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RESEARCH ARTICLE

CLINICO-MICROBIOLOGICAL STUDY OF PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract

Background: Chronic obstructive pulmonary disease is the third leading cause of death worldwide. COPD patients are frequently colonised with potential respiratory pathogens. Use of empirical antibiotics without proper investigations in acute exacerbation leads to emerging resistant strains.

Aim: This study is aimed to record the clinical profile of patients with acute exacerbation of COPD with special reference to microbiological profile so that early adequate treatment can be given.

Material and Methods: This observational cross sectional study was conducted on 104 patients with acute exacerbation of COPD admitted in Medicine department of Jorhat Medical college and hospital from 1st July 2020 to 30th June 2021.After written informed consent detailed history,spirometry, sputum culture and sensitivity with AFB, Gram and fungal staining, chest X- ray, blood parameters and ECG were done.

Result: COPD is common above 40 years of age with male predominance (63.46%).36.54% were active smoker,25% were ex smoker and 38.46% were non smoker. Positive bacteriological culture was obtained in 32.69% of cases, commonest organism being Klebsiella pneumoniae (24%)followed by Pseudomonas aeruginosa (1.92%), Escherichia coli.(0.96%)and Citrobacter freundii(0.96%).32% of Klebsiella pneumoniae,40% of Klebsiella oxytoca and 100% of Citrobacter were found to be multidrug resistant strain.

Conclusion : Gram negative bacteria were more frequently isolated in our study. Early antimicrobial treatment reduces the increasing burden of COPD.

Introduction:-

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by persistent respiratory symptoms and airflow limitation that is not fully reversible.[1]COPD is the third leading cause of death, and also a disease of increasing public health importance around the world which is both preventable and treatable. WHO predicts that COPD will become the fourth leading cause of death world wide by 2030.[2] Exacerbations are episodic acute worsening of respiratory symptoms including increased dyspnea, cough, wheezing and/or change in the

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amount and character of sputum. Acquiring a new strain is associated with increased new term risk of exacerbation.Three classes of pathogens responsible for acute exacerbation, these are respiratory viruses, aerobic Gram positive and Gram-negative bacteria and atypical bacteria.[3] Use of empirical antibiotic without proper investigation leads to the emerging new resistant strains leading to recurrent microbial infection.We have noticed an increasing incidence of microbial infection in acute exacerbations of COPD. The purpose of this study is to record clinical and microbiological observations and find out the etiological agents in COPD patients so that early treatment can be given accordingly which result in decreasing the morbidity and mortality related to acute exacerbations.

Materials And Methods:-

This hospital based cross sectional observational study was conducted in Department of Medicine, Jorhat Medical College & Hospital, Jorhat, Assam on 104 patients over a period of one year from 1st July 2020 to 30th June 2021.

Inclusion Criteria

1. Patients hospitalized with acute exacerbation of COPD in department of medicine, Jorhat Medical College& Hospital.
2. Patients willing to give written informed consent.
3. Age more than 40 years.

Exclusion Criteria

1. All cases with pneumonia or bronchiectasis on chest x-ray
2. HIV positive patients
3. Patient with lung malignancy
4. Active Pulmonary tuberculosis
5. Treatment with any antibiotic within 24 hours before admission
6. Absence of an adequate sputum specimen
7. Sputum specimen not meeting the criteria of Bartlett score.

Patients above 40 years of age presenting with acute exacerbation of COPD were included in this study patient and his / her attendant were interviewed regarding history and clinical examination was done and recorded. Various investigations like biochemical, microbiological, radiological and spirometry done and recorded. All data were compiled and analysed using MS Excel 2007.Data were expressed as percentage, mean and standard deviation. Chi square test was done to find out the association between smoking status & gender and P value <0.05 was considered significant.

Results:-

Table 1:- Age Wise Distribution Copd Cases.

AGE (YEARS)	NO. OF CASES	PERCENTAGE %	MEAN AGE (YEARS)± SD
40-50	13	12.50	64.35±10.9
50-60	27	25.96	
60-70	35	33.65	
>70	29	27.88	

Table 2:- Sex Wise Distribution Of Copd Cases.

