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ASSESSMENT OF PATIENTS HAVING ACUTE EXACERBATION OF BRONCHIECTASIS AND FACTORS LEADING TO MORTALITY IN THE HOSPITALIZED PATIENTS AT PULMONOLOGY DEPARTMENT JINNAH POSTGRADUATE MEDICAL CENTRE KARACHI.

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ABSTRACT

INTRODUCTION: Bronchiectasis is a pathological dilation of the bronchi and bronchioles produced by the disintegration of the elastic and muscular elements of the walls of bronchi and bronchioles. **OBJECTIVES:** The purpose of this study is to assess the frequency of fatalities in subjects admitted with diagnosis of acute exacerbations of bronchiectasis and to evaluate the prevalence of factors responsible for fatality in these admitted subjects, at Jinnah Postgraduate Medical Centre Karachi Pulmonology Unit. **MATERIALS AND METHODS:** Descriptive case series study. The research was carried out at the Jinnah Postgraduate Medical Centre Karachi Pulmonology Unit. Overall 140 subjects were selected in Jinnah Postgraduate Medical Centre Karachi Pulmonology Unit. All those patients fulfilling the inclusion criteria were selected in the study. A short background of the disease's length was taken, as well as a clinical assessment, and written informed consent was obtained. To assess the factors those contribute to death throughout hospitalization and even after discharges for all patients until the end of the four-month follow-up period. **RESULTS:** Mean and standard deviation of age was 47.59±10.96 years. Male were 78(55.7%) and female were 62(44.3%). 87(62.1%) patients did not survived and 53(37.9%) patients were survived from the disease. factors of mortality were compared with mortality **CONCLUSION:** In conclusion, our study identified male gender, history of smoking, steroid use during hospitalization and mechanical ventilation need as independent factors for mortality in AEB patients.

KEY WORDS: Acute Exacerbation of Bronchiectasis; Bronchiectasis; Mortality; FEV_1% Predicted; Systemic Steroids.

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INTRODUCTION

Bronchiectasis is a disease characterized by pathologic dilatation of the bronchi and bronchioles, as well as demolition of the elastic and muscular constituents of their walls, and was first discovered by Laennec in the early nineteenth century.[1,2] Transmural inflammation, edema, fibrosis, and maceration are some of the alterations that might occur in affected locations. Sustained microbial infections and frequent post-obstructive pneumonia can potentially damage the distal lung parenchyma. Bronchiectasis is a lung disease that can be congenital or acquired.[3] Adults and older children develop acquired forms of disease, which require an infectious insult, drainage impairment and blockage of airways, and/or a failure in host defense mechanism. The tissues are additionally harmed by neutrophilic proteases, inflammatory

cytokines, nitric oxide, and oxygen radicals by the host responses. The muscular and elastic constituents of the bronchial wall are harmed as a consequence. Diffuse peribronchial fibrosis can also arise from injury to peribronchial alveolar tissue.[4] Bronchiectasis is still a leading cause of morbidity in developing nations, particularly those with poor access to medical care and antibiotics.[5,6] An epidemiology research of bronchiectasis-related admissions in the United States found that the rate of hospitalisation due to this disorder's has increased from 1993 to 2006, notably among people over 60.[7] This obvious rise in the burden of the disease in the older subjects had not been linked to a single underlying diagnosis. Exacerbations are more common in patients with more severe illness[8] and untreated bronchiectasis.[9] Only a small number of patients brought to the hospital for acute exacerbation of bronchiectasis (AEB) have had their in-hospital and long-term consequences assessed. The debilitation that follows an AEB can enhance fatality.[10] Acute exacerbations of COPD, often called acute exacerbation of chronic bronchitis (AECB), is a short-term deteriorating of shortness of breath, quantity and colour of sputum (COPD symptoms) usually lasting for a number of days. A bacterial or viral infection, as well as environmental contaminants, can cause it. Infectious diseases are responsible for 75 percent or over for exacerbations; bacteria are identified in around 25% of incidents, viruses in another 25% of subjects, and these both ie bacteria and viruses in another 25% of subjects. Throughout an exacerbation, airway inflammation increases, leading to greater hyperinflation, and decrease in both expiratory air flow, and gas exchange.[12,13] Exacerbations of COPD become increasingly common as the disease advances, with an average of three bouts annually.[14] Increasing frequency and severity of cough are related with acute COPD exacerbations.[15] It's frequently accompanied with a worsening of chest congestion as well as uneasiness. In several cases, difficulty in breathing and wheezing are evident.[15] Increased cough and sputum generation, as well as an alteration in the form of sputum, may accompany exacerbations. A sudden deterioration of COPD symptoms might result in a bursting of the lung airways, which can lead to a spontaneous pneumothorax. [14] Weakness, fever and chills are usually associated with infections.

