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ORIGINAL ARTICLE

Risk Factors for Multidrug Resistant organisms in Exacerbation of COPD

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Abstract:

Background & Objective: *Bacterial infections are the major cause of acute exacerbation of COPD (AE-COPD). The natural history of chronic obstructive pulmonary disease is characterized by frequent exacerbations. Majority of exacerbations are infectious and bacteria responsible for 30-50% of these cases. Appropriate use of antibiotic reduce mortality, hospital stay, subsequent exacerbations, further lung damage and also prevention of development of antibiotic resistance.*

Patients & Methods: *This cross sectional observational and analytical study conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from July 2019 – June 2020. A total of 102 patients with acute exacerbation of COPD were enrolled in this study. Early morning Sputum were examined for bacteriological culture and sensitivity. Multidrug-resistance was determined according to European Centre of Disease Prevention and Control classification.*

Result: *One hundred and two exacerbations were included and microorganisms were isolated in 50 cases.* Pseudomonas aeruginosa*15(30%),*Klebsiella pneumoniae*14(28.0%) and Acinetobacter 11(22%) were more frequent. Multidrug-resistant pathogens were found in 35(70%) cases. In multivariateanalysis,preevious hospitalization (Odds ratio2.19,95% CI 1.22-3.91), frequent antibioticuse (OR 3.136, 95% CI 1.37-7.15) and chronic kidney disease (7.560,95%CI 1.82-31.33) were found to be independent predictors for MDR pathogens. Irregular use of antibiotics ($p<0.007$) among the frequent antibiotic users favored growth of MDR pathogen.*

Conclusion: *Recent hospitalization, frequent antibiotic users particularly indiscriminate use of antibiotics and chronic kidney disease were seemed to be the risk factor for multidrug resistant bacteria.So special attention should be warranted in these groups regarding use of antibiotics.*

Key words: *Multidrug Resistant Organism, Exacerbation of COPD, Risk factors*

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Introduction:

Chronic Obstructive Pulmonary Disease (COPD) is a chronic inflammatory condition of the airways, which is associated with significant morbidity and mortality. According to World Health Organization (WHO), COPD will be the third-leading cause of death worldwide by 2030[1,2]. Based on BOLD and other large scale studies, it is estimated that the number of COPD cases was 384 million in 2010, with global prevalence of 11.7% (95% CI 8.4% - 15%)[2]. The overall prevalence of COPD in Bangladesh is 4.3% and in adults with age >40 years is 21.24% with total burden of COPD patients is about 6 million (BOLD-BD, 2007). Globally, there are around three million deaths annually and by 2030 COPD will be the 5th leading cause of loss in DALYs globally, where it was only number 13 in 2004[3].

ATS/ERS guidelines define Acute Exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) as an event characterized by an increase in patient's daily symptoms of dyspnea, cough, and/or sputum beyond normal day-to-day variability and severe enough to require a change in management[4].About 50-78% of acute exacerbations of COPD are caused by respiratory infections[5]. Bacteria as cause of AECOPD are reported from 30% up to 55% and common bacterial pathogens are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis* and in patients with more severe COPD also *Pseudomonas aeruginosa and Klesiella pneumonae*[6].

So, identification and appropriate treatment of these organisms is an essential part in management of AE-COPD.

Optimal antibiotic use is crucial, especially in an era of rising antibiotic resistance and lack of new antimicrobial development[7]. Overprescribing and misprescribing antibiotics are undoubtedly contributing to the growing challenges posed by antibiotic resistant bacteria, and epidemiological studies have clearly demonstrated direct relationships between antibiotic consumption and the emergence and dissemination of resistant strains in hospitals[8].

Infections caused by MDR gram-negative organisms are associated with high morbidity and mortality[9]. Moreover, the financial burden of antimicrobial resistance can be significant as a result of prolonged hospitalizations due to antibiotic treatment failures. The economic impact of antibiotic resistance can be measured not only through direct health care expenses but also through health burden to the individuals affected and to the society[9]. Leaders in world health have described antimicrobial-resistant bacteria as "nightmare bacteria" that account for a substantial number of excess deaths and catastrophic healthcare spending[10].

