EMJ Respir. 2014;2: 104-11.
8. Amberson JB. Significance of unresolved organizing or protracted pneumonia. J Mich State Med Soc. 1943;42:599–603.
9. Welte T , Torres A,Nathwani D. Clinical and economic burden of community-acquired pneumonia among adults in Europe.Europe.Thorax. 2012;67(1):71-79.
10. Fein AM, Feinsilver SH. Non-resolving and slowly resolving pneumonia, Feinsilver SH, Fein AM (eds.), Textbook of bronchoscopy (1995), Baltimore: Williams and Wilkins, . 286–301.
11. Welte T, Torres A, Nathwani D. Clinical and economic burden of community-acquired pneumonia among adults in Europe. Thorax. 2012;67(1):71-79.
12. Fayez K, Tamim H, Walid K, Shadi L. Nonresolving pneumonia. Am J Ther. 2011;18:e177–79.
13. Sialer S, Liapikou A, Torres A. What is the best approach to the nonresponding patient with community-acquired pneumonia? Infect Dis Clin North Am. 2013; 27:189-203.
14. Blasi F, Mantero M, PierAchille S, Tarsia P. Understanding the burden of pneumococcal disease in adults. Clin Microbiol Infections. 2012;18(5):7–14.
15. R oson B,Carratala J,Sabe NF,Tubau F, Manresa F. Causes and factors associated with early failure in hospitalized patients with community-acquired pneumonia. Arch Inter Med 2004;164:502-08.
16. Jayaprakash B, Varkey V, Anithakumari K. Etiology and clinical outcome of non-resolving pneumonia in a tertiary care centre. JAPI. 2012;60:98-101.
17. Chaudhuri AD, Mukherjee S, Nandi S, Bhuniya S. A study on non-resolving pneumonia with special reference to role of fiberoptic bronchoscopy. Lung India. 2013;30(1):27-32.
18. Samokhvalov AV, Irving HM, Rehm J.Alcohol consumption as a risk factor for pneumonia: a systematic review and meta-analysis. Epidemiol Infect.2010;138(12):1789-95.
19. Ramesh PM, Saravanan M. A clinical study on non-resolving pneumonia in tertiary care centre. Int J Adv Med 2018;5:604-07.
20. Avijgan M. Specificity and sensitivity of clinical diagnosis for chronic pneumonia. East Mediterr Health J. 2005;11:1029–37.
21. Begamy T. Thoracic empyema. Is its microbiology changing? Pul Rev Com. 2000;5:10–12.
22. Boyd DH. Failure of resolution. Br J Dis Chest. 1975;69:259–66.
23. Lim WS,Smith DL,M P Wise MP, Welhamet SA . BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax. 2009;64( 3):55 -58.
24. Choudhury G,, Chalmers JD, Mandal P. Physician judgement is a crucial adjunct to pneumonia severity scores in low-risk patients. Eur Respir J. 2011;38(3):643-48.
25. Chalmers JD[1], Singanayagam A, Murray MP.Risk factors for complicated parapneumonic effusion and empyema on presentation to hospital with community-acquired pneumonia.Thorax. 2009;64(7):592-97.
26. FalgueraM, Carratalà J, Bielsa S, García-Vidal C. Predictive factors, microbiology and outcome of patients with parapneumonic effusion. Eur Respir J. 2011;38(5):1173-79.
27. Chalmers JD, Mandal P, Singanayagam A, Akram AR. Severity assessment tools to guide ICU admission in community-acquired pneumonia: systematic review and meta-analysis. Intensive Care Med. 2011;37(9):1409-20.
28. Mandell LA,Richard G. Wunderin K,Anzueto A. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis. 2007;44( 2):72-76.
29. Steel HC, Cockeran R, Anderson R, Feldman C. Overview of community-acquired pneumonia and the role of inflammatory mechanisms in the immunopathogenesis of severe pneumococcal disease. Mediators Inflamm. 2013;2013:490346.
30. Jenkins TC, Sakai J, Knepper BC, Swartwood CJ. Risk factors for drug-resistant Streptococcus pneumonia and antibiotic prescribing practices in outpatient communityacquired pneumonia. Acad Emerg Med. 2012; 19:703-06.
31. Cardinal-Fernández P, García Gabarrot G. Clinical and microbiological aspects of acute community-acquired pneumonia. Rev Clin Esp (Barc). 2013; 213:88-96.
32. Chathamparamb B, Antony A, Nivarthil SU, Paul AM. Non-resolving pneumonia aetiology and clinical profile: a prospective study. J Evolution Med Dent Sci. 2016;5(19):954-58.


**Contribution of Authors: Abdul Rasheed Qureshi**=A,B,C,D Afzal Ullah Khan = A,C,E; Muhammad Irfan=A,B;Aqeel Ahmed=B,C

**Key for Contribution of Authors :** A= Conception/ Study/ Designing /Planning; B= Experimentation/Study conduction;C=Analysis/Interpretation/ Discussion; D= Manuscript writing;E= Critical review;F= Facilitated for reagents/Material/Analysis