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STUDY OF ETIOLOGICAL, CLINICO-RADIOLOGICAL AND MICROBIOLOGICAL PROFILE OF PATIENTS WITH BRONCHIECTASIS AT INSTITUTE OF RESPIRATORY DISEASES, SMS MEDICAL COLLEGE, JAIPUR

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ABSTRACT **Background:** Bronchiectasis has been considered as orphan lung disease since long. There is a geographical variation in clinical features and etiologies of Bronchiectasis. HRCT can accurately diagnose bronchiectasis, along with localizing and describing the areas of parenchymal abnormalities, and identifying bronchiolar abnormalities and mucus plugging. The aim of this present study to evaluate the etiology, clinical-radiological and microbiologicalprofile of patients with bronchiectasis presenting at IRD, SMS Medical College, Jaipur. **Material & Methods:** This was a hospital based prospective observational study carried out on 90 bronchiectasis patients at Department of Respiratory Medicine, Institute of Respiratory Diseases, SMS medical college, Jaipur, over a period of one year (2021- 2022). Patients attending our OPD with cough, purulent expectoration, shortness of breath, fever, with/without hemoptysis and radiological features favoring bronchiectasis or previously known/evaluated cases of bronchiectasis were included in our study. A questionnaire was given to them and information was collected regarding the demographic data, childhood history, symptomatology and significant past and personal history. **Results:** Our study showed that the mean age of the study population was 49.87 years with male preponderance (72.22%) as compared to females (27.78%). The mean BMI was 22.37. Majority were in the normal range of BMI (86.67%). 57.78% of our study population were non smokers with 21.11% as ex-smokers and 21.11% as current smokers. 8 patients died during the study period. Most common etiology associated with mortality was post tubercular as it was the major identified cause followed by Idiopathic, COPD and post pneumonia. Out of 8 deaths, 3 patients died who had Pseudomonas as culture organism. The major complication associated with death was cor pulmonale which has a clinical as well as statistical correlation with a p value = 0.001. **Conclusion:** We concluded some significant differences in patient's etiological, clinical, radiological and microbiological profiles when compared to data from Western World.

INTRODUCTION

Bronchiectasis (broncos, airways; ectasia, dilatation) is a morphologic term used to describe abnormal, irreversibly dilated and thick walled bronchi. Bronchiectasis represents the final stage of a variety of pathological processes that result in the destruction of the bronchial wall and its surrounding supporting tissues.[1] Bronchiectasis can lead to a variety of complications like recurrent lower respiratory tract infections, respiratory failure, deteriorating pulmonary functions and pulmonary hypertension, which can result in the increased morbidity and premature mortality while degrading quality of life.[2] Mucus plugging, bronchial wall thickening, and destruction may also be predisposed by persistent airway inflammation and mucus hypersecretion, which impairs lung function.[3]

Bronchiectasis has been considered as orphan lung disease since long. Since bronchiectasis is the cause of significant morbidity and mortality allover the world, there is a growing interest in this rather neglected disease.There is a geographical variation in clinical features and etiologies of Bronchiectasis. It is associated with microbial colonization of the respiratory tract with recurring infections and progressive pulmonary damage. Hemophilus influenza, Pseudomonas aeruginosa, Moraxella catarrhalis, Staphylococcus aureus and Enterobacteriaceae are commonly isolated pathogens from bronchiectatic airways.[4]

HRCT is now the test of choice for diagnosis of bronchiectasis. HRCTcan accurately diagnose bronchiectasis, along with localizing and describing the areas of parenchymal abnormalities, and identifying bronchiolar abnormalities and mucus plugging.[5]

There are varied pathways that lead to the development of

bronchiectasis. Bronchiectasis commonly develops either due to an incidental event or an episode that usually does not reflect the patient's intrinsic host defenses. It also evolves in accordance with any condition inherent in the genetic makeup of the patient. A prominent concern in understanding the pathogenesis of bronchiectasis is whether the infection has developed due to any underlying predisposing condition or whether it is the proximate cause of bronchiectasis.[6]

