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Original Research Paper

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COMPARISON OF LUNG FUNCTION IN PATIENTS WITH BRONCHIECTASIS DURING ACUTE EXACERBATION AND IN CONVALESCENCE - A PROSPECTIVE STUDY

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ABSTRACT

Background- Bronchiectasis is a common chronic respiratory disease. A noticeable drop in lung function during exacerbations and recovery during convalescence has been revealed in patients with asthma or chronic obstructive pulmonary disease (COPD). Hence this study was planned with the objectives to compare lung functions during acute exacerbation and convalescence in patients with bronchiectasis. **Methods-** This was a prospective cohort study conducted in 50 patients over a duration of 18 months. Measurement of exacerbations and convalescence visits comprised of spirometry, sputum bacteriology, serum and sputum biomarker. Student's paired t test, Fischer's exact test or Chi square test was used to analyze the significance of difference. P value <0.05 was considered as statistically significant. **Results-** In this study, there was a significant association of mMRC dyspnoea score in exacerbation and in convalescence. (p <0.0001). The analysis showed that mMRC dyspnoea score was shifted to lower scores in convalescence compared to that in exacerbation. FEV1, FVC and FEV1/FVC) and 6 MWT distance were significantly lower in patients in exacerbation as compared in convalescence. **Conclusion-** There was marked improvement in lung functions in convalescence as compared to patients in acute exacerbation.

KEYWORDS : Bronchiectasis, Exacerbation, Convalescence, Lung function, Spirometry

INTRODUCTION

Bronchiectasis is a common chronic respiratory disease.[1] Recurrent infection and inflammation leads to chemical and cellular cascade causing permanent changes in airway architecture.[2]

Persistent airway inflammation and mucus hypersecretion may be responsible for mucus plugging along with bronchial wall thickening and destruction causing impairment of lung function. In patients with bronchiectasis, airway obstruction resulting in reduction in Forced expiratory volume in 1 second (FEV1) suggest that spirometry measurement may be helpful for adding further information about functional impairment of lungs.[3] A study reported that greater sputum volume, older age, diffuse disease and concomitant asthma were responsible for worse lung function in patients with bronchiectasis.[4]

The British Thoracic Society (BTS) has defined exacerbations requiring antibiotics based on expert consensus as a deterioration in local symptoms and/or systemic upset.[5] Guan et al.,[6] in their study, revealed that bronchiectasis exacerbations elicit marked reductions in Forced vital capacity (FVC) and FEV1. The 6-Minute Walk Test (6MWT) is a extensively used measure of functional status and is a predictor of prognosis for various respiratory conditions.[7] Though these clinical applications indicate that this simple measurement can reflect the pulmonary and functional status of bronchiectasis patients, evaluation of the 6MWT in this population is limited.

It has been revealed that patients with asthma or chronic obstructive pulmonary disease (COPD) are characterized by noticeable drop in lung function during exacerbations and recovery during convalescence (1 week following a 2-week antibiotic treatment). However, the underlying pathogenesis of bronchiectasis may lead to different magnitude of change in lung function.[6]

There is paucity of studies in literature showing respiratory morbidity in patients with bronchiectasis in acute exacerbation, in India. Hence this study was planned with the aim to study respiratory morbidity in patient with bronchiectasis presenting with acute exacerbation. Objectives of this study were to compare lung functions during acute exacerbation and convalescence and to compare six minute walk test during acute exacerbation and convalescence.

MATERIALS AND METHODS

This was a prospective cohort study conducted in 50 patients in the Department of Respiratory medicine of a tertiary care teaching institute after obtaining approval of institutional ethics committee (IEC). Total duration of study was 18 months from January 2018 to June 2019. Patients satisfying the following inclusion and exclusion criteria and willing to participate in this study were enrolled in the study.