The phlegm might be faintly speckled by blood as well as tinted as yellowish or greenish in bacterial infections.[(15)] Various factors can induce an abrupt exacerbation of COPD that's because the lungs are susceptible organs resulting from exposure to hazardous particulates in the atmosphere. COPD exacerbations are caused by respiratory infections, which account for around half of all COPD exacerbations. Nearly half of them are thought to be caused by viral infections, whereas the other half is thought to be induced by infections due to bacteria.[16] Haemophilus influenzae, Streptococcus pneumoniae, and Moraxella catarrhalis are some of the most common and Chlamydia pneumoniae and MRSA are two less frequent bacterial infections associated with acute exacerbations.[17] Haemophilus parainfluenzae (after repetitive antibiotic use), Mycoplasma pneumoniae, and gram-negative, opportunistic infections like Pseudomonas aeruginosa and Klebsiella pneumoniae are among the pathogens detected more commonly in individuals with decreased lung function (FEV<35 percent of expected).[17] Allergens, such as pollen grains, wood smoke, or cigarette smoke, pollution and toxins, which include a wide range of substances.[15] An suppurative phlegm production[17] that is thicker[15] than usual, though without evidence of pneumonia(that involving principally the alveoli relatively than the bronchioles), is one of the diagnostic criteria for an acute exacerbation of COPD.[15]Increased frequency and severity of cough[15], and also increasing shortness of breath, may be included in diagnostic criteria.[17] Patients with a fever and, specifically, hemoptysis (blood in the sputum) should have a chest X-ray to rule out pneumonia and assess the severity of the exacerbations. Hemoptysis can also be a sign of other, potentially grave health problems. A background of exposure to potential factors and an assessment of symptoms may aid in determining the reason of the exacerbations, allowing the appropriate treatment to be chosen. The strains responsible for a bacterial AECB can be identified by sputum culture.[15] A sample taken as the first thing in the morning is recommended.[17]The capacity of E-nose to detect the source of the aggravation was demonstrated.[18] The description of a COPD exacerbation is frequently referred to as "lost in translation,"[19] implying that there may be no internationally acceptable criteria for describing acute COPD exacerbations. Various associations believe that developing such a standard should be a topmost priority because it would be a significant step forward in COPD diagnostic and treatment quality.

Prevention

Acute exacerbation can be avoided in some cases. Vaccination against viruses like influenza and Streptococcus pneumoniae can help prevent some diseases. Long-acting beta-adrenoceptor agonists (LABAs), long-acting anticholinergics, inhaled corticosteroids, and low-dose theophylline have all been found to lower the incidence of COPD exacerbations when used regularly.[10-13] Quitting smoking and avoidance of dust, passive smoking, and other inhaled irritants are two more measures of prevention.[15] Immunizations for influenza are given once a year, and pneumococcal vaccinations are given every five years.[15] Exercising regularly, adequate relaxation, and a balanced diet are all important components of a healthy lifestyle. Escape from subjects who have currently flu or cold.[15]To assist for decreasing the formation of thick sputum and chest congestion, drink plenty of water and humidify the houses.[15]

MATERIALS AND METHODS:

In the Pulmonology Department Jinnah Postgraduate Medical Centre Karachi this descriptive cross-sectional research was piloted. This study was conducted 6 months after the approval of synopsis. (30, Dec 2016 to 1, july 2017). The sample calculation was done using the WHO sample size calculator by using the least proportion of mechanical ventilation 18.8% with confidence interval 95% and 6.5% margin of error, sample size stand was 140. This information was gathered using a non-probability consecutive survey method. Inclusion criteria of our study was patients having acute exacerbation of Bronchiectasis, age between 20 -60 years both male and female genders included along with all the patients having diabetes and hypertension were part of this research. Patients who had not agreed to participate in the trial and those with a history of cystic fibrosis, bronchial asthma, or chronic obstructive pulmonary disease (COPD) without bronchiectasis were excluded, assessed by radiology and clinically were not the part of the study. This study was performed after the approval of ethical committee of at Jinnah Postgraduate Medical Centre Karachi. Subject was selected through outpatient department (OPD) and Emergency department of Pulmonology Jinnah Postgraduate Medical Centre Karachi. The subjects fulfilling the inclusion criteria were recruited. A short background of the illness's duration was taken, as well as a clinical examination, and written consent was obtained. Acute exacerbation of Bronchiectasis was assessed according to O'Donnell AE[10]criteria. Discharged patient were taken on weekly follow and also contact were continue with contact number. Predictor factors, smoking history, uses of mechanical ventilation were carried out. To assess the factors that contribute to death during admission and after release for all patients until the end of the four-month follow-up period. Clinical features were also observed and recorded platelet count, bilirubin, creatinine, pulmonary function test PFT and serum albumin level.

