



## Bacteriological Profile of Acute Exacerbation of Nonspecific Interstitial Pneumonia (NSIP)

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### Abstract

**Introduction:** Nonspecific interstitial pneumonia (NSIP) is a life-threatening disease of unknown etiology, characterized by distinct radiographic and pathological patterns. Patients with NSIP often experience a progressive decline in respiratory function, or a more acute deterioration referred to as acute exacerbation (AE-NSIP). Among infectious agents, bacterial involvement and its impact on alveolar healing remain underexplored. Recent studies suggest that impaired host defence mechanisms may predispose NSIP patients to infections, thereby influencing disease progression.

**Aim:** This study investigates bacterial isolates from sputum samples in patients with AE-NSIP and evaluates their clinical significance.

**Materials and Methods:** Sputum samples from 120 AE-NSIP patients admitted to a tertiary hospital between January 2021 and January 2022 were analysed. Patients unable to produce sputum or those pre-treated with antibiotics were excluded. Gram staining and culture tests were conducted on high-quality sputum samples. Chi-square tests were used to determine the statistical significance of bacterial isolates.

**Results:** Out of 120 patients, bacterial isolates were identified in 78.3% (n=94), while 21.7% (n=26) showed no isolates. *Streptococcus pneumoniae* (n=26) and *Escherichia coli* (n=24) were statistically significant ( $p < 0.05$ ). Other isolates such as *Haemophilus influenzae* (n=16), *Klebsiella pneumoniae* (n=8), *Enterococcus* (n=4), and *Moraxella catarrhalis* (n=6) were statistically insignificant.

**Conclusion:** Preservation of lung function in NSIP remains critical. The potential role of bacterial infections in worsening NSIP and the use of prophylactic antibiotics warrant larger, geographically diverse studies.

**Keywords:** NSIP, Lung function, Prophylactic antibiotics, Sputum, Tuberculosis, Bacterial infection.

### Introduction

Nonspecific interstitial pneumonia (NSIP) is a severe disease with idiopathic origins, characterized by specific radiographic and pathological findings (1,2). Patients with NSIP may experience progressive respiratory decline or acute exacerbations (AE-NSIP) marked by rapid worsening of dyspnea, new radiographic opacities, and exclusion of alternative causes such as congestive heart failure or pulmonary embolism [2,3,4]. AE-NSIP carries a high mortality rate (>50%) (1,4).

Evidence suggests infections may play a role in AE-NSIP:

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1. Seasonal patterns with increased exacerbations during winter.
2. Similar mortality risks between respiratory infections and AE-NSIP.
3. Diffuse alveolar damage observed in post-mortem examinations of infected patients.
4. Immunosuppression-related vulnerability to exacerbations [5,9].

Bacterial involvement in NSIP remains under-investigated [6,7,8]. Kligerman et al. highlighted impaired host defences and susceptibility to infection as potential contributors to NSIP progression [1]. This study examines the bacterial profile in AE-NSIP patients to explore its clinical significance.

## Material and Methods

This retrospective observational study analysed sputum samples from 120 AE-NSIP patients admitted to Gandhi Medical College, Bhopal, between January 2021 and January 2022.

**Inclusion criteria:** Clinico-radiologically diagnosed AE-NSIP.

**Exclusion criteria:** Inability to produce sputum.  
Prior antibiotic use for the current exacerbation.

## Sample Analysis

Expectorated sputum samples were collected in sterile containers. Quality assessment was performed through macroscopic and microscopic examination. Samples underwent Gram staining, aerobic, and anaerobic cultures. Statistical analysis was conducted using Chi-square tests ( $p < 0.05$  considered significant).

## Statistical Analysis

Chi-Square tests were used to find the significant association ( $p$ -value  $< 0.05$ ) between the bacterial isolates in the sputum samples.

## Results

In the study 120 patients were analyzed. Among them there were isolates in 78.3% ( $n=94$ ) and no isolates in 21.7% ( $n=26$ ) of the subjects. Among the isolates *Streptococcus pneumoniae* was isolated in 24 patients and *Escherichia coli* (E. Coli) in 26 patients. Upon analysis using Chi-square to test the significance of these two isolates, the  $p$  value was found to be 0.042 ( $p < 0.05$ ) and 0.032 ( $p < 0.05$ ) for these two isolates respectively, revealing a statistically significant association [Table-1,2].