Inclusion criteria:

Patients of 18-75 years of age, conscious patients with bronchiectasis in acute exacerbation. Exclusion criteria: Patients requiring invasive ventilation during acute exacerbation, Patients having moderate to severe haemoptysis, Patients with impaired consciousness. [Severity of haemoptysis was classified based on the amount of blood expectorated in 24 hours. Haemoptysis is classified as mild (<30 ml), moderate (31–100 ml), severe (100–600 ml][8] A written informed consent was taken from every patient or from close relative of the patient after explaining the study procedure in detail. The risks and benefits involved in the study and voluntary nature of participation was explained to participants before obtaining consent. Confidentiality of the study participants was maintained.

After initial screening, before subjecting patients to clinical examinations, following parameters were noted in case record form (CRF). Demographic profile - anthropometry (age, sex, height, weight, BMI, smoker/non-smoker profile), clinical profile (Chronic cough with sputum production), past history, family history and personal history was noted. Medical diagnosis was considered after detailed clinical evaluation. Primary investigations such as chest x-ray, HRCT, sputum for AFB stain, gram stain, culture sensitivity, blood investigations (CBC, LFT, KFT) and spirometry were done for every patient and then the patients were started on standard medical treatment.

Acute exacerbation denoted significant changes in three or more of symptoms and for at least 2 days; cough frequency, 24 hours sputum volume, sputum purulence and emerging fever,

dyspnoea or chest pain. Antibiotics were prescribed by integrating previous bacteriological reports. Patients were informed to contact investigators in case of worsening of respiratory symptoms that warrant prompt hospital visit for assessments.

Convalescence is defined as 1 week after cessation of 14 days antibiotic therapy.[6] Patients were requested to undertake reassessment at convalescence stage (at 1 week following antibiotic therapy) regardless of treatment outcome. Measurement of exacerbations and convalescence visits comprised of spirometry, sputum bacteriology, serum and sputum biomarker. PFT of the patients was done in steady state of acute exacerbations and in convalescence period. Patients were started on symptomatic treatment and antibiotics were prescribed according to culture sensitivity reports.

Spirometry was conducted using spirometer. The quality control met guidelines for standardization.[9] Between maneuver variation was less than 5% or 200 ml in FVC and FEV1, with the maximal values being reported. Salbutamol was withdrawn for at least 6 hours and Salmeterol and Formoterol 24 hours prior to spirometry. An individual patient was reported about duration of bronchiectasis, symptoms, duration of diagnosis, no of acute exacerbations within 2 years, sputum characteristics (mucoid/ mucopurulent/ purulent), medications ever taken within 6 months and associated findings.

Spirometry Examination-

Spirometry was performed using Spirobank G by MIR model no. A23- 048.07959 and measured using winspro Pro software. Spirometric procedure was carried out as per ATS/ERS task force recommendation for standardization of lung function testing. Readings of FEV1 (forced expiratory volume in 1 second), FVC (Forced vital capacity), Ratio of FEV1/FVC were taken. At least three forced expiratory manoeuvres were done for each patient of which the test with highest values were accepted.

The HRCT score was assessed on a lobar basis, with lingular lobe being regarded as a separate lobe. For an individual lung lobe, the radiological severity of bronchiectasis were scaled by using modified Reiff score. The maximal total score was 18 for a total of six lobes.[6]

6MWT was performed in accordance with the standard protocol of the American Thoracic Society.[10] The test was conducted in 30 m corridor and patients were instructed to walk at their own pace but to cover as much ground as possible within 6 minutes. Standardised encouragement was provided during the test.[7]

Sample Size was calculated using formula-

$N = Z^2P(1-P)/d^2$

Expected prevalence of respiratory as 8.2%, with 80% power and alpha error of 5%, sample size came out to be 50 patients.

Statistical Analysis: Data was expressed as percentage and mean ± S.D. Kolmogorove-Smirnove analysis was performed for checking linearity of the data. Student's paired t test was used to assess the significance of difference between repeated means. Fischer's exact test or Chi square test was used to analyze the significance of difference between frequency distribution of the data. P value <0.05 was considered as statistically significant. SPSS© for windows™ Vs 17, IBM™ Corp NY and Microsoft excel™ 2007, Microsoft® Inc USA was used perform the statistical analysis.