The data were entered and analyzed in statistical program SPSS version 20. Mean standard deviations were calculated for age, creatinine level, FEV, bilirubin level, platelets count and albumin level. Frequency and percentage were calculated for Diabetes mellitus, hypertension, mortality and factors (gender, smoking history, steroid use during hospitalization and use of mechanical ventilation). Stratification with respective age, creatinine level, FEV1, albumin level, bilirubin level, platelet count, Diabetes mellitus, hypertension was done for mortality and factors leading to mortality. Post stratification Chi-square test was applied. By keeping P value less than <0.05 as significant levels.

RESULTS

In the study 140 patients who fulfill the inclusion criteria were enrolled; In Table 1 mean and standard deviation of age was 47.59±10.96, creatinine level 1.0±0.5, FEV 1.4±0.5, bilirubin level 0.8±0.5, platelets count 0.8±0.5 and albumin level 2.4±1.5. In Table 2 frequency distribution of gender was presented 78(55.7%) patients were male and 62(44.3%) were female. Male participants were more than female. Frequency Distribution of Diabetes mellitus was presented, only 49(35%) patients were diabetic and 91(65%) patients were non diabetics. frequency of hypertension was presented 79(56.4%) patients were hypertensive and 61(43.6%) patients were non hypertensive. frequency of in hospital mortality was observed in 87(62.1%) patients. In Table 3 factors leading to mortality in male cases 54(62.1%), while 48(55.2%) in female cases. Role of mortality was significantly high in male cases as compared to female with (P-value= 0.05). mortality in patients having history of smoking 15(28.3%) which is significantly high with (p-value =0.003), mortality

observed in 43(49.4%) patients used steroid during hospital also showed highly significance with (p-value=0.002), Mechanical ventilation also observed as a factor of mortality, 22(25.3%) patients died who required mechanical ventilation role mortality was significantly high in these patients, within 4 months of follow up. In comparison of all factors of mortality results found significant with p-value less than 0.05. In Table 4 stratification of Mortality with regards to age, diabetes mellitus, hypertension, creatinine level, FEV severity, bilirubin level, platelet count and albumin level was done, where age, diabetes mellitus, hypertension and albumin level were showed significance results with p-values< 0,05. And creatinine level, FEV severity, bilirubin level and platelet count were showed non-significant results with P-value >0.05.

Assessment of patients, having acute exacerbation of bronchiectasis and factors leading to mortality in the hospitalized patients at Pulmonology Department Jinnah Postgraduate Medical Centre Karachi.

Table: 1: **DESCRIPTIVE STATISTICS**

Variables	**N**	**Mean± SD**
Age	140	47.59±10.96
Creatinine level	140	1.0 ± 0.5
FEV1%pred	140	67 ± 25(%)
Bilirubin level	140	0.8 ± 0.5
Platelets count	140	230.6 ± 90.5
Albumin level	140	2.4 ± 1.5

Table: 2: **DISTRIBUTION OF STUDY VARIABLES**(n=140)

Variables		**Frequency**	**percentages**
Gender	Male	78	55.7
	Female	62	44.3
Diabetes Mellitus	Yes	49	35.0
	No	91	65.0
Hypertension	Yes	79	56.4
	No	61	43.6
Mortality	Yes	87	62.1
	No	53	37.9

Table: 3: **FACTORS LEADING TO MORTALITY IN PATIENTS HAVING ACUTE EXACERBATION OF BROCHIECTASIS**(n=140)

