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FACTORS INFLUENCING HOSPITALIZATION OF PATIENTS WITH BRONCHIECTASIS EXACERBATIONS: A COHORT STUDY

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Abstract

Background: In bronchiectasis, exacerbations have been associated with higher mortality and a greater impairment of lung function. This study aims to evaluate factors associated with exacerbations requiring hospitalization, with regard to host characteristics, usual treatments, severity and history of exacerbations and to assess the etiology of bronchiectasis.
Methods: This prospective observational cohort study was conducted among patients with a compatible clinical history consistent of chronic sputum production and/or frequent respiratory infections with confirmed findings of bronchiectasis by HRCT of lungs performed prior to study recruitment. Minimum sample size required for the study was 72. This cohort consisted of 77 patients who were followed up for 1year and separated in two subsets: patients treated as outpatients and those admitted to hospital at least once during the follow-up.
Results: Among the participants, 37 (48.1%) were hospitalized in 1 year follow up period whereas 40 (51.9%) were not hospitalized during the period. All of the patient required hospitalization due to exacerbation were above 50 years. Vaccinated patients were more among OP Patients.29 out of 37 Patients shows any one of culture isolate, from which 32.4% were pseudomonas, 18.9 % were MDR pathogen 27% were other organism. IP Cohort more than half of the patient shows FEV1 less than 50. For OP cohort the entire patient shows FEV1 above 50 with significant P value. Bronchiectasis exacerbation (BE) patients with higher BSI and FACED scores required more hospital admissions because of exacerbation.
Conclusion: Age, Forced Expiratory Volume in 1 second (FEV1), extent of radiological involvement, coexistent COPD, exacerbation in last 1 year, culture isolation of organism, use of Proton Pump Inhibitors (PPI) and Bronchiectasis Severity (BSI) score were found to be risk factors for exacerbation. Pneumococcal and Influenza vaccination is found to be a protective factor.

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Background and Rationale:-

Bronchiectasis is a common chronic structural respiratory disease presenting with cough, sputum production, respiratory infections, and impaired quality of life. One of the key clinical aspects in the prognosis and severity of airway diseases is exacerbations, particularly serious ones that require hospitalization. In bronchiectasis, exacerbations have been associated with higher mortality and a greater impairment of lung function,as well as more severe forms of the disease. As well as substantial concomitant health costs.[1,2]

There is limited data on the mortality after an acute exacerbation of bronchiectasis. Recently, two studies outside of the United States reported the survival in patient with acute exacerbation of bronchiectasis. In these studies, the mortality rate was 40% at one year and 60% at four years. There is still a significant mortality in non-hospitalized patients with bronchiectasis that varies from 13% to 25% according to some other studies.[3,4]

A key challenge in bronchiectasis management lies in the identification of patients at high risk of developing bronchiectasis complications who may benefit from intensification of therapy. We hypothesized that several factors related to host characteristics, to comorbidities, to prior exacerbations, usual treatments along with bronchiectasis severity score must be associated with developing exacerbations requiring hospital admission. Hence this study aim to evaluate factors associated with exacerbations requiring hospital admission, with regard to host characteristics, usual treatments, severity scores (FACED and BSI) and history of prior exacerbations.

Objectives:-

1) To evaluate factors associated with exacerbations requiring hospitalization, with regard to host characteristics, usual treatments, severity and history of exacerbations
2) To assess the etiology of bronchiectasis