**Table 1:** Association of E. Coli between isolates and no isolates.

E. coli	Group			p-value
	No isolates (n=26)	Isolates (n=94)	Total	
Absent	26 (100.0)	68 (72.3)	94 (78.3)	0.032*
Present	0 (0.0)	26 (27.7)	26 (21.7)	
Total	26 (100.0)	94 (100.0)	120 (100.0)	

**Table- 2:** Association of *S. Pneumoniae* between isolates and no isolates.

S. Pneumoniae	Group			p-value
	No isolates (n=26)	Isolates (n=94)	Total	
Absent	26 (100.0)	70 (74.5)	96 (80.0)	0.042*
Present	0 (0.0)	24 (25.5)	24 (20.0)	
Total	26 (100.0)	94 (100.0)	120 (100.0)	

In contrast the other isolates were *Haemophilus influenza* in 18 patients ( $p$  value=0.087), *klebsiella pneumonia* in 16 patients ( $p$  value =0.110), *Enterococcus* in 4 patients ( $p$  value=0.449) and *Moraxella catarrhalis* in 6 patients ( $p$  value=0.350). all these were found to be statistically insignificant [Table- 3-6].

**Table- 3:** Association of *Klebsiella* between isolates and no isolates.

Klebsiella pneumonia	Group			p-value
	No isolates (n=26)	Isolates (n=47)	Total	
Absent	26 (100.0)	78 (82.9)	104 (86.7)	0.110 (N.S)
Present	0 (0.0)	16 (17.1)	16 (13.3)	
Total	26 (100.0)	94 (100.0)	120 (100.0)	

**Table- 4:** Association of *H. Influenza* between isolates and no isolates. Chi-Square: 2.553; N.S: Not significant

H. Influenza	Group			p-value
	No isolates (n=26)	Isolates (n=47)	Total	
Absent	26(100.0)	78 (82.9)	104 (86.7)	0.110 (N.S)
Present	0 (0.0)	16 (17.1)	16 (13.3)	
Total	26(100.0)	94 (100.0)	120 (100.0)	

**Table- 5:** Association of *Enterococcus* between isolates and no isolates. Chi-Square: 2.553; N.S: Not significant

Enterococcus	Group			p-value
	No isolates (n=26)	Isolates (n=94)	Total	
Absent	26 (100.0)	90 (95.7)	116 (96.7)	0.449 (N.S)
Present	0 (0.0)	4 (4.3)	4 (3.3)	
Total	26 (100.0)	94 (100.0)	120 (100.0)	

**Table- 6:** Association of *M. catarrhalis* between isolates and no isolates.

M. catarrhalis	Group			p-value
	No isolates (n=26)	Isolates (n=94)	Total	
Absent	26 (100.0)	88 (93.6)	114 (95.0)	0.350 (N.S)
Present	0 (0.0)	6 (6.4)	6 (5.0)	
Total	26 (100.0)	94 (100.0)	120 (100.0)	

## Discussion

The study identified *E. coli* and *S. pneumoniae* as the most common and statistically significant bacterial isolates in AE-NSIP patients. These findings align with prior studies such as Seth J. Kligerman et al [1], which documented similar pathogens in NSIP patients using culture-independent methods. Other reports, like those by Hochegger B et al [2], have also demonstrated positive cultures in NSIP patients, supporting the potential role of bacteria in disease progression. Unlike other pulmonary diseases where exacerbations are truly acute events, the onset of an acute exacerbation in NSIP is generally insidious [6]. Recently, molecular culture independent techniques have identified complex microbial species in the lower airways with distinct alterations in the microbiome occurring in many of respiratory diseases [7, 8]. In a Sambataro G et al [5], where they analyzed the microbial flora in the BAL of 20 patients with interstitial lung diseases including idiopathic pulmonary fibrosis, non-specific interstitial pneumonia and acute interstitial pneumonia using bacterial culture & gel electrophoresis. Both classic respiratory pathogens (e.g., *Haemophilus influenza*) and a variety of previously unrecognized or under-recognized organisms were identified.

## Limitation

1. Long-term follow-up was not conducted to evaluate recurrent isolates or colonization patterns.
2. Viral and fungal co-infections were not analysed.

## Conclusion

Infectious agents may contribute to NSIP progression, but their exact role remains unclear. Larger, multi-centre studies are needed to explore the impact of bacterial infections on disease outcomes and the potential benefits of prophylactic antibiotics in reducing mortality and morbidity in NSIP patients.

## Transparency

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**Declaration of financial other relationship-** The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony,

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**Authors contributions-** All authors participated in the conception and design of the work or the collection, interpretation or analysis of the study data, and in the drafting, critical revision, and approval of the final version of the manuscript.

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