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The Pattern of Antibiotics Resistance among Critically Ill Patients Admitted At a Tertiary Hospital in Chattogram

Authors
Dr Md. Mahade Hassan[1], Prof. Dr Alak Nandy[2], Prof. Dr Nahida Sultana[3], Dr Md. Saif Uddin Azad[4], Dr Tarequr Rahaman[5]
[1]Assistant Professor, Department of Intensive Care Unit and Acute Medicine Unit, Chattogram Maa O Shishu Hospital Medical College, Bangladesh
[2]Professor and HOD Department of Anaesthesia, Chattagram Maa O Shishu Hospital Medical College, Bangladesh
[3]Professor and HOD Department of Microbiology, Chattagram Maa O Shishu Hospital Medical College, Bangladesh
[4]Registar, ICU, Chattogram Maa O Shishu Hospital Medical College, Bangladesh
[5]Medical Officer, ICU, Chattogram Maa O Shishu Hospital Medical College, Bangladeh
Corresponding Author
Dr Md. Mahade Hassan
Assistant Professor, Department of ICU and Medicine, Chattagram Maa O Shishu Hospital Medical College

Abstract

Background: *Antimicrobial resistance (AMR) has been a major concern to the successful treatment of an ever- increasing spectrum of illnesses that are caused by bacteria, parasites, viruses, and fungi for a number of decades now. This risk has become even more serious since the number of infections that need treatment has been steadily raising over the last several years. Because antibiotic resistance reduces the efficacy of drugs used to treat bacterial infections, it becomes more difficult, costly, and maybe even impossible to treat patients.*

Objective: *To assess the antibiotic resistance pattern of antibiotics resistance among critically ill patients admitted at a tertiary hospital in Chattogram.*

Materials and Methods: *This prospective observational research was undertaken from January to June 2022 at the Microbiology Lab of Chattagram Maa O Shishu Hospital Medical College. After receiving clearance from the CMC Ethical and Review Committee and authorization from the laboratory authorities, the research colleagues and research assistant gathered 79 data points from various labs in the form of MS-Excel files and entered them into a case record form.*

Results: *The Mean±SD age of the patients was 52.70±18.361 years. Among the patients 5.063% was adolescent, 51.9% was adult and 43.09% senior adult. Nearly, 64.6% of samples were collected from tracheal and 1.3% of samples were collected from pus culture. Furthermore, 55.7% Klebsiella, 16.5% Pseudomonas, 12.7% Acinetobacter, 7.6% Staph Aureus, 5.1% E. coli, and 2.5% Enterococcus bacteria were found in the patients. Microbe Klebsiella is highly resistant to most of the multidrug except Netilmicin and Mecillinum. Multidrug resistance such as Amikacin (p=0.006), Cefuroxime (p=0.041), Ampicillin (p=0.005), Vancomycin (p=0.000), Linezolid (p=0.000), Nitrofurantoin (p=0.000), Cloxacillin (p=0.005) and Mecillinum (p=0.02) were significantly associated with the micro-organisms. Prevalence of co-morbidities and antibiotic resistance among critically ill patient's shows that most of antibiotics resistant with co morbidities which is higher than sensitivity and very few antibiotics are intermediate with co-*

morbidities.
Significant association observed between COTRIM vs COPD (p=0.007), CHLORAM vs HTN and IHD, CIPRO vs DM, AMOXICLAV vs IHD, CEFIXIME vs CVD, AMIKACIN vs CVD and PIPERCILLIN vs CVD. This study also identified that multidrug resistance has association with Specimen in some cases. Six antibiotics such as COTRIM, MECILLINUM, TETRACYCLINE, CEFOTAXIME, TIGECYCLINE and COLISTIN significantly associated with Specimen.
Conclusion: *The primary scenario of rational anti-microbial medication for critically sick patients is presented in this research. There was a catastrophic scenario due to the gradual rise in the number of E. coli and Klebsiella organisms, as well as their resistance to popular antibiotics like Ampicillin, Ciprofloxacin, and Cefuroxime. This condition was worrying and severe.*
Keywords: *Antibiotics resistance, Critically Ill Patients, Bacterial infections, microbiotic infections, antiviral infections.*