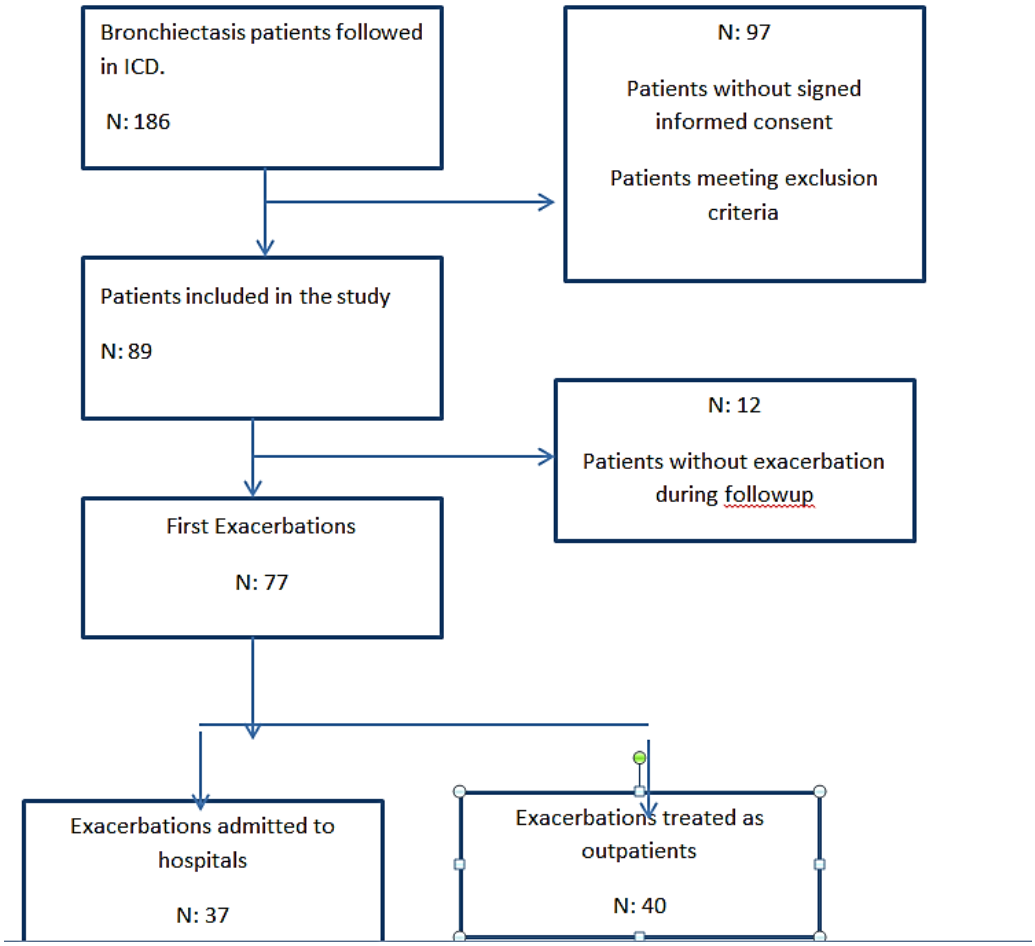
Methods:-

This prospective observational cohort study was conducted among patients attending institute of chest disease -govt medical college Kozhikode during the period December 2017 to May 2019. The study population included all patients with a compatible clinical history consistent of chronic sputum production and/or frequent respiratory infections with confirmed findings of bronchiectasis by HRCT of lungs performed prior to study recruitment. Those with severe immunosuppression, active tuberculosis, cystic fibrosis, interstitial lung disease was excluded from the study.

IEC clearance was obtained. Data collection was started only after getting ethics committee approval for the study, informed written consent was obtained from all the participants. Confidentiality has been ensured and maintained.

Minimum sample size required for the study was calculated as 72. In this study, the cohort consisted of 77 patients who were followed up for 1year and separated in two subsets: patients treated as outpatients and those admitted to hospital at least once during the follow-up period (Figure1). The decision of hospital admission was made by BTS 2010 guideline.

Data collected from the participants include demographic data, diagnosis of bronchiectasis, comorbidities, smoking, alcohol intake, and vaccine status (flu and pneumococcal vaccines). Comorbid conditions recorded were diabetes, chronic obstructive pulmonary disease (COPD), asthma, chronic heart failure, myocardial infarction and prior tuberculosis. In this study, COPD was recorded as comorbidity similar to other studies and defined bronchiectasis associated with COPD in the presence of a smoking history of at least 10 pack-years with airflow obstruction (FEV1/FVC ratio < 0.7) according to the Global Initiative for Chronic Obstructive Lung Disease recommendations.[5]Data were analyzed using spss software: descriptive and inferential statistical analysis has been carried out in the present study.



Results:-

The cohort consisted of 77 patients followed up for 1 year and separated in two subsets: patients treated as outpatients and those admitted to hospital at least once during the follow-up period. Among the participants, 37 (48.1%) were hospitalized in 1 year follow up period whereas 40 (51.9%) were not hospitalized during the period.