In a retrospective analysis, chest computerized tomography findings in health screening examinees revealed a very high prevalence of bronchiectasis (9.1%) in Korean adults, including asymptomatic and mild cases.[7] Bronchiectasis is still regarded as an "orphan" disease due to the lack of clinical suspicion, commercial interest and research activity.[8] As a consequence,scientific concern in non- cystic fibrosis bronchiectasis diminished, with limited literature about this issue compared to other "obstructive lung diseases" and "pneumonia".[9]

Prior to the development of antibiotics, it was a frequent crippling condition, but since the introduction of vaccine and antibiotics, its occurrence has decreased. According to estimates, it affects 4.2 people out of every 100,000 in the US, and 272 people out of every 100,000 who are 75 years or older. 60% of the people afflicted in the majority of serieswere women. Between 1993 and 2006, the average annual hospitalization rate for bronchiectasis-related conditions was 16.5 per 100,000, with an average yearly percentage rise of 2.4% for men and 3% for women.[6]

The true prevalence of bronchiectasis in communities in the Asia-Pacific region is largely unknown and should be considered a potential diagnosis in all populations. Important etiologies of bronchiectasis seen in other regions including

immunodeficiency syndromes such as, common variable immunodeficiency, secondary immunoglobulin disorders (frequently drug related) and mucociliary defects including primary ciliary dyskinesia, chronic aspiration, autoimmune/ connective tissue diseases, particularly rheumatoid arthritis, and ABPA are described and in some cases result in a delayed diagnoses.

The clinical characteristics and etiologies of bronchiectasis vary geographically as a result of the heterogeneous nature of this chronic,debilitating condition. Therefore, the goal of this study was to identify the common etiologies, clinical presentation, radiological type and involvement, spirometric pattern, microbiological profile and complications of the disease so that comorbidities can be prevented and management, outcome and patient'squality of life can be improved.

MATERIAL & METHODS
This was a hospital based prospective observational study carried out on Bronchiectasis patients at Department of Respiratory Medicine, Institute of Respiratory Diseases, SMS medical college, Jaipur, over a period of one year (2021- 2022).

Inclusion Criteria
1. Patients who have given written informed consent
2. Age above 18 years
3. Radiologically diagnosed Bronchiectasis patients

Exclusion Criteria
1. Other pulmonary diseases like ILD with traction bronchiectasis.
2. Uncooperative and/or hemodynamically unstable patients
3. Pregnant females

METHODS
This study was approved by the Ethical Committee and Institutional Review Board, SMS Medical College, Jaipur. Patients attending our OPD with cough, purulent expectoration, shortness of breath, fever, with/without hemoptysis and radiological features favoring bronchiectasis or previously known/evaluated cases of bronchiectasis were included in our study. A register was maintained for bronchiectasis patients in OPD to facilitate data collection and follow up. After giving full explanation regarding the study, written consent was obtained from all enrolled patients. Patients were selected on the basis of inclusion and exclusion criteria. A questionnaire was given to them and information was collected regarding the demographic data, childhood history, symptomatology and significant past and personal history.

X ray Chest PA view and HRCT chest was done to assess the radiological involvement.

Sputum for AFB smear, CBNAAT, NTM Culture and Pyogenic culture & sensitivity was done to assess the microbiological colonization.

Spirometry was performed as per ATS standards using helios 401 spirometer to detect the pattern of impairment.

Diagnosis of bronchiectasis secondary to COPD was made in patients with a history of significant smoking i.e. >10-15 pack years with spirometric diagnosis of post-bronchodilator obstructive airway impairment and evidence of background emphysema.