Introduction

Antibiotics are essential for fighting infections which are developed by bacterial attack, but many bacteria are likely to develop resistant to antibiotics. Critically sick patients admitted to intensive care units (ICU) are always more likely to develop nosocomial infections caused by resistant bacteria.[1] Because of limited mobility and increasing use of intrusive equipment, patients admitted to ICUs are more vulnerable to infection. Antimicrobial resistance (AMR) threatens the effective treatment and prevention of wide range of diseases and infections caused by bacteria.[2] Infection with resistant strains in intensive care units increases mortality and costs.[3]In ICU patients, the patterns of organisms producing infections and their antibiotic resistance vary greatly from hospital to hospital, nation to country, and even between ICUs within the same institution. Bacteria create resistant against antibiotics because of various reason, such as: genetic mutations, bacteria are become multiple in presence of therapeutic level of antibiotic doses & bacteria become resistance in the presence of other species. Furthermore, some diseases are becoming more frequent in each local population and are a significant risk factor for the morbidity and death of ICU patients.[4] Themost prevalent species in an Indian ICU investigation were Acinetobacter sp., Escherichia coli, Klebsiella sp., Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pyrogen, andothers.[5]

In a European intensive care unit, however, Staphylococcus aureus was found to be the most often isolated bacterium (30.1%) followed by Pseudomonas aeruginosa (28.7%), Coagulase negative staphylococcus (19.1%), and Yeast (17.1%).

Several antibiotic stewardship initiatives, or techniques for optimizing antibiotic usage, have been created. These treatments are divided into two types: instructional and restrictive or coercive. Both types of interventions may be beneficial in lowering the number of antibiotics administered and therapy costs while preserving quality of care. Restrictive tactics, on the other hand, are seen to be more successful and have a longer lasting influence than instructional techniques.[5-7]

This study tried to identify the bacterial resistance patternagainst antibiotics among critically ill patients admitted at a tertiary hospital in Chattogram. In addition, this study also tried to understand the widely uses of antibiotics among critically ill patients in tertiary medical centre in Bangladesh.

Materials and methods

This prospective observational research was undertaken from January to June 2022 at the Microbiology Lab of Chattagram Maa O Shishu Hospital Medical College. After receiving clearance from the CMC Ethical and Review Committee and authorization from the laboratory authorities, the research colleagues and research assistant gathered 79 data points from various labs in the form of MS-Excel files and entered them into a case record form.

Data was noted in a case record form (CRF). The

CRF had four parts.

- Client's information from the record
- Specimen with growth
- Name(s) of the bacteria
- Drug sensitivity profile

Inclusion Criteria

Infection has been shown by bacterial testing, with laboratory results indicating positive findings against microorganisms.

Exclusion Criteria

Samples taken in duplicate, each with a unique sensitivity.

Statistical Analysis

The data was examined using descriptive statistics, such as total numbers and percentages when appropriate. Microsoft Word, Microsoft Excel, and Statistical Package for Social Service (SPSS) version 23 have been used in the United States.

Results

In table-1 shows demographic status of the patients where majority were belong to 59-69 years age group, 23(29.1%). Followed by 20(25.3%) belong to 48-58 years age group, 13(16.5%) belong to >69 years age group, 10(12.7%) belong to 15-25 years age group. The mean ± SD age was 52.70±18.361**.** Besides that, 51.9% were male. The following table is given below in detail:

Table-1: Demographic status of the patients (N=79)

Age group	Frequency (n)	Percent (%)	Mean ± Std
15-25 years	10	12.7	**52.70±18.361**
26-36 years	8	10.1	
37-47 years	5	6.3	
48-58 years	20	25.3	
59-69 years	23	29.1	
>69 years	13	16.5	
Gender			
Male	41	51.9	
Female	38	48.1	