SEX	NO. OF PATIENTS	PERCENTAGE %
MALE	66	63.46
FEMALE	38	36.54
TOTAL	104	100

Table 3:- Association Of Smoking With Gender.

SMOKING STATUS	MALE		FEMALE		Chi square test& P value
	NO.	%	NO.	%	
SMOKER	48	72.7	16	42.1	
NON-SMOKER	18	27.3	22	57.9	P=0.001*
TOTAL	66	100	38	100	SIGNIFICANT

Table 4:- Pathogens Isolated From Copd Patients With Acute Exacerbation.

PATHOGENS	NO.	PERCENTAGE %
Klebsiellapneumoniae	25	24%
Klebsiellaoxytoca	5	4.80%
Pseudomonas aeruginosa	2	1.92%
Escherichia coli	1	0.96%
Citrobacterfreundii	1	0.96%

Table 5:- Multi Drug Resistant Strains Among The Isolates.

PATHOGEN	NO. OF MULTI DRUG RESISTANT ISOLATE	PERCENTAGE %
Klebsiellapneumoniae n (25)	8	32
Klebsiellaoxytoca n (5)	2	40
Pseudomonas aeruginosa n(2)	0	0
Escherichia coli n (1)	0	0
Citrobacterfreundii n (1)	1	1OO

Table 6:- Antimicrobial Sensitivity Pattern Of Isolates.

ANTIBIOTICS	***Klebsiellapneumoniae* n= 25**		***Klebsiellaoxytoca* n = 5**		***Pseudomonas aeruginosa* n = 2**		***Escherichia coli* n= 1**		***Citrobacterfreundii* n = 1**	
	NO	%	NO	%	NO	%	NO	%	NO	%
CEFEPIME	9	36	3	60	2	100	1	100	0	0
AMIKACIN	15	60	4	80	1	50	1	100	0	0
PIPERICILLIN + TAZOBACTUM	14	56	2	40	2	100	1	100	0	0
DOXYCYCLINE	15	60	2	40	1	50	1	100	1	100
COTRIMOXAZOLE	10	40	2	40	2	100	1	100	1	100
CIPROFLOXACIN	15	60	4	80	1	50	1	100	0	0
LEVOFLOXACIN	10	40	4	80	2	100	0	0	0	0
AZTREONAM	9	36	2	40	0	0	1	100	0	0
CEFOTAXIME	8	32	1	20	1	50	0	0	0	0
IMIPENEM	6	25	2	40	2	100	0	0	0	0

Out of 104 COPD patients majority of the cases were in the age group of 60-70 years which was 35 cases (33.65%) followed by 29 cases (27.88%) above 70 years, 27 cases (25.96%) in the age group of 50-60 years and 13 cases (12.50%) of age group 40-50years. Mean age ±SD of the study population was 64.35±10.9.In the present study out of 104 patients 66(63.46%) were male and 38(36.54%) were female. The male: female ratio is 1.7:1. Out of 66 male COPD cases, 48 (72.7%) were smoker and 18 (27.3%) were non-smoker. Out of total 38 female COPD patients 16 (42.1%) were smoker and 22 (57.9%) were non-smoker. A P value of 0.001 was obtained which was statistically significant. Positive sputum culture was isolated from 34 patients (32.69%) among 104 patients. The most common

organism found was *Klebsiella pneumoniae* 25 cases (24%) followed by *Klebsiella oxytoca* 5 cases (4.80%), *Pseudomonas aeruginosa 2* cases (1.92%0, *Escherichia coli* 1 case (0.96%) and 1 case of *Citrobacter freundii* (0.96%).In the present study the number of multidrug resistant strains were 8(32%) out of 25 *Klebsiella pneumoniae*, 2 (40%) out of 5 *Klebsiella oxytoca*, 0 out of 2 *Pseudomonas aeruginosa*, 0 out of 1 *Escherichia coli* and 1(100%) of *Citrobacter freundii*. Among the *Klebsiella pneumoniae* strains 60% were sensitive to amikacin, doxycycline and ciprofloxacin .56% are sensitive to piperacillin and tazobactam, 40% were sensitive to cotrimoxazole and levofloxacin,36% are sensitive to cefepime and aztreonam, 32% were sensitive to cefotaxime and 25% are sensitive to imipenem .Similarly out of 5 *Klebsiella oxytoca* strain, 80% ere sensitive to amikacin, ciprofloxacin and levofloxacin, 60% were sensitive to cefepime, 40% were sensitive to piperacillin and tazobactam, doxycycline, cotrimoxazole, aztreonam and imipenem. Out of *Pseudomonas aeruginosa* 100% are sensitive to piperacillin + tazobactam, cefepime and levofloxacin. Escherichia coli was found to be sensitive to cefepime, amikacin, piperacillin and tazobactam, doxycycline, cotrimoxazole. *Citrobacter freundii* was 100% sensitive to doxycycline and cotrimoxazole.

