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ORIGINAL ARTICLE

Factors Affecting Antibiotic Resistance Among Patients With Community Acquired Pneumonia In A Tertiary Care Hospital

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Abstract:

Background: *Community Acquired Pneumonia (CAP) is a major health problem leading to significant morbidity and mortality worldwide. Bacteriological profile of CAP is different in different countries and changing with time within the same country. Bacterial resistance to antibiotics is also an increasing problem, which may cause infection that is difficult to treat.*

Aims: *To identify the factors affecting antibiotic resistance among indoor patients of NIDCH.*

Materials & Methods: *This cross sectional, observational study conducted at the Department of Respiratory Medicine in National Institute of Diseases of the Chest and Hospital from May 2019 to September 2020. Of 195 patients with CAP, 87 patients with positive sputum bacterial growth were enrolled in this study.*

Results: *A total number of 87 patients with community acquired pneumonia were selected and among them, majority patients were male 65(74.7%), male to female ratio was 2.9:1. The mean age was found 50.6±16.7 years with range from 18 to 85 years. Among the co morbidities diabetes mellitus was the highest 34(39.1%) followed by hypertension 23(26.4%), chronic obstructive pulmonary disease (COPD) 20(23.0%). Most frequent pathogens were* Klebsiella pneumoniae *35(40.2%) followed by* Streptococcus pneumoniae *15(17.2%),* Pseudomonas aeruginosa *11(12.6%). In this study it was observed that multidrug-resistant pathogens was found 54(62.1%) with 95% CI 51.9 to 72.3%. In multivariate logistic regression analysis, previous antibiotic use, history of self medication and history of previous hospitalization were found to be independent predictors for multidrug resistance.*

.***Conclusion:*** *Gram negative bacteria are the main pathogenic bacteria in CAP. Identification of bacteriological profile and susceptibility pattern of pathogens could enable accurate diagnosis and treatment of CAP. The growing prevalence of multidrug resistant bacteria represents an important issue in choosing empiric antimicrobial management in hospitalized patients. The widespread antibiotic resistant microorganisms necessitate the implementation of antibiotic stewardship strategies, to ensure that antibiotics are used only when necessary and appropriate.*

Keywords: *Factors Affecting, Antibiotic Resistance, Multi Drug Resistance (MDR), Community Acquired Pneumonia.*

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Introduction:

Pneumonia is broadly defined as acute infection and inflammation of lung parenchyma[1]. Pneumonia can be classified as- community acquired pneumonia (CAP), nosocomial pneumonia, aspiration pneumonia and pneumonia in immunocompromised host[2].

Infectious Diseases Society of America (IDSA) defines CAP as "an acute infection of the pulmonary parenchyma that is associated with at least some symptoms of acute infection, accompanied by the presence of an acute infiltrate on a chest radiograph or auscultatory findings consistent with pneumonia in a patient not hospitalized or residing in a long-term care facility for more than 14 days before onset of symptoms[3-5].

Bacterial resistance to the effects of antibioti-cs is an increasing problem around the world. Multi-drug resistant organisms (MDRO), which in de-veloped countries would result in the selection of an alternative treatment but in poor countries, may cause infections that are difficult to treat[6] .

Unfortunately, the three major bacterial respiratory pathogens; *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Haemophilus influenzae*; have increasing prevalence of antibiotic resistance in developed world[5,7,8].

Moreover, resistance surveillance data from parts of the developing world remain poor. Relatively few surveillance data are available for countries in South-East Asia[9].

We are living through an antibiotic resistance crisis, mainly because antibiotics tend to lose their efficacy over time due to the emergence and dissemination of resistance among bacterial pathogens, principally caused by the overuse and inappropriate use of antibiotics, as well as the extensive use of antibiotics in agriculture and the food industry.