In figure-1 shows sample distribution of the patients where 51(64.56%) patients' sample were taken from Tracheal, followed by 16(20.25%) patients' sample were taken from Blood, 7(8.86%) patients' sample had taken from urine, 4(5.06%) patients' specimen was taken from Sputum and only 1 (1.27%) sample taken from Pus Culture. The following figure is given below in detail:

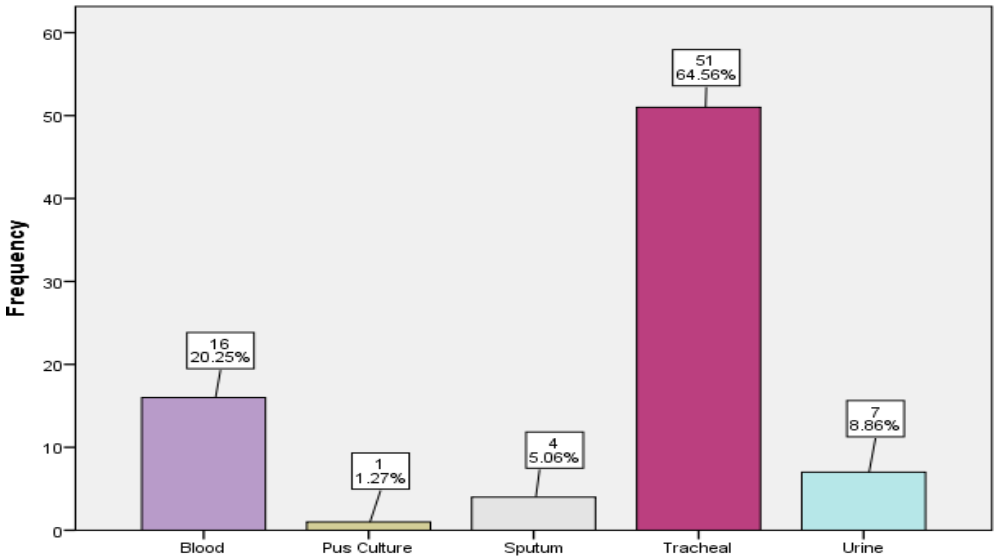

Figure 1: Sample Distribution of the Patients (N=79)

The following figure-2 shows distribution of microorganism isolate from patients sample where 55.7% Klebsiella, 16.5% Pseudomonas, 12.7% Acinetobacter, 7.6% Staph Aureus, 5.1% E. coli, and 2.5% Enterococcus bacteria were found in the patients. The following table is given below in detail:

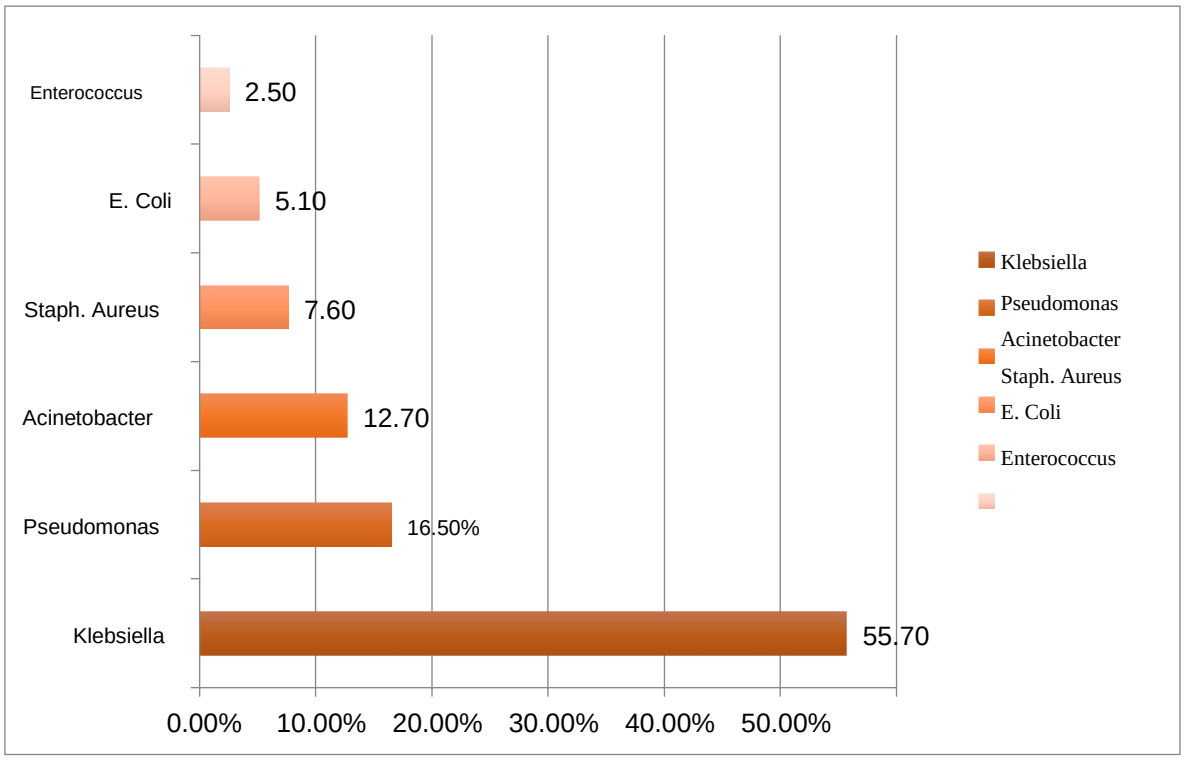

Figure 2: Distribution of microorganism that isolate from patients sample (N=79)

In association between types of sample and microorganism E. coli was found in only tracheal (1) and urine (3) samples. Besides Acinetobacter, it was found in blood (7) and tracheal (3) samples. Similar findings for Enterococcus bacteria Besides, Klebsiella and Pseudomonas found most of the samples that were collected from the patients. In addition, p-value less than 0.05 (typically $p \leq 0.05$) is statistically significant. Here we found p= 0.000*. That means significant relationship between the specimen and the micro-organism. The following table 3 is given below in detail:

Table 2: Association between types of specimen and microorganism (N=79)

Specimen	**Microbes**						
	Gram Negative					**Gram Positive**	**p value**
	Klebsiella (n=44)	Pseudomonas (n=13)	Acinetobacter (n=10)	E.coli (n=4)	Enterococcus (n=2)	Staph. aureus (n=6)	**0.000***
Blood	3(18.75%)	4 (25%)	7(43.75%)	-	1 (6.25%)	1 (6.25%)	
Pus	-	1(100%)	-	-	-	-	
Sputum	4 (100%)	-	-	-	-	-	
Tracheal Sample	34(66.66%)	8 (15.68%)	3 (5.88%)	1 (1.96%)	-	5 (9.80%)	
Urine	3 (42.85%)	-	-	3 (42.85%)	1(14.28%)	-	

Note: $p \leq 0.05$ (significant)

* P=0.000 (highly significant)

Distribution of multiple antibiotics among the critically ill patients shows levofloxacin antibiotic used in 94.9% cases followed by amikacin used in 93.7% cases, cefuroxime used in 92.4% cases, cefixime and ciprofloxacin used in 86.1% cases. The following table 4 is given below in detail:

Table 3: Prescribe of Multiple Antibiotic for the critically ill patients (N=79)