It is necessary to find out the resistant pathogens so that treatment can be planned accordingly which may decrease the mortality and morbidity.

Materials and Methods:

This cross-sectional analytical study was carried out in the Department of Respiratory Medicine, National Institute of Diseases of the Chest & Hospital (NIDCH), Mohakhali, Dhaka over a period of one year between July 2019 to June 2020.Adult patients presented with exacerbation of COPD admitted to the inpatient Department of Respiratory Medicine were the study population. Patients with concomitant pulmonary tuberculosis were excluded from the study. A total of 102 cases were taken in the study. Study samples were selected by purposive sampling.

Results:

Out of 102 patients with acute exacerbation of exacerbation of COPD mean age was 62.0±8.5 years with range from 42 to 84 years. Male patients were predominant 88(86.3% with M:F 6.3:1. Smoker was found in 89(87.2%). Among them majority 81(79.5%) patients took e"20 pack per year. The mean BMI was found 23.0±1.9 kg/m$^{2.}$

Sputum for C/S showed bacterial growth in 50(49.0%) with multidrug-resistant organism in 35 (70%) cases.

Majority 47(46%) patients used frequent antibiotic, 15(14.7%) had previous exacerbation in last year, and 10(9.8%) patients required hospital admission and I/V antibiotics. 25(24.5%) had DM and 15(14.7%) had CKD.

According to Winnipeg criteria 14 (13.7%) patients were in mild group, 53 (52.0%) were in moderate

and 35 (34.3%) were in severe exacerbation group. 26(52%) in moderate and 15(30%) in severe exacerbation group showed growth of organism which was insignificant (p>0.05).

Patients presented with no respiratory failure were 22 (21.5%) and rest 80 (78.5%) with respiratory failure of which 45 (44.1%) presented with non-life threatening and 35 (34.4%) with life threatening failure. 5 (10%) patients in no respiratory failure and 45 (90%) in respiratory failure group had growth of organism which was statistically significant (p<0.005).

In univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens.

In multivariable analysis, recent hospitalization, frequent antibiotic use and chronic kidney disease were found to be independent predictors for MDR pathogens.

Table-I

Demographic Characteristics of the Study Cases (n=102)

Demographic characteristic	Number of patients	Percentage
Sex		
Male	88	86.3
Female	14	13.7
Mean age (years)	62.0	±8.5
Range (min-max)	(42.0-84.0)	
Economic status		
Low	69	67.6
Lower middle	11	10.8
Upper middle	20	19.6
High	2	2.0
Smoker		
No	13	12.8
Yes	89	87.2
<20 pack/yr	8	7.7
>20 pack/yr	81	79.5

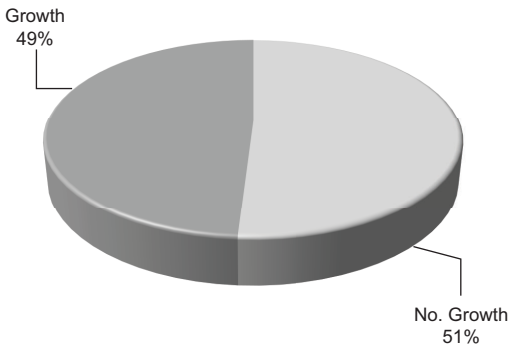

Fig.-1: *Sputum for C/S of the study patients*

Table 7 showed 14 (13.7%) patients were in mild group, 53 (52.0%) were in moderate and 35 (34.3%) were in severe exacerbation group according to Winnipeg criteria. 52% in moderte and 30% in severe exacerbation group showed growth whereas 53% and 35% didn't show any growth respectively. The chi-square statistic is 0.326. the p value is 0.568 and not significant at p <0.05.

Table III showed patients presented with no respiratory failure were 22 (21.5%) and rest 80 (78.5%) with respiratory failure of which 45 (44.1%) presented with non-life threatening and 35 (34.4%) with life threatening failure. 5 (10%) patients in no respiratory failure and 45 (90%) in respiratory failure group had growth of organism.

Chi square statistics was 7.7592 and p value is 0.0053. p value was significant (<0.01) for growth of organism between respiratory failure and no respiratory group which indicated respiratory failure favored growth of organism in this study.

In univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens

Table VI showed multivariable regression analysis using age, sex, smoking status, past exacerbation, past hospitalization, frequent use of antibiotics, presence of respiratory failure, DM and CKD for growth of MDR pathogens. P value was significant (p<0.05) for patients with previous hospitalization, frequent antibiotic use and presence of concomitant CKD.

Table II

Exacerbation of COPD according to Winnipeg criteria and growth of organisms (n=102)

Severity	Growth of organism				Total	P value
	Yes (n=50)		No (n=52)			
	N	%	N	%		
Mild	9	18.0	5	9.6	14(13.7%)	
Moderate	26	52.0	27	51.9	53(52.0%)	0.568[ns]
Severe	15	30.0	20	38.5	35(34.3%)	

ns= not significantP-value reached from chi square test

Table III

Association between growth of organism with exacerbation according to respiratory failure (n=102)

Exacerbation according to respiratory failure (GOLD guideline-2019) of organism	Growth				Total	P value
	Yes (n=50)		No (n=52)			
	n	%	N	%		
Acute respiratory failure- non life threatening	27	54.0	18	34.6	45(44.1%)	0.285[ns]
Respiratory failure (life threatening)	18	36.0	17	32.7	35(34.4%)	0.005[s]
No respiratory failure	5	10.0	17	32.7	22(21.5%)	

s= significant P-value reached from chi square test

Table-IV

Distribution of the study patients according to risk factors (n=102)

Risk factors	Number of patients	Percentage
Previous exacerbation in last year	15	14.7
Hospitalization in last year	10	9.80
Frequent antibiotic use	47	46.0
Previous I/V antibiotics in last year	10	9.80
Diabetes mellitus	25	24.5
Chronic kidney disease	15	14.7

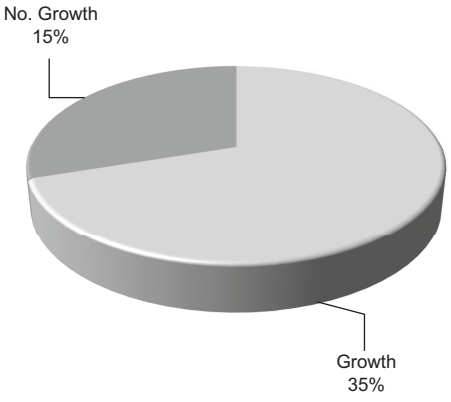

Fig.-2: *Distribution of Multidrug-resistant Pathogens of the Study Cases (n=50)*

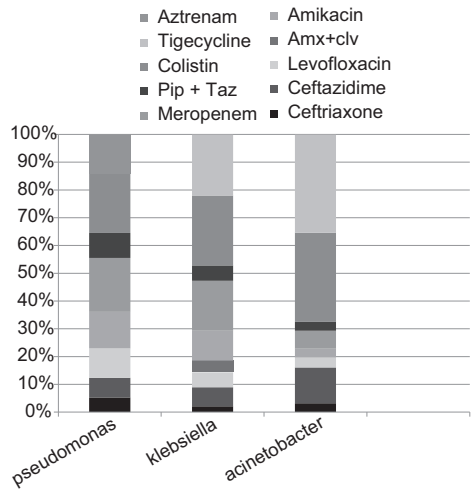

Fig.-3: *Antibiotic sensitivity of predominantly isolated organisms in component bar chart.*

Table-V

Univariate regression analysis for MDR pathogens

	Adjusted OR	95% CI		P value
		Lower	Upper	
Previous exacerbation	4.380	1.327	14.452	0.015[s]
Recently hospitalization	3.733	1.905	7.318	0.001[s]
Frequent antibiotic use	4.079	2.043	8.142	0.001[s]
Diabetes mellitus	3.451	1.762	6.759	0.001[s]
Chronic kidney disease	8.857	2.555	30.707	0.001[s]

s= significantP-value reached from univariate analysis by binary logistic regression analysis