Variables		**Mortality**		**Total (n=140)**	**P-Value**
		Yes (n=87)	**No (n=53)**		
Male gender	Yes	54(69.23%)	24(30.77%)	78(100%)	0.05*
	No	33(53.23%)	29(46.77%)	62(100%)	
H/O smoking	Yes	48(76.19%)	15(23.81%)	63(100%)	0.003*
	No	39(50.65%)	38(49.35%)	77(100%)	
Steroid use	Yes	43(78.18%)	12(21.82%)	55(100%)	0.002*
	No	44(51.76%)	41(48.24%)	85(100%)	
Mechanical Ventilation	Yes	22(91.67%)	2(8.33%)	24(100%)	0.001*
	No	65(56.03%)	51(43.97%)	116(100%)	

Applied Chi-square.
Significance level<0.05*

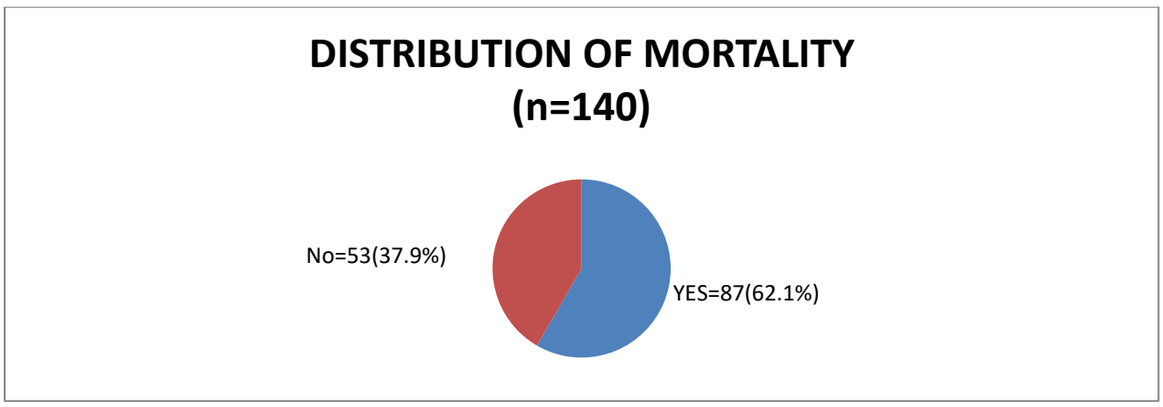

Table: 4: **STRATIFICATION OF MORTALITY WITH RESPECT TO EFFECT MODIFIERS** (n=140)

Variables		**Mortality**				**Total**		**P-value**
		Yes (n=87)		**No (n=53)**				
		No. of cases	**%**	**No. of cases**	**%**	**No. of cases**	**%**	
Age	<45	24	40.67	35	59.3	59	100	0.001*
	45 or >45	63	77.77	18	22.2	81	100	
Diabetes Mellitus	Yes	21	42.85	28	57.14	49	100	0.009*
	No	66	72.52	25	27.47	91	100	
Hypertension	Yes	66	83.5	13	16.4	79	100	0.001*
	No	21	34.4	40	65.5	61	100	
Creatinine level	>1.5mg/dl	55	66.2	28	33.7	83	100	0.28
	<1.5mg/dl	32	56.1	25	43.8	57	100	
FEV	Mild	10	66.67	5	33.3	15	100	0.84
	Moderate	37	59.67	25	40.3	62	100	
	Severe	40	63.49	23	36.5	63	100	
Bilirubin level	>1.9mg/dl	57	62.63	34	37.36	91	100	0.89
	<1.9mg/dl	30	61.22	19	38.8	49	100	
Platelets count	<130	46	66.7	23	33.33	69	100	0.23
	>130	41	57.74	30	42.25	71	100	
Albumin level	<3.5g/dl	47	51.64	44	48.35	91	100	0.005*
	>3.5g/dl	40	81.63	9	18.36	49	100	