Diagnosis of Post TB or Post Pneumonia bronchiectasis was made when the suggesting symptoms followed soon after a severe infection. Patients with a history of Asthma and evidence of proximal bronchiectasis were evaluated further with Serum IgE and Aspergillus specific IgE. These patients

were labelled to have underlying ABPA based on ISHAM criteria for the diagnosis of ABPA. For the patients with a history suggestive of Arthritis and Connective Tissue Disease, workup including Rheumatoid factor, anti-CCP and ANA Profile were sent.

Statistical Analysis
Statistical analysis was done using the Microsoft Excel and SPSS software (22.0V) with the help of a statistician. P value is used to assess the significance of correlation between variables. Chi- square test was performed between two groups and its statistical significance was calculated.

RESULTS
Our study showed that the mean age of the study population was 49.87 yrs. The maximum patients 36.67% were in the age group of 41-50 years and 30% in 51–60 years with male preponderance (72.22%) as compared to females (27.78%). The mean BMI was 22.37 kg/m^2. Majority were in the normal range of 18.5 – 24.9(86.67%). 57.78% of our study population were non smokers with 21.11% as ex-smokers and 21.11% as current smokers (table 1).

8 patients died during the study period. Most common etiology associated with mortality was post tubercular as it was the major identified cause followed by Idiopathic, COPD and post pneumonia (table 2).

Cystic type bronchiectasis was more associated with death (12.5%), followed by Mixed type in 10% and Cylindrical type in 7.69%. There were no mortality seen in Varicose type, which was statistical non significant (P=0.82 NS) (table 3).

Out of 8 deaths, 3 patients died who had Pseudomonas as culture organism, followed by 2 patients with S.pneumoniae, 1 patient with Klebsiella, 1 patient with E.coli and 1 patient with H. influenza (table 4).

Though respiratory failure was the most common complication in our study, the major complication associated with death was cor pulmonale which has a clinical as well as statistical correlation with a p value = 0.001 (table 5).

DISCUSSION
Infection and chronic airway inflammation that results in the destruction and remodeling of the bronchial wall cause bronchiectasis, a permanent and typically progressive bronchial dilation. Chronic, purulent expectoration, multiple exacerbations, and progressive, incapacitating dyspneaare all symptoms of bronchiectasis. The affected patients' lung function and health-related quality of life gradually deteriorate as a result of these events. A number of factors have contributed to the rise in bronchiectasis diagnoses, hospital admissions, mortality rates, and associated costs in recent years, including the disease's detrimental effects on underlying diseases as well as the quality of life and pulmonary function of patients (annual loss of nearly 50 mL of forced expiratory volume in 1 second (FEV1).

In developing nations, bronchiectasis incidence and prevalence are underreported and poorly understood. Despite the fact that the prevalence has decreased in recent years in societies with high socioeconomic status, likely as a result of the advancement of preventive medicine, particularly childhood immunizations, as well as improvements in living conditions and the widespread use of antibiotics, bronchiectasis is now more widely recognized, primarily because high-resolution computerized tomography (HRCT) is used more frequently.

In our study the mean age of the study population was 49.87 years which was compatible with Sharif et al[10] showed 49 years & Dhivya et al[11] showed higher prevalence of

bronchiectasis in 5th and 6th decade which is well documented in literature.

The present study showed that 25 (27.78%) were females and 65 (72.22%) males. This is in accordance to studies which show a higher male preponderance. Dhivya et al observed similar result to that of ours. The ratio of male to female sex ratio was slightly higher on the female side which reflects the higher prevalence of bronchiectasis in female gender.[11]

Patients were more prone to recurrent respiratory tract infections, hypoproteinemia and persistent breathlessness in advanced stages causing a low mean BMI. Chandrasekaran et al[12] and Dhivya et al[11] found that about 11 subjects i.e. 34% of the study population belonged to overweight category. Majority of the subjects 135 i.e. 81.8% were included under normal BMI. 19 of the subjects i.e.11.5 % were underweight.