Considering the age, all of the patient required hospitalization due to exacerbation is above 50 years of age (with significant P value). Most of the hospitalization due exacerbation is with 61-70 years (56.8%). Distribution of male and female is almost similar in two groups. (table 1).

Table 1:- Association of age and Gender in relation to Hospitalization I years follow up of patients studied.

variables	**Hospitalization 1year follow-up**		**Total (n=77)**	**P value**
	No (n=40)	**Yes (n=37)**		
Age in years				
• <40	4(10%)	0(0%)	4(5.2%)	<0.001**
• 40-50	16(40%)	0(0%)	16(20.8%)	
• 51-60	16(40%)	16(43.2%)	32(41.6%)	
• 61-70	4(10%)	21(56.8%)	25(32.5%)	
Gender				
• Female	22(55%)	20(54.1%)	42(54.5%)	0.934
• Male	18(45%)	17(45.9%)	35(45.5%)	

**Statistically significant

Vaccinated patients were more among OP Patients: 35 % patients were taken influenza vaccine and 47.5% were taken pneumococcal vaccine [8.1% and 21.6% for IP patient respectively] with significant p value. 8 out of 32 patients were smokers in IP cohort whereas 3 out of 40 patients were smokers in OP group. (table2)

Table 2:- Association of Smoking status, Influence vaccine and pneumococcal vaccine in relation to Hospitalization I years follow up of patients studied.

variables	Hospitalization 1year follow-up		Total (n=77)	P value
	No (n=40)	Yes (n=37)		
Smoking Status	3(7.5%)	8(21.6%)	11(14.3%)	0.077+
Influence vaccine	14(35%)	3(8.1%)	17(22.1%)	0.004**
Pneumococcal vaccine	19(47.5%)	8(21.6%)	27(35.1%)	0.017*

Chi-Square/Fisher Exact Test

Considering isolated organism from culture, 29 out of 37 Patients shows any one of culture isolate, from which 32.4% were pseudomonas, 18.9 % were MDR pathogen 27% were other organism. Whereas, for 31 out of 40 OP patient not isolated any organism in culture. (figure2)