Risk factors for the spread of resistant bacteria in hospitals and the community are overcrowding, lapses in hygiene or poor infection control practices, unnecessary use of antibiotics for conditions where they are not indicated, such as common colds or viral pharyngitis, non compliance and inadequate duration or dosage, veterinary use of antibiotics[10]. Prior hospitalization, previous colonization, history of antibiotic use, non ambulatory status, prior use of inhaled corticosteroid are the risk factors associated with drug resistant organism of community acquired pneumonia[11,12].

Identification of patients with drug-resistant pathogens at initial diagnosis is also essential for treatment of pneumonia[11].

Hence, this study was conducted to address the factors associated with antibiotic resistance among patients admitted in Inpatient Department of NIDCH.

Methods:

This cross-sectional observational study was conducted in National Institute of Diseases of the Chest and Hospital (NIDCH), Dhaka, Bangladesh. This study was carried out from May 2019 to September 2020. Community acquired pneumonia patients admitted in Inpatient Department of NIDCH fulfilling the inclusion and exclusion criteria were included in this study.

The patients were selected by non-randomized purposive sampling method. Community acquired pneumonia patients with positive sputum bacterial growth admitted in Inpatient Department of NIDCH were included.

The patients with co-infection with Tuberculosis and those who refused to enroll in the study were excluded.

Patients of community acquired pneumonia were selected by history, clinical examination and radiological examination from the Inpatient Department of Respiratory Medicine of NIDCH according to inclusion and exclusion criteria.

Early morning sputum samples were collected in a sterile container and sent to International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR, B) for Gram staining, culture sensitivity test. Sputum for AFB, sputum for Gene X-pert MTB/RIF were sent to Department of Microbiology of NIDCH. For scanty sputum production, sputum was collected after nebulization by hypertonic saline (3% sodium chloride).

All the data were recorded systematically in a preformed data collection sheet and analyzed by descriptive and analytic techniques. Chi square test was used for categorical variables. Multivariate logistic regression was performed to assess independent relationship between factors.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software version 23 for windows.

Sputum samples were collected from all patients enrolled in the study. Representative sputum originated from the lower respiratory tract was defined as that containing >25 granulocytes and <10 epithelial cells per low power field microscopic view. Validated sputum was cultured in blood agar, chocolate agar and McConkey's agar media. Isolation and identification of microorganism was done by semiquantitative method.

Antibacterial susceptibility testing was done by using modified Kirby-Bauer disk diffusion method[13] and interpreted according to Clinical and Laboratory Standard Institute guideline.

Results:

Table-I

Socio-demographic distribution of the study respondents (n=87)

Demographic characteristics	Number of patients	Percentage
Sex		
Male	65	74.7
Female	22	25.3
Mean age (years)	50.6	±16.7
Range (min-max)	18.0	-85.0
Marital status		
Married	78	89.7
Unmarried	9	10.3
Residence		
Rural	36	41.4
Urban	51	58.6
Educational status		
Illiterate	13	14.9
Primary	19	21.8
Secondary	41	47.1
College	9	10.3
University	5	5.7

Table I shows that male patients were predominant 65(74.7%) and female was 22(25.3%), male female ratio was 2.9:1. The mean age was found 50.6±16.7 years with range from 18 to 85 years. Married patients were found 78(89.7%), 41(47.1%) patients completed secondary education level. Other results are depicted in the table.

Table-II

Distribution of the respondents according to risk factors (n=87)

Risk factors	Number of patients	Percentage
Previous antibiotic use	63	72.4
History of self medication	40	46.0
Sharing of antibiotic with others	24	27.6
Use of left over antibiotics	21	24.1
History of non adherence to antibiotic	47	54.0
History of previous hospitalization	48	55.2
Vaccination is status against *S. pneumoniae*	4	4.6
Use of inhaled corticosteroid	25	28.7

Regarding risk factors, 63(72.4%) patients had history of previous antibiotic use, 48(55.2%) had history of previous hospitalization, 47(54.0%) had history of non adherence to antibiotic, 42(46.0%) had history of self medication, 24(27.6%) sharing of antibiotic with others, 21(24.1%) used of left over antibiotics and 25(28.7%) used inhaled corticosteroid.