OBSERVATIONS AND RESULTS

All the 50 patients were found to have breathlessness and 40 (80%) patients had cough with expectoration while 10 (20%) patients had dry cough. Haemoptysis was observed in 17 (34%) patients while chest pain was noted in 13 (26%) patients. Out of 50 patients in total, 33 (66%) patients were found non-tobacco smokers while, 9 (18%) were former tobacco smokers and 8(16%) were current tobacco smokers. Duration of symptoms in study patients was noted. Out of 50 patients in total 30 (60%) patients were found to have symptoms since last 6-10 years and 17 (34%) patients were found to have symptoms since </=5 years. While, 3 (6%) patients had symptoms since last 11-15 years.

Duration of diagnosis in study patients was noted. Out of 50 patients in total 37 (74%) patients were diagnosed in </=5 years and 12 (24%) patients were found to be diagnosed in 6-10 years while only 1 (2%) patient was diagnosed in 11-15 years.

Exacerbation in previous year in study patient was noted. 18 (36%) patients were found to have exacerbation twice in previous year. This was followed by 13 (26%) and 12 (24%) patients who had exacerbation 4 and 3 times respectively. 5 (10%) patients had exacerbation once in previous year while, 2 (4%) patients had exacerbation 5 times in previous year. Past history in study patients was noted. PTB was observed in 18 (36%) patients and Pneumonia was observed in 13 (26%) patients. This was followed by other causes (congenital immunodeficiency syndrome, developmental defects, rheumatic arthritis and SLE) in 9 (18%) patients and infection (like measles, pertussis, adenovirus) in 8 (16%) patients. While, PTB and pneumonia both was observed in 2 (4%) patients. Distribution of bronchiectatic lobes involved in study patients was noted. 16 (32%) patients were found to have bronchiectasis in 5 lobes followed by 14 (28%) patients having 3 bronchiectatic lobes involved. 13(26%) patients involved 4 lobed, while 7 (14%) were found to have 2 lobes involved.

Distribution of HRCT score in study patients was noted. 11 (22%) patients were found to have HRCT score 5. While, 9 (18%) patients had score 6 as well as another 9 (18%) patients were found to have score 7. HRCT score 5 was observed in 8 (16%) patients. 4 (8%) patients had HRCT score 3 while another 4 (8%) patients had HRCT score 8. HRCT score 2 and 9 were respectively noted in 3 (6%) and 2 (4%).

Distribution of microorganism in study patients was noted. *P. aeruginosa* was observed in 19 (38%) patients and *H. influenza* was observed in 12 (24%) patients. This was followed by *H. parainfluenzae* in 9 (18%) patients and methylsilline sensitive *S.aureus* in 6 (12%) patients. In 3 (6%) patients no growth was observed and fungal spore was found in 1 (2%) patient. Comparison of blood eosinophils in exacerbation and in convalescence in study patients was assessed using Pearson Chi square test. No significant difference was noted between them.

Distribution of triple therapy in convalescence in study patients was performed. All the study patients were found to undergo LABA and 47 (94%) patients underwent ICS while LAMA was given to 15 (30%) patients.

Table 1: Patient demographics

Age (Years)	Frequency	Percent
</=30	6	12.0
31-40	8	16.0
41-50	3	6.0
51-60	20	40.0
>60	13	26.0
Gender	Frequency	Percent
Female	25	50.0
Male	25	50.0
BMI	Frequency	Percent

Underweight	21	42.0
Normal range	11	22.0
Overweight	11	22.0
Obese I	3	6.0
Obese II	4	8.0
Total	50	100.0