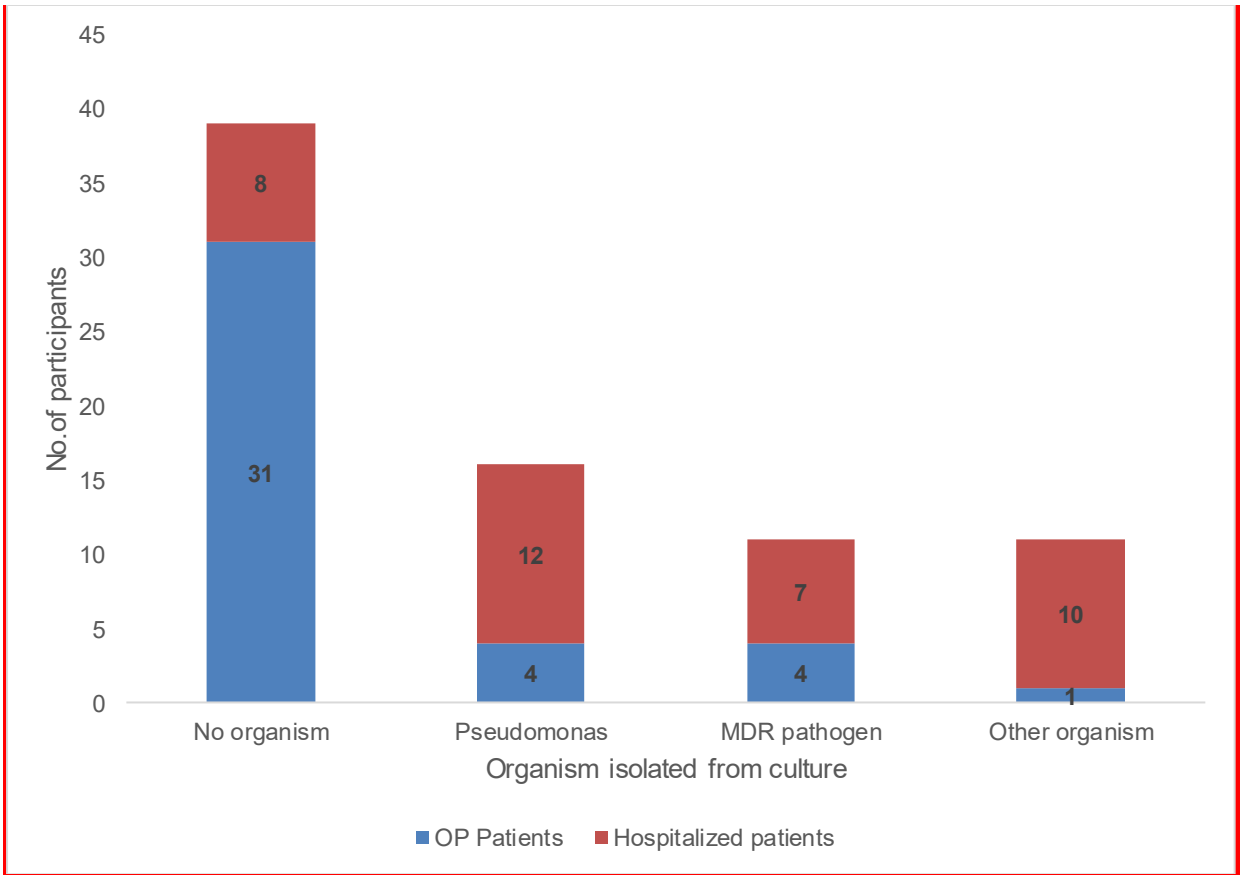


Figure 2:- Organism distribution in relation to Hospitalization I years follow up of patients studied.

Association between various factors and hospitalization was analysed and the following results were observed. For the IP Cohort more than half of the patient shows FEV1 less than 50. For OP cohort the entire patient shows FEV1 above 50 with significant P value.COPD has got association with exacerbation, which is more with IP patient that is 12 out of 37 patients [32.4%] with significant P value. 53% patient from IP cohort shows involvement of more than 2 lobes, and 70 % patient from OP cohort shows less than 3 lobes, with significant P value. (table3)

Most of the patients from both groups, almost 83% were using LABA and ICS.Considering LTOT, 16% patient using from IP patients and 3 patients using from OP cohort. From IP cohorts 73% patients were using mucolytic whereas from OP cohort 87.5% using mucolyticsOut of 40 OP patients, 35 patients were uses PPI and from 37 IP cohort 25 patient were using PPI.Almost 70% patients from IP cohort and 82.5 % patients from OP cohort were regularly using chest physiotherapy.Considering hospitalization due to exacerbation in last year is more with IP cohort [48.6%] compared to OP cohort [30%] with significant p value.From the IP cohort 64.9 % patient had history of previous hospitalization due to bronchiectasis at any time, where as in OP cohort, it is 50%.(table3)

An underlying etiology was identified in 48.06% of the patients. Most commonly, bronchiectasis was post-infectious (83%) due to tuberculosis (25.97%), childhood infections (10.38%), pneumonia (3.89%), whooping cough (1.29%) and measles (1.29%) There were three patient with immunoglobulin deficiency and one case ABPA.(Figure 3)

Bronchiectasis exacerbation (BE) patients with higher BSI and FACED scores required more hospital admissions because of exacerbation. Regardless of its recognized differences in classifying BE patients in the severe phases, BSI classified more patients as severe than FACED. According to BSI score, patients were classified into low (0–4 points, n =12), intermediate (5–8 points, n =23), and high BSI scores (9 or more points, n = 42).There was a clear difference in hospitalization due to exacerbation between patients classified as low, intermediate, and high BSI scores with significant p value[P value <.001]. (Table4)

Table 3:- Association of various factors in relation to Hospitalization I years follow up of patients studied.