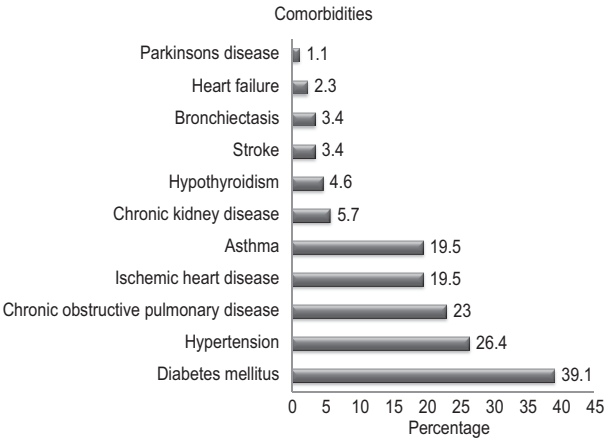

Fig.-1: *Comorbidities of the study respondents (n=87)*

Figure 1 shows that among the comorbidities diabetes mellitus was the highest 34(39.1%), followed by hypertension 23(26.4%), chronic obstructive pulmonary disease (COPD) 20(23.0%), ischemic heart disease 17(19.5%), asthma 17(19.5%), chronic kidney disease 5(5.7%),

Table-III

Distribution of the respondents according to isolated bacteria (n=87)

Name of the bacteria	Number of patients	Percentage
Single bacterial agent		
Klebsiella pneumoniae	35	40.2
Streptococcus pneumoniae	15	17.2
Pseudomonas aeruginosa	11	12.6
Acinetobactor	4	4.6
Haemophilus influenzae	4	4.6
Staphylococcus aureus	3	3.4
E. coli	2	2.3
Staphylococcus haemolyticus	2	2.3
Serratia	1	1.1
Mixed bacterial agent		
Klebsiella pneumoniae+ Acinetobactor	3	3.4
Acinetobactor+ Pseudomonas aeruginosa	2	2.3
Acinetobactor+ Staphylococcus aureus	1	1.1
Klebsiella pneumoniae+ Enterobactor	1	1.1
Klebsiella pneumoniae+ Enterococcus faecium	1	1.1
Klebsiella pneumoniae+ Staphylococcus haemolyticus	1	1.1
Pseudomonas aeruginosa+ Strptococcus pneumoniae	1	1.1

hypothyroidism 4(4.6%), stroke 3(3.4%), bronchiectasis 3(3.4%), heart failure 2(2.3%) and parkinson's disease 1(1.1%).

Table III shows that the most frequent pathogens were *Klebsiella pneumoniae* 35(40.2%), *Streptococcus pneumoniae* 15(17.2%), *Pseudomonas aeruginosa* 11(12.6%), *Acinetobactor* 4(4.6%), *Haemophilus influenzae* 4(4.6%), *Staphylococcus aureus* 3(3.4%), *E.coli* 2(2.3%), *Staphylococcus haemolyticus 2(2.3%) and Serratia* 1(1.1%). Regarding mixed(dual) pathogens *Klebsiella pneumoniae+ Acinetobactor* were 3(3.4%), *Acinetobactor+ Pseudomonas aeruginosa* 2(2.3%). Other results are depicted in the table.