Name of Antibiotics	Responses	ent of Multiple Antibiotic
	Number of cases (n)	
LEVOFLOXACIN	75	94.9%
AMIKACIN	74	93.7%
CEFUROXIME	73	92.4%
CEFTRIAXONE	68	86.1%
CEFIXIME	68	86.1%
CIPRO	67	84.8%
COTRIM	64	81.0%
CEFTAZIDIME	62	78.5%
GENTA	61	77.2%
MEROPENEM	59	74.7%
AMPICILLIN	57	72.2%
TIGECYCLINE	50	63.3%
COLISTIN	36	45.6%
CEFOTAXIME	35	44.3%
CEFEPIME	32	40.5%
AZITHRO	25	31.6%
AMOXICLAV	22	27.8%
PIPERCILLIN	15	19.0%
PENICILLIN	15	19.0%
VANCOMYCIN	13	16.5%
TEICOPLANIN	12	15.2%
CHLORAM	11	13.9%
LINEZOLID	9	11.4%
ERYTHRO	7	8.9%
NITROFURANTOIN	7	8.9%
CLOXACILLIN	5	6.3%
DOXYCYCLINE	5	6.3%
CEPHALEXIN	2	2.5%
CARBENECILLIN	2	2.5%
TETACYCLINE	2	2.5%
IMIPENAM	2	2.5%
CLINDAMYCINE	2	2.5%
NETILMICIN	1	1.3%
MECILLINUM	1	1.3%

Levofloxacin has shown to be resistant to klebsiella (35.4%), followed by pseudomonas (8.9%), Acinebacteria (5.1%), Staph Aureus (3.8%) and E. coli (2.5%). There is no significantly association between Levofloxacin and the micro-organisms, p = 0.923. Amikacin has also shown resistance to maximum microbe, Klebsiella (30.4%) and moderate resistant to other micro-organism such as; Acinetobacter (7.6%), E. coli (2.25%), pseudomonas (8.9%) and Staph Aureus (2.25%). There was significantly association between amikacin and the microbes, p=0.006. Cefuroxime has also shown similar result where it has shown resistance to Klebsiella

(49.4%), followed by pseudomonas (15.2%), Acinetobacter (11.4%), E.coli (5.1%) and Staph Aureus (1.3%) and is significantly associated, p=0.041. Multidrug ceftriaxone is also resistant to Klebsiella (31.8%) followed by pseudomonas (16.5%) and Acinetobacter (10.1%). Cefriaxone is also resistant to E. coli and Staph. Aureus; 5.1% and 1.3%, respectively. There isnot significant association, p=0.374. Cefixime is resistant to klebsiella (48.1%), followed by pseudomonas (13.9%), Acinetobacter (8.8%), E.coli (5.1%) and Staph Aureus (5.1%). There is no significantly association between cefixime and the micro-organism, p=0.628.

Other multidrug such as Ampicillin (p=0.005), vancomycin (p=0.000), linezolid (p=0.000), nitrofurantoin (p=0.000), cloxacillin (p=0.005) and mecillinum (p=0.02) were significantly associated with the micro-organisms. Table 5 shows in details.

In this study the result of prevalence of co-morbidities and antibiotic resistance among critically ill patient's shows that most of antibiotics resistant with co morbidities which is higher than sensitivity and very few antibiotics are intermediate with co-morbidities. Pearson Chi-Square Tests shows the association between antibiotics resistant and co-morbidities among critically ill patients. Significant association observed between COTRIM vs COPD (p=0.007), CHLORAM vs HTN and IHD, CIPRO vs DM, AMOXICLAV vs IHD, CEFIXIME vs CVD, AMIKACIN vs CVD and PIPERCILLIN vs CVD (Table 6).

This study identified that multidrug resistance has association with Specimen in some cases. Six antibiotics such as COTRIM, MECILLINUM, TETRACYCLINE, CEFOTAXIME, TIGECYCLINE and COLISTIN significantly associated with Specimen (Table 7).