Variables	**Category**	**Hospitalization 1year follow-up**		**Total**
		No	**Yes**	
FEV1	<50	0(0%)	22(59.5%)	22(28.6%)
	50-70	32(80%)	15(40.5%)	47(61%)
	>70	8(20%)	0(0%)	8(10.4%)
Co morbidities	DM	10(25%)	16(43.2%)	26(33.8%)
	COPD	2(5%)	12(32.4%)	14(18.2%)
	Heart Failure	3(7.5%)	8(21.6%)	11(14.3%)
Radiology distribution	1	14(35%)	6(16.2%)	20(26%)
	2	14(35%)	11(29.7%)	25(32.5%)
	3	11(27.5%)	15(40.5%)	26(33.8%)
	4	1(2.5%)	5(13.5%)	6(7.8%)
LABA/ICS	1	7(17.5%)	6(16.2%)	13(16.9%)
	2	33(82.5%)	31(83.8%)	64(83.1%)
Long Term O2	No	37(92.5%)	31(83.8%)	68(88.3%)
	Yes	3(7.5%)	6(16.2%)	9(11.7%)
Mucolytic distribution	No	5(12.5%)	10(27%)	15(19.5%)
	Yes	35(87.5%)	27(73%)	62(80.5%)
PPI distribution	No	15(37.4%)	5(13.5%)	17(22.1%)
	Yes	25(62.6%)	32(86.5%)	60(77.9%)
Chest Physio- distribution	No	7(17.5%)	11(29.7%)	18(23.4%)
	Yes	33(82.5%)	26(70.3%)	59(76.6%)
Hospitalization due to Exacerbation in last year	No	28(70%)	19(51.4%)	47(61%)
	Yes	12(30%)	18(48.6%)	30(39%)
Previous hospitalization due to BE at any time	No	20(50%)	13(35.1%)	33(42.9%)
	Yes	20(50%)	24(64.9%)	44(57.1%)