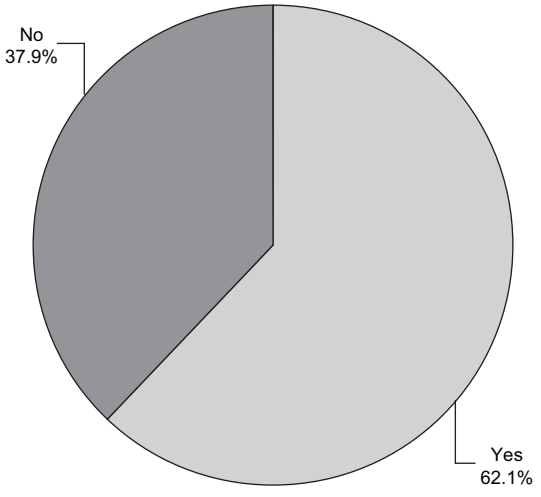

Fig.-2: *Multidrug resistance of the study respondents (n=87)*

Multidrug resistant organism (MDRO): non susceptibility to at least one agent in three or more antimicrobial categories. Figure 2 shows that multidrug resistance was found 54(62.1%) with 95% CI 51.9 to 72.3%.

Table IV shows that hypertension, chronic obstructive pulmonary disease, previous antibiotic use, history of self medication, sharing of antibiotic with others, use of left over antibiotics, history of non adherence to antibiotic, history of previous hospitalization, vaccination status against *S. pneumoniae* and antibiotic prescribed by pharmacy were significantly associated with multidrug resistance. However, other risk factors were not significantly associated with multidrug resistance.

In multivariate logistic regression analysis, previous antibiotic use, history of self medication and history of previous hospitalization were found to be independent predictors for multidrug resistance.

Table-IV

Association between Multidrug resistance with risk factors (n=87)

Risk factors	Multidrug-resistance				P value
	Yes (n=54)		No (n=33)		
	n	%	n	%	
Age (>60 years)	18	33.3	9	27.3	0.364^{ns}
Male	42	77.8	23	69.7	0.400^{ns}
Smoking	34	63.0	20	60.6	0.826^{ns}
Consumption of broiler chicken	51	94.4	28	84.8	0.132^{ns}
Consumption of pasteurized packet milk	31	57.4	13	39.4	0.103^{ns}
Diabetes mellitus	25	46.3	9	27.3	0.078^{ns}
Hypertension	19	35.2	4	12.1	0.015^{s}
Chronic obstructive pulmonary disease	18	33.3	2	6.1	0.003^{s}
Ischemic heart disease	10	18.5	7	21.2	0.759^{ns}
Asthma	8	14.8	9	27.3	0.155^{ns}
Chronic kidney disease	4	7.4	1	3.0	0.368^{ns}
Hypothyroidism	2	3.7	2	6.1	0.490^{ns}
Stroke	3	5.6	0	0.0	0.234^{ns}
Bronchiectasis	3	5.6	0	0.0	0.234^{ns}
Heart failure	2	3.7	0	0.0	0.383^{ns}
Using inhaled steroid	15	27.8	10	30.3	0.800^{ns}
Previous antibiotic use	47	87.0	16	48.5	0.001^{s}
History of self medication	34	63.0	6	18.2	0.001^{s}
Sharing of antibiotic with others	21	38.9	3	9.1	0.003^{s}
Use of left over antibiotics	19	35.2	2	6.1	0.002^{s}
History of non adherence to antibiotic	37	68.5	10	30.3	0.001^{s}
History of previous hospitalization	42	77.8	6	18.2	0.001^{s}
Vaccination status against *S. pneumoniae*	0	0.0	4	12.1	0.018^{s}
Antibiotic prescribed by pharmacy	21	46.3	3	9.1	0.040^{s}

s= significant, ns= not significant
p-value reached from chi square test

Table-V

Multivariate logistic regression analysis for Multidrug resistance

	Adjusted	95% CI		P value
	OR	Lower	Upper	
Hypertension	12.261	0.466	82.788	0.133^{ns}
Chronic obstructive pulmonary disease	0.547	0.022	13.800	0.714^{ns}
Previous antibiotic use	22.708	2.542	92.846	0.005^{s}
History of self medication	4.352	1.250	15.151	0.021^{s}
Sharing of antibiotic with others	0.936	0.024	36.946	0.972^{ns}
Use of left over antibiotics	18.182	0.374	82.768	0.143^{ns}
History of non adherence to antibiotic	0.264	0.017	4.182	0.345^{ns}
History of previous hospitalization	10.257	1.537	68.456	0.016^{s}
Vaccination is status against *S. pneumoniae*	1.025	0.447	2.349	0.954^{ns}
Antibiotic prescribed by pharmacy	1.721	0.262	11.288	0.572^{ns}

s= significant, ns= not significant
p-value reached from multivariate analysis by binary logistic regression analysis
OR=Odd's Ratio