DISCUSSION

There are inadequate statistics regarding the death rate related to bronchiectasis. The bronchiectasis is commonly encountered in routine practice inspite of that it is considered an orphan illness. Age, coexisting illnesses, and distinct clinical characteristics all substantially increased the disease-related death rate, which was determined to be 62.1 percent after a four-month follow-up period. After an average follow-up of four years, Onen et al. found a 16.3 percent death rate.[20] Age, comorbid illnesses, and distinct clinical aspects were all significantly higher in male group in other studies than in ours. After an average follow-up of 5.18 years, Goemminne et al. found a 20.4 percent overall death rate.[21] The patient population in that study had an identical range of ages and gender dispersion to ours, but the number of participants with COPD was much larger. Earlier researches have shown that the elderly have a greater death rate than the general population. According to Dupont et al., death in individuals with bronchiectasis over 65 years old was more than doubled (relative risk [RR], 2.70; 95 percent confidence interval [CI], 1.15 to 6.29). (80,81). An elevated mortality rate may be caused by age > 65, comorbidities, and therapeutic noncompliance. In our analysis, smoking status had an impact on death. According to Loebinger et al., in smokers death rate was not raised, (RR: 1.78 (CI: 0.87 – 3.63), P = 0.120).[24] According to Onen et al., smoking background and the existence of COPD as a concomitant illness had no effect on bronchiectasis mortality.[21] In the current study patient populations were with a much higher co morbidity rate. There was a strong association between Charlson co morbidity scores and predicted 10-year survival rates calculated by comorbidities assessment and fatality. In view of the effect of co morbidity on the disease prognosis,

severity, and fatality, it may be suggested that a systemic inflammatory response may be caused by bronchiectasis. Assessing and treating concomitant diseases may help to minimize the death rate in subjects suffering from bronchiectasis.[22-24] Cor pulmonale was identified more frequently in the deceased group than in the people who survived. Hypoxic pulmonary vasoconstriction, pulmonary vascular remodeling, small vessel damage, and fibrosis are all part of the pathogenesis of pulmonary hypertension in chronic lung illness. The intensity of pulmonary hypertension in bronchiectasis is usually mild to moderate. In chronic lung diseases, the development of pulmonary hypertension is a bad prognostic indicator. Impaired cardiac functions and pulmonary gas exchange are consequences of severe bronchiectasis due to capillary bed injuries and left-to-right shunting, perfusion is compromised. It could explain why pulmonary hypertension in bronchiectasis is a poor predictive indicator.[24] Coexisting bronchiectasis has been linked to increased COPD morbidity and death, according to accumulating data. Furthermore, there is a paucity of data on the factors that influence the occurrence and severity of bronchiectasis in COPD patients. We revealed that male status, smoking background, steroid use, and mechanical ventilation are all independent risk factors for death in COPD patients with bronchiectasis. COPD patients with bronchiectasis were primarily men, according to the study. Male gender was found to be a risk factor for bronchiectasis in patients with mild to severe COPD in our study. This tendency, according to Ni and coworkers[25] could be explained by males having a higher smoking rate. In our study, however, there was no significant effect of smoking status on the presence and degree of bronchiectasis. New evidences suggest that sex hormones may play a role in the etiology of chronic obstructive pulmonary disease (COPD).[26] More research is needed to determine whether sex hormone levels are linked to the presence of bronchiectasis in COPD patients.

COPD patients with bronchiectasis had a worse nutritional quality. A prolonged illness course, additional respiratory symptom, a higher frequency of acute exacerbations, a more substantial inflammatory response, poorer lung functions, and a increased positive rate of phlegm P aeruginosa. The above findings of the current study are consistent with previous studies. Our findings strongly suggest that COPD with bronchiectasis is a clinically significant phenotype that may require additional medicines in addition to standard COPD treatments. We also discovered that male gender was linked to a higher fatality rate in our research. In contradiction to Pasteur et al., who discovered a preference for females with bronchiectasis, lung injury occurred with simultaneous rates across both sexes. In the two prior trials done in the ICU with AEB, gender had no effect on death.[27,28] In the ICU trial, the proportion of females was identical (Females were 58 percent in Dupont et al., 60 percent in Alzeer et al., and 68 percent in our study). Moreover, within this research, intubation was required, that might be considered as a predictor for poor outcome, although it should be viewed with caution due to the small sample size. When the creatinine levels of the two groups were compared, the results revealed a substantial variation. During an AEB, this minor elevation in creatinine could indicate decreasing renal function, which can result in increased in fatality. Renal impairment has previously been used to predict poor outcomes in community-acquired pneumonia patients. As a result, deteriorating renal function in AEB may be linked to a bad prediction.[29] The use of systemic glucocorticoids for a short period of time in patients with an AEB has not been studied. We discovered a higher mortality rate related with the acute administration of systemic glucocorticoids during hospitalization in this study of patients with an AEB. Even though acute steroid use in bronchiectasis has not been researched, it has been studied in the COPD populations.[30] Regretfully, due to the nature of the trial, steroid procedure for deciding whether individuals with AEB should receive steroids was not established. As a result, the steroid dosage given to each patient differed and was not reported routinely in the electronic health records. The etiology of mortality could not be determined because of the use of the social security death index.[31] Because we only had a small number of patients on inhaled steroids during our research, that will be difficult to establish particular recommendations about their use. Inhaled steroids have been shown to be useful in individuals with relatively stable bronchiectasis in the past, and yet no data on patients with an AEB utilizing inhaled steroids has been reported.[32]