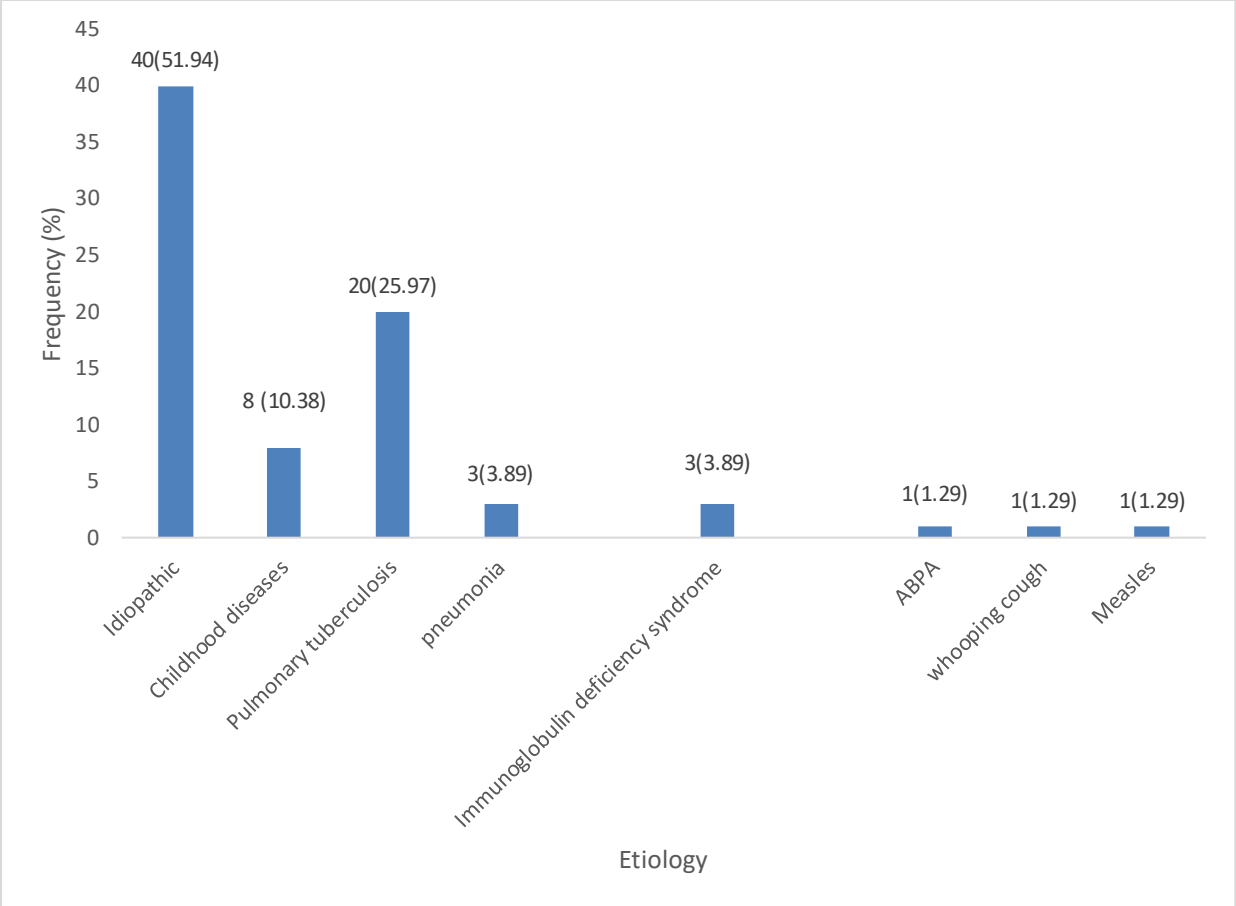


Figure 2:- Etiology of bronchiectasis among the study population.

Table 4:- Association of FACED and BSI according to Hospitalization 1year follow-up of patients studied.

variables	Hospitalization 1year follow-up		Total (n=77)	P value
	No (n=40)	Yes (n=37)		
Faced				
• Mild	27(67.5%)	8(21.6%)	35(45.5%)	<0.001**
• Moderate	12(30%)	12(32.4%)	24(31.2%)	
• Severe	1(2.5%)	17(45.9%)	18(23.4%)	
BSI				
• Mild	10(25%)	2(5.4%)	12(15.6%)	<0.001**
• Moderate	20(50%)	3(8.1%)	23(29.9%)	
• Severe	10(25%)	32(86.5%)	42(54.5%)	

Discussion:-

In this study, a total of 77 patients with bronchiectasis were included. They were divided in to two groups, one which required hospitalisations and the others who were managed as out patients. Males constituted 45.6% of the study population. Mean age of the population was 52.6 years. When the possible aetiology of bronchiectasis were analysed in this study, majority were found to have idiopathic or post infective bronchiectasis.

Majority of patients requiring hospitalization due to exacerbation in this study were above 51 years of age, (P value<.001).Whereas in OP cohort, 40% of the patients were above 50 years of age. menendez et al found that mean age for severe exacerbation of bronchiectasis is73(68-80).[6] Gender difference does not seems to be a factor responsible for difference in exacerbations and hospital admissions among the two groups in this study. Finklea et al

found that male gender was associated with an increased mortality rate.[7] This was contrary to Pasteur et al. who found a predilection to females with bronchiectasis, but lung damage developed at the same rate in both genders.[8]

The data for FEV1 in this study population showed 59.5 percent of the patients from the inpatient group have FEV1 less than 50% of predicted, whereas in the OP patient group, all of them have FEV1 more than 50% (P value <.001). Chalmers et al found that FEV1 < 50% has significant relation with mortality and exacerbation of bronchiectasis.[2]Roberts et al. have found that the degree of airflow obstruction correlated with the degree of radiographic findings on CT, specifically the severity of bronchial wall thickening and disease of the small airways.[9]Evaluation of the isolation of organism from culture in patients with exacerbations in this study showed that, there was significantly higher culture isolation in patients with any one of the bacterial isolate, compared with non-isolated patients. The mortality rate varied significantly depending on the type of organism, with the highest mortality rates being associated with the isolation of Pseudomonas aeruginosa. Menendez et al also found exacerbation are more with pseudomonas infection (40.7%).[6]Pseudomonas aeruginosa infection in the respiratory tract of bronchiectasis patients is associated with worsening airway clearance and airway obstruction, resulting in worsening of lung function and impaired health-related quality of life.[10]The analysis of radiological severity is presented in this study showed significant relationship between radiological severity and hospitalization due to exacerbations (p value=.087). Study of Charmers et al shows no Significant relationship between radiological severity and mortality (P = 0.3) but a significant relationship between the Reiff score and hospital admissions. This Relationship was statistically significant above a score of 3 or more (indicating three or more lobes involved or a lobe with cystic bronchiectasis) but Menendez et al has got no significant relationship between radiological severity and exacerbation.[2,6]