Discussion:

This cross sectional observational study was carried out with an aim to identify the bacteriological profile of community acquired pneumonia and their antibiotic susceptibility pattern among patients admitted in Inpatient Department of NIDCH. This study also to find out the multidrug resistance and factors affecting multidrug resistance.

Of 195 patients with community acquired pneumonia, 87 fulfilled the inclusion and exclusion criteria during the period from May 2019 to September 2020 were included in this study. Community acquired pneumonia patients with positive sputum bacterial growth and patient willing to participate were enrolled in this study. Patients suffering from co-infection with active pulmonary tuberculosis and patient not willing to be included in this research were excluded from the study. The present study findings were discussed and compared with previously published relevant studies.

Regarding risk factors in this study it was observed that 63(72.4%) patients had history of previous use, 48(55.2%) had history of previous hospitalization, 47(54.0%) had history of non adherence to antibiotic, 42(46.0%) had history of self medication, 24(27.6%) sharing of antibiotic with others, 21(24.1%) used of left over antibiotic. Ishida et al.[14] had observed that previous antibiotic treatment was found 31.4%. Gross et al.[15] consisted that antibiotic use in the last 90 days was found 31.9%. Another study documented by Lauderdale et al.[16] which showed antibiotic used 16.1%.

Regarding history of antibiotic use of the respondents, majority 32(50.8%) respondent 1st time complete full course and 7(77.8%) respondent 4th time demand of antibiotic. 16(25.4%) respondent 1st time prescribed by registered doctor.

In this study it was observed that among the comorbidities diabetes mellitus was the highest 34(39.1%) followed by hypertension 23(26.4%), chronic obstructive pulmonary disease (COPD) 20(23.0%), ischemic heart disease 17(19.5%), asthma 17(19.5%), chronic kidney disease 5(5.7%), hypothyroidism 4(4.6%), stroke 3(3.4%), bronchiectasis 3(3.4%), heart failure 2(2.3%) and parkinsons disease 1(1.1%). In a study conducted by Jeong et al.[17] where they found diabetes was 23.0%, cerebrovascular disease 19.0%, chronic heart disease 8.0%, chronic kidney disease 6.0%, chronic liver disease 8.0%. Prina et al.[18] reported that COPD was 35.0%, bronchiectasis 11%, diabetes mellitus 23.0%, chronic kidney disease 16.0%, neurologic disease 19.0%. Ishida et al.[14] consisted that congestive heart failure 32.1%, chronic obstructive pulmonary disease 21.6%, bronchiectasis 15.7%, chronic kidney disease 11.8%, cerebrovascular disease 22.9% and diabetes 13.7%. Gross et al.[15] had observed COPD was 27.6%, congestive heart failure 16.5% and diabetes 28.4%. Another study conducted by El-Sokkary et al.[19] which showed that diabetes mellitus was 31.48%, hypertension 25.93%, COPD 18.52%, ischemic heart disease 16.67%.

In this present study it was observed that multidrug-resistant pathogens was found 54(62.1%) with 95% CI 51.9 to 72.3%. In a study of El-Sokkary et al.[19] reported that overall, 76.2% of isolates showed a multidrug resistant phenotype. Another study conducted by Prina et al.[18] which showed although MDR pathogens were more frequently isolated in HCAP (26.6%), they were also detected in CAP (8.6%).