57.78% of our study population was non smokers with 21.11% as ex-smokers and 21.11% as current smokers. Smoking further accentuates airway inflammation increasing breathlessness and worsening prognosis. Smoking history is important because COPD is an important co-morbidity for patients with bronchiectasis, which is associated with severe morbidity and poor outcome.[12]

The most important aspect for disease treatment and preventing complications in patients with bronchiectasis is microbiology. In our study sputum culture is an important parameter in the management of bronchiectasis. Pseudomonas and Streptococcus pneumoniae were the most common microorganisms isolated in 28.88% and 14.44% of study population respectively. According to studies, pseudomonas is the common isolated organism which also has a destructive nature and tendency for chronic colonization further worsening the symptoms. It was followed by H. influenza, streptococcus pneumonia which was seen predominantly. Other organisms isolated were Klebsiella, staphylococcus aureus, acinetobacter etc. Non tuberculous mycobacteria is emerging as one of the important cause for colonization even in immune-competent individuals. 15– 20% of patients may alsobe negative for any pathogenic bacterial growth.[13]

There was not much clinical or statistically significant association of presence of comorbidities and death in our study population. Pseudomonas aeruginosa was the most common organism isolated in patients with bronchiectasis as well as those who died during the study period. In our study, 3 patients out of 26 patients infected with Pseudomonas died. Pseudomonas has tendency to form persistent colonies, with 50% patients having pseudomonas growth even on repeated cultures. It is also commonly seen in the destructive cavitatory type and more prone to develop complications of morbidity and mortality. Thus susceptible antibiotics should be initiated earlier to prevent colonization and complications.

Though respiratory failure was the most common complication in our studypatients, the major complication associated with death was cor pulmonale (4 patients) which has a clinical as well as statistical correlation with a p value = 0.001. Chronic bronchiectasis leads to pulmonary hypertension, right atrial and ventricular dilatation eventually leading to cor pulmonale. Supported with our results by Dhivya et al[11], showed major complication associated with death was cor pulmonale which had a clinical as well as statistical correlation with a p value =0.001.

Table 1 : Demographic Profile Of Study Patients

Demographic profile		Frequency (N=90)	Percentage
Age (Mean)		49.87 yrs	
Gender	Male	65	72.22%
	Female	25	27.78%

BMI (Kg/m2)	<18.50	8	8.89%
	18.5 to 24.9	78	86.67%
	25-29.9	4	4.44%
Smoking history	Smoker	19	21.11%
	Ex- Smoker	19	21.11%
	Non Smoker	52	57.78%

Table 2: Correlation Between Etiology And Mortality

ETIOLOGY	Total	Alive		Mortality	
		No.	%	No.	%
Post Tubercular	48	44	91.66%	4	8.33%
Post Pneumonia	9	8	88.88%	1	11.11%
Connective Tissue Disorder	8	8	100%	0	0%
COPD	5	4	80%	1	20%
ABPA	4	4	100%	0	0%
Idiopathic	12	10	83.33%	2	16.66%
Primary Ciliary Dyskinesia	2	2	100.00%	0	0.00%
Non Tubercular Mycobacteria (NTM)	2	2	100.00%	0	0.00%
Total	90	82	91.11%	8	8.89%

Table 3: Correlation Between Morphological Pattern Of Bronchiectasis And Mortality In Study Patients

Morphological Pattern	Alive		Dead		Total
	No.	%	No.	%	
Cylindrical	48	92.31%	4	7.69%	52
Cystic	21	87.50%	3	12.50%	24
Mixed	9	90.00%	1	10.00%	10
Varicose	4	100.00%		0.00%	4
Total	82		8		90

Table 4: Correlation Between Culture Organism And Mortality In Study Patients

Sputum culture	Total	Alive		Mortality	
		No.	%	No.	%
Pseudomonas	26	23	88.46%	3	11.53%
Klebsiella	9	8	88.88%	1	11.11%
E. Coli	7	6	85.71%	1	14.28%
H. Influenza	7	6	85.71%	1	14.28%
Streptococcus pneumoniae	13	11	84.62%	2	15.38%
Staphylococcus aureus	8	8	100.00%	0	0.00%
No Organism grown / Sterile	14	14	100.00%	0	0.00%
Aspergillus species	4	4	100.00%	0	0.00%
NTM	2	2	100.00%	0	0.00%