Discussion:-

In the present study a total of 104 patients were included over a period of 1 year 1st July 2020 to 30th June 2021. The observations made in our study were compared with other similar studies. In the present study, the age ranged from minimum 43 years to maximum 87 years. Mean age ± standard deviation of the study population was 64.32±10.87 years. Out of 104 COPD patients, majority of the cases were in the age group of 60-70 years which was 33.65%, followed by 27.88% above 70 years. This is similar to a study by Bajpai *et al*. 2019 where the mean age of smokers with COPD was 59.29±10.28 years.[4] Our finding is also consistent with a study by Hoogendoorn *et al*. 2006 where the mean age of the patients with COPD patients were 63.8 years.[5] John *et al*. 2005 reported in their study that mean age was 61± 1 years.[6]

In the present study, out of 104 patients, 66(63.46%) were male and 38 (36.54%) were female. The male: female ratio is 1.7:1. This study showed male predominance.

This is similar to other studies conducted by Almagro *et al*. 2010 who reported 89% men and 11% women out of 398 patients & Ferrari *et al*, 2010 who reported 60 males and 30 females out of 90 COPD patients.[7,8] Similarly Kundu *et al*. 2015 and Tamakuwala *et al*. 2017 reported the number of male and female COPD patients were (88.75% and 11.25%) and (80% and 20 %) respectively.[9, 10]

In the present study, out of 66 male COPD cases, 48 (72.7%) were smoker and 18 (27.3%) were non-smoker. Out of total 38 female patients 16 (42.1%) were smoker and 22 (57.9%) were non-smoker. P value was calculated for association of smoking with gender using chi square test and it was found to be statistically significant which was 0.001.

This finding is similar to a study by Xu X *et al*. (1994) who stated that as compared to women, men had a much higher smoking prevalence developing COPD.[11] A study by Greaves LJ *et al*. in 2007 also had similar findings & reported that smoking was more in male COPD patients as compared to female. [12]A study by Torres JP *et al*. in 2005 also showed that women were younger, smoked less than men.[13]

In the present study positive sputum culture was isolated from 34 patients (32.69%) among 104 patients. The most common organism found was *Klebsiella pneumoniae* 25 cases (24%) followed by *Klebsiella oxytoca* 5 cases (4.80%), *Pseudomonas aeruginosa 2* cases (1.92%0, *Escherichia coli* 1 case (0.96%) and 1 case of *Citrobacter freundii* (0.96%).

This is similar to a study by Lin SH *et al*. 2007, who isolated potential pathogenic microorganisms in 66.4% patients with acute exacerbation of COPD. The predominant bacteria were *Klebsiella pneumoniae* (19.6%), Pseudomonas *aeruginosa* (16.8%) and *Haemophilus influenzae (*7.5%) followed by *Acinetobacter baumanni* (6.9%), *Enterobacter* species (6.1%), *Staphylococcus aureus* (6.1%).[14]

In contrast to the present study, Groenewegen *et al*. 2003 found in their study that most frequently isolated organism was *Haemophilus influenzae* (45%), *Streptococcus pneumoniae* (27%) and *Pseudomonas aeruginosa*.[15] Again, Moghoofei M *et al*. 2020 found in their study that prevalence of bacterial infection was 49.59% in acute

exacerbation of COPD patients and those were *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*.[16]