In my study it was observed that hypertension, chronic obstructive pulmonary disease, previous antibiotic use, history of self medication, sharing of antibiotic with others, use of left over antibiotics, history of non adherence to antibiotic, history of previous hospitalization, vaccination is status against and antibiotic prescribed by pharmacy were significantly associated with multidrug-resistant pathogens. However, other risk factors were not significantly associated with multidrug-resistant pathogens. Gross et al.[15] reported that statistically significant associations with MDRO included the following: history of cerebrovascular accident, congestive heart failure, presence of HCAP, number of days hospitalized in the previous 180 days, antibiotic use in the previous 90 days.

In multivariate logistic regression analysis in this study it was observed that previous antibiotic use, history of self medication and history of previous

hospitalization were found to be independent predictors for multidrug resistance. In a study of Luan et al.[20] had observed that prior multiple antibiotic treatment was the only independent risk factor for MDRCAP (OR: 3.542; 95% CI: 1.141–14.827, P=0.002) Although frequent use antibiotics might significantly inhibit bacterial growth, it also might lead to frequent bacterial mutation and drug resistance. When more than one antimicrobial agent is present in the microorganism environment, pressure from these antimicrobial agents results in selection of bacteria using multiple or polyvalent resistance mechanisms. Therefore, bacteria optimize one resistance mechanism to survive in variable environments or increase mutational events during situations of bacterial stress[21]. Self medication commonly associated with inappropriate drug use practices include- short duration of treatment, inadequate dose, sharing of medicines, and avoidance of treatment upon the improvement of disease symptoms[22]. This may be the cause of antibiotic resistance in self medication.

Prina et al.[18] showed that the following six independent factors were described for MDR pathogens: prior hospitalization; immuno-suppression; previous antibiotic use; use of gastric acid–suppressive agents; tube feeding; and nonambulatory status. Moreover, they defined some additional risk factors for MRSA (including chronic dialysis during the preceding 30 days, positive MRSA history within the previous 90 days, and congestive heart failure). Gross et al.[15] reported that in the propensity score-adjusted multivariate logistic regression analysis, duration of previous hospitalization in the last 90 or 180 days, *P. aeruginosa* colonization/infection in the previous year, antimicrobial use in the last 90 days, and admission from a nursing home were all predictors of MDRO. Another study conducted by Jeong et al.[17] where they found logistic regression analysis identified 5 variables that were independently associated with the identification of PDR pathogens. Recent history of hospitalization for e" 2 days in the preceding 90 days (adjusted OR 2.324 and 95% CI 1.241–4.352, p = 0.008) and recent antibiotic therapy within the past 30 days (adjusted OR 2.699 and 95% CI 1.366–5.334, p = 0.004) were independently associated with PDR pathogens. Chronic lung disease (adjusted OR 1.970 and 95% CI 1.075–3.612, p = 0.028) were also independently associated with the recovery of PDR pathogens.

Conclusion:

In multivariate analysis, previous antibiotic use, history of self medication and history of previous hospitalization were found to be independent predictors for multidrug resistance. The growing prevalence of multidrug resistant bacteria represents an important issue in choosing empiric antimicrobial management in hospitalized patients. The widespread antibiotic-resistant microorganisms necessitate the implementation of antibiotic stewardship strategies. Microbiological profile of community acquired pneumonia varies geographically. There is a need to conduct regular prevalence and antibiogram studies to develop empirical guidelines for treatment of community acquired pneumonia in that particular region.

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Author Contributions: Dr.Mohammad Zannatul Rayhan had full access to all data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis.

Dr. Mohammad Zannatul Rayhan contributed to study conception and design, data collection, analysis and interpretation of data, drafting of the manuscript and critical revisions of the article.

Prof. Krishna Chandra Ganguly, contributed to case selection, critical revisions & section writing of the manuscript. Bipul Kanti Biswas, Most Mehenaz Alam, Tazrin Farhana also contributed to critical revisions of the manuscript.

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