Table 5: Antibiotic resistance and its association with microorganism (N=79)

ANTIBIOTICS	Microbes																		Total R	p-value
	Klebsiella(n=44)			Pseudomonas(n=13)			Acinetobacter(n=10)			Staph.aureus(n=6)			E.coli(n=4)			Enterococcus(n=2)				
	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R	S	I	R		
LEVOFLOXACIN	10 (12.7)	3 (3.8)	28 (35.4)	5 (6.3)	1 (1.3)	7 (8.9)	5 (6.3)	-	4 (5.1)	3 (3.8)	-	3 (3.8)	2 (2.5)	-	2 (2.5)	1 (1.3)	-	1 (1.3)	45 (56.9)	0.923
AMIKACIN	19 (24.1)	1 (1.3)	24 (30.4)	6 (7.6)	-	7 (8.9)	3 (3.8)	-	6 (7.6)	1 (1.3)	-	2 (2.5)	2 (2.5)	-	2 (2.5)	1 (1.3)	-	-	41 (51.9)	0.006
CEFUROXIME	3 (3.8)	1 (1.3)	39 (49.4)	1 (1.3)	-	12 (15.2)	-	-	9 (11.4)	-	-	3 (3.8)	-	-	4 (5.1)	-	-	1 (1.3)	68 (86.0)	0.041
CEFTRIAXONE	5 (6.3)	-	33 (31.8)	-	-	13 (16.5)	1 (1.3)	-	8 (10.1)	1 (1.3)	-	3 (3.8)	-	-	4 (5.1)	-	-	1 (1.3)	62 (78.5)	0.374
CEFIXIME	2 (2.5)	-	38 (48.1)	1 (1.3)	-	11 (13.9)	1 (1.3)	-	7 (8.9)	-	-	4 (5.1)	-	-	4 (5.1)	-	-	1 (1.3)	65 (82.3)	0.628
CIPRO	10 (12.7)	-	27(34.2)	5 (6.3)	-	7 (8.9)	4 (5.1)	-	3 (3.8)	4 (5.1)	-	2 (2.5)	1 (1.3)	-	3 (3.8)	-	-	2(2.5)	44 (55.7)	0.309
COTRIM	13 (16.5)	1 (1.3)	22 (27.8)	4(5.1)	-	9 (11.4)	4(5.1)	-	4 (5.1)	3 (3.8)	-	1 (1.3)	3 (3.8)	-	-	1 (1.3)	-	-	36 (45.6)	0.544
CEFTAZIDIME	1 (1.3)	-	33 (41.8)	-	-	12(15.2)	-	-	8 (10.1)	-	-	4 (5.1)	-	-	3 (3.8)	-	-	1 (1.3)	61 (77.2)	0.953
GENTA	8 (10.1)	-	26 (32.9)	2 (2.5)	-	7 (8.9)	-	-	9 (11.4)	-	-	5 (6.3)	1 (1.3)	-	2 (2.5)	2 (2.5)	-	-	49 (62.0)	0.091
MEROPENEM	10 (12.7)	1 (1.3)	2 (30.4)	2 (2.5)	1 (1.3)	7 (8.9)	2 (2.5)	-	4 (5.1)	3 (3.8)	-	2 (2.5)	1 (1.3)	-	1 (1.3)	1 (1.3)	-	-	16 (20.3)	0.827
AMPICILLIN	-	-	34(43.0)	2 (2.5)	-	9 (11.4)	-	-	4 (5.1)	1 (1.3)	-	2 (2.5)	1 (1.3)	-	3 (3.8)	1 (1.3)	-	1 (1.3)	35 (44.3)	0.005
TIGECYCLINE	16 (20.3)	4 (5.1)	7 (8.9)	3 (3.8)	-	6 (7.6)	3 (3.8)	1 (1.3)	3 (3.8)	1 (1.3)	-	1 (1.3)	2 (2.5)	-	1 (1.3)	2 (2.5)	-	-	18 (22.8)	0.546
COLISTIN	13 (16.5)	3 (3.8)	3 (3.8)	3 (3.8)	1 (1.3)	2 (2.5)	3 (3.8)	-	3 (3.8)	1 (1.3)	-	1 (1.3)	2 (2.5)	-	-	1 (1.3)	-	-	9 (11.4)	0.906