In the present study the number of multidrug resistant strains were 8(32%) out of 25 *Klebsiella pneumoniae*, 2 (40%) out of 5 *Klebsiella oxytoca*, 0 out of 2 *Pseudomonas aeruginosa*, 0 out of 1 *Escherichia coli* and 1(100%) of *Citrobacter freundii*. Among the *Klebsiella pneumoniae* strains 60% were sensitive to amikacin, doxycycline and ciprofloxacin, 56% are sensitive to piperacillin and tazobactam, 40% were sensitive to cotrimoxazole and levofloxacin,36% are sensitive to cefepime and aztreonam, 32% were sensitive to cefotaxime and 25% are sensitive to imipenem .Similarly out of 5 *Klebsiella oxytoca* strain, 80% ere sensitive to amikacin, ciprofloxacin and levofloxacin, 60% were sensitive to cefepime, 40% were sensitive to piperacillin and tazobactam, doxycycline, cotrimoxazole, aztreonam and imipenem. Out of *Pseudomonas aeruginosa* 100% are sensitive to piperacillin + tazobactam, cefepime and levofloxacin. Escherichia coli was found to be sensitive to cefepime, amikacin, piperacillin and tazobactam, doxycycline, cotrimoxazole.

This is similar to a study by Kulkarni G *et al*. 2017 who found in their study that *Klebsiella* and *Pseudomonas* were the most common organisms and they were mostly sensitive to ciprofloxacin and amikacin followed by amikacin and cephalosporin. Another best monotherapy was piperacillin and tazobactam or cefoperazone with sulbactam .[17]

Similarly, Zohaib A *et al*. 2020 also found that, *Klebsiella pneumoniae* (27.2%) was the most frequent microorganism followed by *Pseudomonas* (19.1%) and *Staphylococcus aureus* (18.2%). Amikacin was found to be most sensitive antibiotic followed by gentamycin and ciprofloxacin.[18]

In contrast to our study, Soumya S *et al*. 2018 found that *Klebsiella Pneumoniae*, *Pseudomonas* and *E. coli* were mostly sensitive to aminoglycosides and Piperacillin with tazobactam but these are quinolones resistant.[19] Multidrug resistant strains of *Klebsiella* and *Pseudomonas* were also isolated in their study by Jones *et al*. 2011 and Engler *et al*. 2012.[20,21]

Limitation

Due to ongoing Covid 19 crisis, sample size of the present study was limited to 104. It will be more reliable on conducting the study with a large sample size. As the study had relatively smaller population and conducted in a shorter duration of time, the finding cannot be extrapolated to patients in general. Another limitation of the study is that viral and fungal isolates were not isolated from the sputum culture of the patients with acute exacerbation of COPD, which also contributes a major portion of the organisms causing acute exacerbation COPD.

Conclusion:-

In the present study, which included 104 COPD patients with acute exacerbation, it was found that the disease is more prevalent in male and in elderly age group. Smoking is one of the dominant risk factors and more common in male having COPD. Positive sputum culture was found in 32.69% of cases and mainly they were gram negative organisms. *Klebsiella pneumoniae* was the most common organisms isolated. Other organisms isolated were *Klebsiella oxytoca*, *Pseudomonas aeruginosa*, Escherichia coli and *Citrobacter freundii*. Multidrug resistant organisms were also isolated. The most sensitive antibiotics were amikacin, doxycycline and ciprofloxacin. The second most sensitive antibiotic was piperacillin with tazobactam. So, we come to a conclusion that with continuously changing bacterial flora of COPD, choice of antibiotics should be based on the local bacterial resistance pattern and periodic study will reduce the emergence of drug resistance.

References:-

1. Silverman EK, Crapo JD, Make BJ. Chronic obstructive pulmonary disease. In; Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J, editor. Harrisons principles of internal medicine 20thednvol 2. America: McGraw –Hill education; 2018. P 1961-9
2. World Health organization (WHO). The world Health Report 2000[internet]. Geneva:WHO;2000.Availablefrom:URL:http://www.who.int/whr/2000/en/satisties.htm;2000
3. Rakesh G, Kasturi T, Yuvarajan S. Bacterial agents causing acute exacerbations in Chronic Obstructive Pulmonary Disease (COPD) patients, their antibiograms to Extended Spectrum Beta-Lactamases (ESBL) production. Int J CurrMicrobiol App Sci 2013; 2(11):273-82

