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Original Research Article

Bacteriological Profile of Acute Exacerbation of IPF

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Abstract

Introduction: Idiopathic pulmonary fibrosis (IPF) is a fatal disease with unknown or idiopathic aetiology, characterized by a radiographic and pathologic pattern of usual interstitial pneumonia (UIP)[1,2]. Patients with IPF have either a progressive course of worsening respiratory function, or a more rapid decline described as acute exacerbation (AE-IPF). Out of the infectious agents, bacterial exacerbation and the possible alteration of alveolar healing by bacteria are the least explored [6-8]. A recent study by Jonathan J Smith *et al* [13], has pointed to a disordered host defense and thus susceptibility to infection, as an important contributor to disease progression in IPF.

Aim: This study analyses the sputum for bacterial isolates in patients with acute exacerbation of IPF and aims to find the significance of such association.

Materials and Methods: Sputum samples of 120 patients who came with acute exacerbation of IPF to a Tertiary Medical College and Hospital between January 2021 to January 2022 were analyzed. Patients who were unable to produce sputumand who had received antibiotics for the present exacerbation prior to admission were excluded. Expectorated sputum samples were subjected to gram staining and after assessing the sputum quality. Chi-Square tests were used to find the significant association between the bacterial isolates in the sputum samples.

Results: Among the 120 patients, there were isolates in 78.3% (n=94) and rest had no isolates. Streptococcus pneumoniae was isolated in 24 patients and Escherichia Coli in 26 patients and these were found to have significant association statistically in patients presenting with acute exacerbation of IPF. Whereas the rest of the isolates like Klebsiella (n=18), Haemophillus influenza (n=16), Enterococcus (n=4) and Moraxella catarrhalis (n=6) were found to have insignificant association.

Conclusion: Preserving the lung functions in patients with IPF is the main aim of treatment. Whether infectious causes play a role in decreasing lung function and treating these with prophylactic antibiotics needs to be seen with larger studies in different geographic areas.

Keywords: IPF, Lung function, Prophylactic antibiotics, Sputum

Introduction

Idiopathic pulmonary fibrosis (IPF) is a fatal disease with unknown or idiopathic aetiology, characterized by a radiographic and pathologic pattern of usual interstitial pneumonia (UIP) [1,2]. Patients with IPF have either a progressive course of worsening respiratory function, or a more rapid decline described as acute exacerbation (AE-IPF) [2-4]. The criteria for AE-IPF include IPF with acute worsening of dyspnea in the preceding one month, new radiographic opacities or ground glass on computed tomography (CT), and exclusion of alternative causes (e.g. Congestive heart failure, and pulmonary embolism). AE-IPF is a dangerous condition with a high mortality (often >50%) [1-4].

There are a number of factors supporting a role for infection; i) seasonal patterns exist with increased AE-IPF occurring during the winter months, ii) respiratory tract infections in individuals with IPF confer a mortality risk indistinguishable from that seen with acute exacerbations, iii) post mortem examination in cases of confirmed infection frequently discloses diffuse alveolar damage identical to that seen during an AE-IPF and iv) immunosuppression is associated with an increased rate of acute exacerbations [5-9].

Out of the infectious agents, bacterial exacerbation and the possible alteration of alveolar healing by bacteria are the least explored [6-8]. A recent study by Jonathan J Smith *et al* [13], has pointed to a disordered host defense and thus susceptibility to infection, as an important contributor to disease progression in IPF.

Recent evidences points towards a potential role of an altered lung microbiome in triggering IPF progression, including AE-IPF [10,11]. In this study we analyze bacterial profile of patients who came with acute exacerbation of IPF.

Material and Methods

This was a retrospective observational study of sputum samples of 60 patients who came between January 2021 to January 2022 with acute exacerbation of IPF, in department of respiratory medicine Gandhi medical college which is a Tertiary center in Bhopal (M.P.)

Inclusion criteria: All patients who came with acute exacerbation of IPF, diagnosed clinico-radiologically.

Exclusion criteria: Patients who were unable to produce sputum and who had received antibiotic for the present exacerbation prior to admission.

Expectorated sputum samples were collected in wide mouth sterile containers after giving appropriate instructions for all patients. The quality of the sputum was assessed by both macroscopic and microscopic examination. All sputum samples were subjected to Gram staining and aerobic & anaerobic culture

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, thep 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/Fig-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)	

Chi-Square: 4.149, *p<0.05

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/Fig-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.

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)	

Chi-Square: 2.553; N.S: Not significant

Table 5: Association of *Enterococcus* between isolates and no isolates.

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)	

Chi-Square: 2.553; N.S: Not significant

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)	

Chi-Square: 2.553; N.S: Not significant

Discussion

In our study most common infection was E. coli followed by streptococcus pneumonia, H. influenza, klebsiella, Enterococcus & Moraxella. Significant association of E.coli ,S. pneumonia with isolate & non isolates seen, rest showed no correlation.

In a study done by Jonathan J Smith *et al* [13], BAL samples were analyzed from 25 patients with IPF using culture-independent metagenomic analysis. Their findings were similar to us. In their study the phylum Firmicutes (Streptococcus and Veillonella species), Proteobacteria, and Bacteroidetes were most encountered. Also in this study authors were able to show by longitudinal analysis of patients with IPF in serum and Bronchoalveolar Lavage (BAL) samples that specific genes, were present in patients with IPF and such expression increased over time, supporting that the pathogens may provide chronic antigenic stimuli in patients with IPF.

One observational evidence comes from Richter AG *et al* [14], who in 2008 demonstrated positive BAL cultures in eight of 22 stable IPF patients . A large multicenter, randomized, placebo-controlled study observed that the high mortality associated with bacterial respiratory tract infection in IPF, this suggests that bacteria may play a role in driving IPF disease progression.

Unlike other pulmonary diseases where exacerbations are truly acute events, the onset of an acute exacerbation in IPF is generally insidious [16]. 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 [17,18]. In a study FriazaV *et al* [15], 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

The patients who presented with recurrent and similar bacterial isolates need to be followed up and determine whether they have a pattern of colonization. We did not check the viral and fungal co- infections in these patients.

Conclusion

Therefore, the role of infectious agents in the development and progression of IPF is unknown. Although a variety of bacterial, viral, and fungal pathogens can be isolated, the causal nature of these organisms in IPF remains uncertain. Whether these organisms alter the alveolar healing mechanism and host response to injury, leading to accelerated decline in lung function, needs to be investigated in long-term studies. Whether treatment of these bacterial infections in IPF patients with both active isolates and latent infections can prophylactically reduce mortality and morbidity remains to be investigated in a larger study in different settings.

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