Analysing the use of Proton Pump Inhibitors (PPI) showed that out of 37 in the inpatient group, 32(86.5%) patients were using PPI and from the 40 OP cohort, 25 (62.6%) were using PPI. Which shows association with significant p value (This is additional valuable information, which is not included in any of the validated score related to bronchiectasis. charmers et al not mentioned about the use of PPI and mortality.[2] Pathophysiological mechanism behind this association is not clearly defined, some studies states that, PPIs modify the composition of the gut microbiome, and increasing levels of oral and upper gastro-intestinal tract commensals due to changes in pH.[11]

In this study, at enrolment, 48.6% of the patients gave a history of hospitalization with exacerbation or respiratory tract infection in the preceding 1 year. This shows that a prior history of hospital admissions predict future mortality, hospital admissions, exacerbations, and quality of life. Charmers et al and Menendez et al Prior hospitalization has been clearly identified as the most decisive risk factor for severe exacerbation in other chronic respiratory diseases.[2,6]

As expected, bronchiectasis exacerbation (BE) patients with higher BSI and FACED scores required more hospital admissions because of exacerbation. Regardless of its recognized differences in classifying BE patients in the severe phases, BSI classified more patients as severe than FACED. According to BSI score, patients were classified into low (0–4 points, n =12), intermediate (5–8 points, n =23), and high BSI scores (9 or more points, n = 42).

The relationship between these severity classes and hospitalization due to exacerbations are shown in Table 23. There was a clear difference in hospitalization due to exacerbation between patients classified as low, intermediate,and high BSI scores with significant p value[P value <.001]. Menendez et also shows BE patients with higher BSI andFACED scores required more hospital admissions,regardless its recognized differences in classifying BEpatients in the severe phases: -BSI classified morepatients as severe than FACED.[6] The mathematical models retained identicalrisk and protective factors with minor changes in theOR when both scales (BSI or FACED) are evaluated separately. Recently the new E-FACED[12] and Exa- FACED scores[13], which incorporates the number of exacerbations, has demonstrated a better prognostic capacity for subsequent exacerbations and 1 yearhospitalization.Vaccination against influenza and pneumococci are associated with protective effect in bronchiectasis. [56]. This study also shows that vaccinated patients are more in the non-hospitalized group, ie 35 % patients were taken influenza vaccine and 47.5% were taken pneumococcal vaccine,whereas 8.1% and 21.6% in hospitalized patient respectively[p value=0.004]. Pneumococcal vaccine has been recommended in bronchiectasis patients in the literature.[14,15]

In this study, several factors like DM, heart failure, smoking status, and inhaled beta2 agonist, chest physio, use of LTOT and corticosteroid use were not associated with mortality or hospital admissions. Almost all patients in this

study group were using ICS/LABA. In the past, inhaled corticosteroids have been found to be beneficial in patients who are in a steady state bronchiectasis, but no data were found on patients with an acute exacerbation using inhaled steroids.Smoking has been known to be associated with lung disease. In this study it was found that smoking was not associated with risk for exacerbation, it may be because of small study population and less proportion of smoking patient. whereas in many studies smoking was found to be a risk factor. Possible causes are defects in the ability to clear secretions predisposing them to an increased risk of infections and increased inflammation of the lung parenchyma caused by the toxic chemicals in tobacco.[16,17] In this study only 11(14.3%) out of total 77 were smokers. Probably the low number of smokers in the study group might not have sufficient power to impact the exacerbation and hospitalisation.

Conclusion:-

This study found that the risk factors associated with bronchiectasis patients likely to develop exacerbations requiring hospitalization during one-year follow-up period are age, Forced Expiratory Volume in 1 second(FEV1), extent of radiological involvement, coexistent COPD, exacerbation in last 1 year, culture isolation of organism, use of Proton Pump Inhibitors (PPI) and Bronchiectasis Severity (BSI) score.Possible aetiological cause could not be found in majority of our study population (Idiopathic). Infective causes like Tuberculosis and childhood infections were found to be the other prominent underlying aetiological factors. Pneumococcal and Influenza vaccination is found to be a protective factor.Association of use of PPI to increased exacerbation is new information to be added to the validated scale and more studies regarding the role of PPIs are warranted.

Abbreviations :

Conflicts of interest :

Nil.

Financial support:

Nil.

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