Table 5: Correlation Between Complications And Mortality In Study Patients

Complications	Total	Alive		Dead	
		No.	%	No.	%
No complications	25	25	100.00%	0	0.00%
Hemoptysis	18	16	88.89%	2	11.11%
Respiratory failure	32	30	93.75%	2	6.25%
Cor Pulmonale	20	16	80%	4	20%
Pneumothorax	6	6	100.00%	0	0.00%

CONCLUSION

The majority of patients were middle aged males. Post-tubercular bronchiectasis was the commonest etiology. Pseudomonas was the most common isolated pathogen and respiratory failure was the most frequent complication. To conclude, our study highlights some significant differences in patient's etiological, clinical, radiological and microbiological profiles when compared to data from Western World.

REFERENCES
1. Fishman's pulmonary diseases and disorders Fifth edition
2. Habesoglu MA, Ugurlu AO, Eyuboglu FO. Clinical, radiologic, and functional evaluation of 304 patients with bronchiectasis. Ann Thorac Med. 2011 Jul;6(3):131-6.
3. Guan WJ, Gao YH, Xu G, Lin ZY, Tang Y, Li HM, Lin ZM, Zheng JP, Chen RC, Zhong NS. Characterization of lung function impairment in adults with bronchiectasis. PLoS One. 2014 Nov 18;9(11):e113373.

4. Sharif N, Baig MS, Sharif S, Irfan M. Etiology, Clinical, Radiological, and Microbiological Profile of Patients with Non-cystic Fibrosis Bronchiectasis at a Tertiary Care Hospital of Pakistan. Cureus. 2020 Mar 8;12(3):e7208.
5. King PT, Holdsworth SR, Freezer NJ, Villanueva E, Holmes PW. Characterisation of the onset and presenting clinical features of adult bronchiectasis. Respir Med. 2006 Dec;100(12):2183-9.
6. Murray and Nadel's Textbook of Respiratory Medicine sixth edition
7. Kwak HJ, Moon JY, Choi YW, Kim TH, Sohn JW, Yoon HJ, Shin DH, Park SS, Kim SH. High prevalence of bronchiectasis in adults: analysis ofCT findings in a health screening program. Tohoku J Exp Med. 2010 Dec;222(4):237-42.
8. Barker AF, Bardana EJ Jr. Bronchiectasis: update of an orphan disease.Am Rev Respir Dis. 1988 Apr;137(4):969-78.
9. Martinez-Garcia, MA. Bronchiectasis: Still an Orphan Disease?. Archivos de bronconeumología. 2005;41:407-9.
10. Sharif N, Baig MS, Sharif S, Irfan M. Etiology, Clinical, Radiological, and Microbiological Profile of Patients with Non-cystic Fibrosis Bronchiectasis at a Tertiary Care Hospital of Pakistan. Cureus. 2020 Mar8;12(3): e7208.
11. Dhivya R. Study the Clinical, Radiological and Microbiological Profile ofPatients with Bronchiectasis in a Tertiary Care Hospital (Doctoral dissertation, Kilpauk Medical College, Chennai).
12. Chandrasekaran R, Mac Aogáin M, Chalmers JD, Elborn SJ, Chotirmall SH. Geographic variation in the aetiology, epidemiology and microbiology of bronchiectasis. BMC Pulm Med. 2018 May 22;18(1): 83.
13. Schäfer J, Griese M, Chandrasekaran R, Chotirmall SH, Hartl D. Pathogenesis, imaging and clinical characteristics of CF and non-CFbronchiectasis. BMC Pulm Med. 2018 May 22;18(1):7