Table 2: Association of mMRC dyspnoea score acute exacerbation and mMRC dyspnoea in convalescence

mMRC Dyspnoea score in exacerbations	mMRC Dyspnoea score in convalescence				Total
	1	2	3	4	
2	15	5	1	0	21
	93.8%	20.8%	14.3%	.0%	42.0%
3	1	18	0	0	19
	6.2%	75.0%	.0%	.0%	38.0%
4	0	1	6	3	10
	.0%	4.2%	85.7%	100.0%	20.0%
Total	16	24	7	3	50
	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests

Table 3: Comparison of different parameters between exacerbation and convalescence

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	62.916a	6	.000
Likelihood Ratio	59.770	6	.000
Linear-by-Linear Association	31.617	1	.000
N of Cases	50		

DISCUSSION

In the present study, the duration of symptoms in study patients was noted. Out of 50 patients in total 30 (60%) patients were found to have symptoms since last 6-10 years and 17 (34%) patients were found to have symptoms since </=5 years. While, 3 (6%) patients had symptoms since last 11-15 years. Supporting our findings, in a study by **Guan et al.[6] (2014)** also reported the mean duration of symptoms of 10 years in patients with bronchiectasis exacerbation. Duration of diagnosis in study patients was noted. Out of 50 patients in total, 37 (74%) patients were diagnosed in </=5 years and 12 (24%) patients were found to be diagnosed in 6-10 years while only 1 (2%) subject was diagnosed in 11-15 years. **Guan et al.,[6] (2014)** reported the mean duration of diagnosis as 5 years in patients with bronchiectasis exacerbation which is in relation with our study.

Exacerbation in previous year in study patients was noted. 18 (36%) patients were found to have exacerbations twice in previous year. This was followed by 13 (26%) and 12 (24%) patients who had exacerbations 4 and 3 times respectively. 5 (10%) patients had exacerbation once in previous year while, 2 (4%) patients had exacerbations 5 times in previous year. In consistency with our study, in a study by **Chalmers and collegues.,**[11] 3 or more exacerbations were noted in majority 15(55.6%) patients, 2 exacerbations were seen in 8(29.6%) patients and 4(14.8%) patients had only one exacerbation per year.

Past history in study patients was noted. PTB was observed in 18(36%) patients and Pneumonia were observed in 13 (26%) patients. This was followed by other causes (congenital immunodeficiency syndrome, developmental defects, rheumatic arthritis and SLE) in 9 (18%) patients and infection (like measles, pertussis, adenovirus) in 8 (16%) patients. While, PTB and pneumonia both was observed in 2 (4%) patients. In relation with our study, in a study by **Lopes et al.**[12] in patients of bronchiectasis, out of 112 individuals who were included in the study, 34 had sequelae of tuberculosis, 29 had a history of non-tuberculosis infections, 21 had Cystic Fibrosis, 11 had primary ciliary dyskinesia (PCD), and 17 had rheumatoid arthritis. Similarly, **Utpat et al.,**[13] in their study reported that 27(54%) patients had past history of infection followed by 7(14%) patients with past history of PTB.

In present study, distribution of bronchiectatic lobes in study patients was noted. 16 (32%) patients were found to have bronchiectasis in 5 lobes followed by 14 (28%) patients having 3 bronchiectatic lobes involved. 13 (26%) patients involved 4 lobed, while 7 (14%) were found to have 2 lobes involved. Similarly, in a study by **Guan et al.,[6] (2014)** majority of patients involved 4 bronchiectatic lobes. Also, in study by **Alzeer et al.,**[14] out of 94 patients with bronchiectasis, majority 63 (67%) patients involved <5 lobes and 31(33 %) patients involved >5 lobes involvement. Distribution of HRCT score in study patients was noted. 11 (22%) patients were found to have HRCT score 5. While, 9 (18%) patients had score 6 as well as another 9(18%) patients were found to have score 7. HRCT score 4 was observed in 8 (16%) patients.4 (8%) patients had HRCT score 3 while another 4 (8%) patients had HRCT score 8. HRCT score 2 and 9 were respectively noted in 3 (6%) and 2 (4%). High-resolution CT scan (HRCT) and its score changes and pulmonary function impairment in patients with bronchiectasis.[30] In consistency with our study, mean HRCT score was 7 in a study by **Guan et al.[6] (2014)** Also, in a study by **Guan et al.**[15] (2015), the mean chest HRCT score in patients with exacerbation of bronchiectasis was 8.3±4.1. Aberrant HRCT features have also been associated with poor lung function. This has been supported by the fact that lung clearance index correlated with chest HRCT scores in patients with bronchiectasis.[6] **Lee et al.**[7] in their study, to find out the clinical determinants of bronchiectasis reported that HRCT score was >9 in 37% patients, 6-9 in 33% patients and 1-5 in 30% patients.