Table-VI

Multivariable regression analysis for MDR pathogens

	Adjusted OR	95% CI		P value
		Lower	Upper	
Age (>60 years)	0.622	0.221	1.749	0.368[ns]
Male	1.224	0.493	3.039	0.663[ns]
Smoker	1.548	0.626	3.828	0.344[ns]
Previous exacerbation	1.434	0.358	5.745	0.610[ns]
Previous hospitalization	2.192	1.228	3.914	0.008[s]
Frequent antibiotic use	3.136	1.375	7.152	0.007[s]
Respiratory failure	0.879	0.263	2.935	0.834[ns]
Diabetes mellitus	1.781	0.774	4.098	0.175[ns]
Chronic kidney disease	7.560	1.824	31.331	0.005[s]

s= significant, ns= not significant
P-value reached from multivariate analysis by binary logistic regression analysis

Discussion:

This cross sectional observational and analytical study was carried out with the aim to identify the possible risk factors for the development of multidrug resistant pathogens. In this study, the age of the patients ranged from 42 years to 84 years with a mean of 62.0±8.5yearswith male predominance (86.3%) which was consistent with results found in another studies[11].

Smoker was found in 89(87.2%). Among them majority 50(49.0%) patients taken e"20 pack per year. Similar results were found in other studies[12].

In this present study it was observed that there was no significant association between growth of organism with exacerbation according to Winnipeg criteria. It was found that the number of patients in severe exacerbation were lower as compared to mild and moderate grade, the growth percentage of a pathogenic organism was found to be highest (71.4%) in severe exacerbation followed by moderate (55.9%) and least (35.2%) in mild exacerbation cases and this difference was found to be statistically significant (p = 0.004)[13].

In this study it was observed that 45(44.1%) patients had acute respiratory failure-non life threatening, 15(14.7%) had respiratory failure (life threatening) and 42(41.2%) were no respiratory failure. Respiratory failure slightly higher than other studies as only hospital admitted patients were considered[14,15]. In this study it was observed that presence of respiratory failure was statistically significant (p<0.05) when compared between growth of organism and no growth of organism group which was similar to other study[15].

This study showed bacterial growth found in 50 cases (49.0%). These results are comparable with previous studies[6,7,14,15] and are not supported by the study[13] where bacteriological isolation was found in 35% of cases.

In this study multidrug-resistance was found in 35 (70%) while it was 20.1% in another study[18].

This study also showed hospitalization in last year 9(66.7%) and chronic kidney disease 13(87.0%) were found in multi-drug resistance, which were statistically significant ($p<0.05$) when compared between multidrug-resistant and non multi drug-resistant pathogens. Another study[19]reported that exacerbation in last year was 87.5%, hospitalization in previous year was 81.2%, long term oral antibiotics use was 12.5%, Diabetes mellitus was 21.9%, Renal disease was 21.9 %. Hospitalization in previous year and renal disease was statistically significant ($p<0.05$) between groups.

This study observed that in univariate analysis, previous exacerbation, recent hospitalization, frequent antibiotic use, diabetes mellitus and chronic kidney disease were found to be independent predictors for MDR pathogens. Another study[12] documented MDR pathogens were more frequently encountered in patients with more chronic conditions and in those required prior hospitalization.

In multivariate analysis, previous hospitalization (Odds ratio (OR)2.92, 95% CI 1.23-3.91), frequent antibiotic use (OR 3.136, 95% CI 1.37-7.15) and chronic kidney disease (OR 7.56, 95%CI 1.82-31.33) were found to be independent predictors for MDR pathogens. Another similar study[20] found three independent MDR risk factors: chronic renal disease (Odds ratio (OR), 7.60, 95% CI 1.92-30.09), hospitalization in the previous year (OR, 3.88 95% CI 1.37-11.02) and prior multidrug-resistant isolation (OR, 5.58, 95% CI 2.02-15.46).

Limitations of the study:

Adequate past treatment history of patients was not available due to lack of records. It was necessary to evaluate the reason for such high antibiotic resistance pattern observed in this study.Also,atypical organisms and viruses could not be detected due to unavailability of serological tests.

Conclusion:

Presence of multidrug resistant bacteria were very high 35 (75%) in admitted cases. Previous hospitalization, repeated use of antibiotics, DM and CKD were found as important predictors for development of multi-drug resistance.

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