4. Bajpai J, Kant S, Bajaj DK, Pradhan A, Srivastava K. Clinical, demographic and radiological profile of smoker COPD versus non-smoker COPD patients at a tertiary care centre in North India. Fam. Med. Prim. Care Rev 2019; 8(7):2364
5. Hoogendoorn M, Feenstra TL, Schermer TRJ, Hesselink AE. Severity distribution of chronic obstructive pulmonary Disease (COPD)in Dutch general practice. Respir. Med 2006; 100(1): 83-6
6. John M, Hoering S, Doehner W, Okonko DD, Witt C, Anker SD. Anaemia and inflammation in COPD. Chest 2005; 127(3): 825-9
7. Almagro P, Garcia FL, Cabrera FJ, Montero L, Morchon D, Diez J *et al*. Comorbidity and gender- related differences in patients hospitalized for COPD. The ECCO Study. Respir.Med.2010; 104(2): 253-9
8. Ferrari R, Tanni SE, Lucheta PA, Faganello MM, Amaral RAF, Godoy I. Gender differences in predictors of health status in patients with COPD. J Bras Pneumol 2010; 36(1):37-43
9. Kundu A, Maji A, Sarkar S, Saha K, Jash D, Maikap M. Correlation of six-minute walk test with spirometric indices in chronic obstructive pulmonary disease patients: A tertiary care hospital experience. J Assoc Chest physicians 2015; 3(1):9
10. Tamakuwala G, Khyati S, Mahendraz P, Bhoomika P. A study of corelation of 6-minute walk test (6MWT) &spirometry findings in COPD patients. Int J Res Med 2017; 6(3):12-20
11. Xu X, Li B, Wang Li. Gender differences in smoking effect on adult pulmonary function. EurRespir. J. 1994; 7(3): 477-83
12. Greaves LJ, Richardson LA. Tobacco use, women, gender and chronic obstructive pulmonary disease: are the connections being adequately made? Proc Am ThoracSoc 2007 Dec 1;4(8): 675-9
13. de Torres JP, Casanova C, Hernandez C, Abreu J, Aguirre- Jaime A, Celi BR. Gender and COPD in patients attending a pulmonary clinic. Chest. 2005 Oct 1; 128(4): 2012-6
14. Lin SH, Kuo PH, Hsuehp R, Yang PC, KUOSH. Sputum bacteriology in hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease in Taiwan with an emphasis on *Klebsiellapneumoniae* and *Pseudomonas aeruginosa*. Respirology 2007; 12(1):81-7
15. Groenewegen KH, Wouters EF. Bacterial infections in patients requiring admission for an acute exacerbation of COPD; a 1-year prospective study. Respir. Med. 2003; 97(7): 7707
16. Moghoofie M, Jamalhandi SA, Moein M, Salmain J, Ahmadi A. Bacterial infection in acute exacerbation of chronic obstructive pulmonary disease: a systematic review and meta- analysis. Infection. 2020; 48(1):19-35
17. Kulkarni G, Chaudhary D, Bhoyar A, Dugad S. Bacteriological profile in Sputum and their Antibiogram among the patients of Acute Exacerbation of COPD. MVP J Med Sci 2017;4(2):113-7
18. Zohaib A. Khan FA, Ahmed M. Khalid T, Malik T *et al*. Antimicrobial susceptibility pattern among patients presenting with Acute Exacerbation of COPD. J Islamabad Med Dent College 2020; 9(1):23-7
19. Soumya S, Vagarali M, Nagamoti J. Sputum Bacteriology and antibiotic Sensitivity pattern in patients with COPD. A Hospital based Study. J Med SciClin Resarch.2018; 6(8): 47-53
20. Jones PW, Chen WH, Wilcox TK, Sethi S, Leidy NK, EXACT-PRO study group. Characterizing and quantifying the symptomatic features of COPD exacerbations. Chest 2011; 139(6):1388-94
21. Engler K, Muklemann K, Garzoni C, Pfakler H, Geiser T, Von Garnier C. Colonisation with *Pseudomonas aeruginosa* patients in COPD patients. Swiss medical weekly. 2012; 142(0506).