It has long been known that smoking causes lung illness. Inside this analysis, it was discovered that smoking was linked to a higher risk of death. Impairment in the order to extract secretions could be one of the

causes, putting them at danger of infection. It showed that older individuals who were given steroids during their stay had a higher mortality risk. The reason of such an elevated fatality trend could be related to the facts stated previously in patients who took steroids.[33,34] Male gender, acutely utilized systemic steroids throughout hospitalization, increased creatinine, lower FEV1.0 percent expected, background of smoking, and use of mechanical ventilation throughout hospitalization were all associated with the greatest death rates.

This would be the first research to our knowledge that demonstrated a link in the mortality amongst patients who were admitted with an AEB and were given systemic steroids. Ultimately, this research showed that this illness can be extremely debilitating, although there is currently very little research on it.[35]

CONCLUSION

In conclude, this research found that male sex, smoking background, steroid use during hospitalizations, and the necessity for mechanical ventilation were all predictive factors in AEB patient fatality. Furthermore, aberrant clinical characteristics such as bilirubin, creatinine, FEV severity, platelet count, and albumin levels were significantly linked with the severity of bronchiectasis, implying that these parameters may play a significant role in the development of bronchiectasis in COPD. Future studies using high sample size are required to assess longitudinal changes in these parameters and their impact on the disease's natural course. It may be clinically advantageous for people with COPD and bronchiectasis, but more research is needed.

LIMITATION OF THE STUDY: Our study's main weakness is its limited sample strength. As a result, the whole sample had a limited number of variables influencing fatality, resulting in lower statistical inferences between the research parameters.

ETHICS APPROVAL: The ERC gave ethical review approval **CONSENT TO PARTICIPATE:** written and verbal consent was taken from subjects and next of kin **FUNDING:** The work was not financially supported by any organization. The entire expense was taken by the authors. **ACKNOWLEDGEMENTS:** We would like to thank the all contributors and staff and other persons for providing useful information. **AUTHORS' CONTRIBUTIONS:** All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript. **CONFLICT OF INTEREST:** No competing interest declared.

REFERENCES

1. Finklea JD, Khan G, Thomas SH, Song J, Myers D, Arroliga AC. Predictors of mortality in hospitalized patients with acute exacerbation of bronchiectasis. Respiratory Medicine 2010;104;816-21
2. Athanazio R. Airway disease: similarities and differences between asthma, COPD and bronchiectasis. Clinics. 2012 Nov;67(11):1335-43.
3. Luce JM. Bronchiectasis.Murray JF, Nadel JA. Textbook of Respiratory Medicine. 2nd ed. Philadelphia, Pa: WB Saunders and Co; 1994. 1398-1417
4. Morrissey D. Pathogenesis of Bronchiectasis. Clin Chest Med. 2007. 28:289-296.
5. Habesoglu MA, Ugurlu AO, Eyuboglu FO. Clinical, radiologic, and functional evaluation of 304 patients with bronchiectasis. Ann Thorac Med 2011;6(3):131–36.
6. Sehitogullari A, Bilici S, Sayir F, Cobanoglu U, Kahraman A. A long-term study assessing the factors influencing survival and morbidity in the surgical management of bronchiectasis.Journal of cardiothoracic surgery. 2011;11;6(1):1.
7. Seitz AE, Olivier KN, Steiner CA. Trends and burden of bronchiectasis-associated hospitalizations in the United States, 1993-2006. Chest. 2010;138(4):944-9.
8. Neves PC1, Guerra M, Ponce P, Miranda J, Vouga L. Non-cystic fibrosis bronchiectasis. Interact CardiovascThoracSurg 2011;13(6):619-25.
9. Karadag B, Karakoc F, Ersu R. Non-cystic-fibrosis bronchiectasis in children: a persisting problem in developing countries.Respiration2005;72:233–8
10. McShane PJ, Naureckas ET, Tino G, Strek ME. Non–cystic fibrosis bronchiectasis.American journal of respiratory and critical care medicine. 2013;15;188(6):647-56.
11. O'Donnell AE, Barker AF, Ilowite JS, Fick RB. Treatment of idiopathic bronchiectasis with aerosolized recombinant human DNase I. CHEST Journal 1998;113(5):1329-34.
12. Rabe KF, Hurd S, Anzueto A, et al. (2007). "Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary". Am. J. Respir. Crit. Care Med. 176 (6): 532–55.
13. van Geffen WH, Slebos DJ, Kerstjens HA. "Hyperinflation in COPD exacerbations". The Lancet Respiratory Medicine.3 (12): 43–44.
14. "Chronic Obstructive Pulmonary Disease (COPD)". Merck Sharp & Dohme Corp. Retrieved 19 May 2014.
15. Uppsala Academic Hospital > Guidelines for treatment of acute lung diseases. August 2004. Authors: Christer Hanson, Carl-Axel Karlsson,
16. The British Society for Antimicrobial Chemotherapy > Acute exacerbations of