In this study, there was a significant association of mMRC dyspnoea score in exacerbation and in convalescence. (p <0.0001). The analysis showed that mMRC dyspnoea score was shifted to lower scores in convalescence compared to that in exacerbation. Similarly, **Ozalp et al.,**[16] in their study including patients with bronchiectasis used MMRC to evaluate dyspnoea, which is being considered as a major factor while defining bronchiectasis and affects the survival along with airway obstruction, lung hyperinflation and frequency of disease. They confirmed that dyspnoea perception was evidently higher in patients with bronchiectasis. Also, **Qi et al.**[17] confirmed the mean mMRC dyspnoea score of 1.95 demonstrating a moderate severity of breathlessness in patients with bronchiectasis.

In our study, when comparison of FEV_1%, FVC% and FEV_1/FVC between exacerbation and convalescence was done, FEV_1%, FVC% and FEV_1/FVC in exacerbation was found to be significantly lower in study patients in exacerbation as compared with that in convalescence. Supporting our study, in a study by **Guan et al.**,[15] (2015), it was confirmed that during exacerbations of bronchiectasis, there were significant reductions in FVC, FEV1 and maximum mid-expiratory flow (P= .01, <.01, and .04, respectively while for comparing between bronchiectasis exacerbations and stable state), but not FEV1/FVC. In relation with our study, results of the study by **Guan and collegues**.[6](2014) stated that there was significant reduction in FVC and FEV1 at exacerbations and recovery during convalescence in patients with bronchiectasis (P<0.05). In spite of the trend toward decline during bronchiectasis exacerbations and recovery during convalescence, the mean changes in spirometry were 5% or less in most patients, compared with baseline levels.

In the present study, mean of 6 MWD in exacerbation was 386.3±49.05 meters and mean of 6 MWD in convalescence was 519.56±44.27 meters. In accordance with this study, **Chalmers et al.,**[18] in their study, reported that mean 6 MWD in

patients with exacerbation was 434 meters and 448 meters after standard treatment. In a study by **Prasad et al.,**[19] it was found that among bronchiectatic patients, mean 6 MWD was 418±114.69 meters which can be correlated with our study. In this study, when comparison of 6 MWT was done between exacerbation and convalescence, 6 MWT in exacerbation was found to be significantly lower in patients in exacerbation as compared to that in convalescence. These findings can be correlated with the findings by **Chalmers et al.**,[18] in which the 6 MWT distance was improved 8 weeks post-exacerbation after giving standard therapy or pulmonary rehabilitation as a management for exacerbation of bronchiectasis. Although, improvement seen was not statistically significant.

Limitations:

It was a single centre, short duration study. Because of small sample size of the study, it should be acknowledged that these differences may be the result of chance.

CONCLUSION

From this study, it can be concluded that past history of PTB and >1 exacerbation in previous year were the risk factors for developing exacerbation of bronchiectasis. There were marked reductions in PFT parameters such as (FEV1, FVC and FEV1/FVC) and 6 MWT distance along with increase in mMRC dyspnoea score in patients of exacerbation of bronchiectasis which were improved in same patients after 14 days of standard antibiotic treatment in convalescence reflecting improvement in lung function.

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