chronic bronchitis (AECB). Retrieved March 13, 2010
17. Geffen, Wouter H. van; Bruins, Marcel; Kerstjens, Huib A. M. (2016-01-01). "Diagnosing viral and bacterial respiratory infections in acute COPD exacerbations by an electronic nose: a pilot study". Journal of Breath Research. 10 (3): 036001.
18. Makris D, Bouros D (January 2009). "COPD Exacerbtion: Lost in Translation". BMC Pulm Med. 9 (6): 6.
19. Calverley PM, Anderson JA, Celli B, et al. (2007). "Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease". N. Engl. J. Med.356 (8): 775–89.
20. Onen ZP, Gulbay BE, Sen E, Yıldız OA, Saryal S, Acican T, Karabiyikoglu G. Analysis of the factors related to mortality in patients with bronchiectasis. Respir Med 2007; 101: 1390-1397.
21. Goeminne PC, Nawrot TS, Ruttens D, Seys S, Dupont LJ. Mortality in non-cystic fibrosis bronchiectasis: a prospective cohort analysis. Respir Med 2014; 108: 287-296.
22. Dupont M, Gacouin A, Lena H, Lavoue S, Brinchault G, Delaval P, Thomas R. Survival of patients with bronchiectasis after the first ICU stay for respiratory failure. Chest 2004; 125: 1815-1820.
23. Keistinen T, Saynajakangas O, Tuuponen T, Kivela SL. Bronchiectasis: an orphan disease with a poorly-understood prognosis. Eur Respir J 1997; 10: 2784-2787.
24. Loebinger MR, Wells AU, Hansell DM, Chinyanganya N, Devaraj A, Meister M, Wilson R. Mortality in bronchiectasis: a long-term study assessing the factors influencing survival. Eur Respir J 2009; 34: 843-849.
25. Ni Y, Shi G, Yu Y, et al. Clinical characteristics of patients with chronic obstructive pulmonary disease with comorbid bronchiectasis: a systemic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2015; 10:1465–1475.
26. Raghavan D, Jain R. Increasing awareness of sex differences in airway diseases. Respirology 2016; 21:449–459.
27. A.H. Alzeer, M. Masood, S. Jani Basha, ***et al.*** Survival of brochiectatic patients with respiratory failure in ICU.BMC Pulm Med, 7 (2007), p. 17
28. M. Dupont, A. Gacouin, H. Lena, ***et al.*** Survival of patients with bronchiectasis after the first ICU stay for respiratory failure.Chest, 125 (2004), pp. 1815–1820
29. Vestbo J, Hurd SS, Agusti AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187:347-65.
30. Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J 1977;1:1645-8.
31. Goh F, Shaw JG, Savarimuthu Francis SM, et al. Personalizing and targeting therapy for COPD - the role of molecular and clinical biomarkers. Expert Rev Respir Med 2013;7:593-605.
32. Vestbo J, Edwards LD, Scanlon PD, et al. Changes in forced expiratory volume in 1 second over time in COPD. N Engl J Med 2011;365:1184-92.
33. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Medical Communications Resources, Inc., 2014. Accessed 12 July 2014. Available online: www.goldcopd.com
34. Vestbo J, Agusti A, Wouters EF, et al. Should we view chronic obstructive pulmonary disease differently after ECLIPSE? A clinical perspective from the study team. Am J Respir Crit Care Med 2014;189:1022-30.
35. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095-128.