CEFOTAXIME	-	-	17 (21.5)	1 (1.3)	-	7 (8.9)	1 (1.3)	-	7 (8.9)	-	-	2 (2.5)	-	-	-	-	-	-	33 (41.8)	0.114
CEFEPIME	-	-	20 (25.3)	-	-	4 (5.1)	-	-	4 (5.1)	-	-	1 (1.3)	-	-	-	-	-	-	29 (36.7)	0.286
AZITHRO	2(2.5)	-	12 (15.2)	1 (1.3)	-	2 (2.5)	-	-	2 (2.5)	1 (1.3)	-	4 (5.1)	-	-	1 (1.3)	-	-	1 (1.3)	22 (27.8)	0.440
AMOXICLAV	-	-	13 (16.5)	1 (1.3)	-	4 (5.1)	-	-	3 (3.8)	-	-	1 (1.3)	-	-	-	-	-	-	21 (26.6)	0.615
PIPERCILLIN	-	1 (1.3)	5 (6.3)	1 (1.3)	-	4 (5.1)	1 (1.3)	-	2 (2.5)	-	-	-	-	-	1 (1.3)	-	-	-	12 (15.2)	0.739
PENICILLIN	-	-	7 (8.9)	-	-	2 (2.5)	-	-	3 (3.8)	-	-	1 (1.3)	-	-	1 (1.3)	-	-	2 (2.5)	10 (12.6)	0.099
VANCOMYCIN	-	-	3(3.8)			2 (2.5)	-	-	1 (1.3)	4 (5.1)	-	2 (2.5)	-	-	-	1 (1.3)	-	-	8 (10.1)	0.000
TEICOPLANIN	1 (1.3)	-	3 (3.8)	-	-	2 (2.5)	-	-	3 (3.8)	-	-	3 (3.8)	-	-	-	-	-	-	11 (13.9)	0.273
CHLORAM	1 (1.3)	0	7 (8.9)	-	-	-	-	-	1(13)	-	-	2 (2.5)	-	-	-	-	-	-	10 (12.6)	0.776
LINEZOLID	-	-	1(1.3)	-	-	1 (1.3)	-	-	2 (2.5)	3 (3.8)	-	1 (1.3)	-	-	-	1 (1.3)	-	-	5 (6.3)	0.000
ERYTHRO	-	-	4 (5.1)	-	-	-	-	-	2 (2.5)	-	-	1 (1.3)	-	-	-	-	-	-	7 (8.9)	0.573
NITROFURANTOIN	-	-	3 (3.8)	-	-	-	-	-	1 (1.3)	-	-	-	1 (1.3)	-	1 (1.3)	1 (1.3)	-	-	5 (6.3)	0.000
CLOXACILLIN	-	-	1 (1.3)	-	-	-	-	-	1 (1.3)	1(1.3)	-	2 (2.5)	-	-	-	-	-	-	4 (5.0)	0.005
DOXYCYCLINE	-	-	2(2.5)	-	-	2 (2.5)	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	5 (6.3)	0.521
CEPHALEXIN	-	-	1 (1.3)	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	-	-	-	2 (2.5)	0.712
CARBENECILLIN	-	-	1 (1.3)	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	-	-	-	2 (2.5)	0.712
TETRACYCLINE	1 (1.3)	-	1 (1.3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1 (1.3)	0.998
IMIPENAM	-	-	1 (1.3)	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	-	-	-	2 (2.5)	0.712
CLINDAMYCINE	-	-	1 (1.3)	-	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	-	-	-	0.218
NETILMICIN	-	-	-	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	-	-	-	1 (1.3)	0.221
MECILLINUM	-	-	-	-	-	-	-	-	-	-	-	-	1 (1.3)	-	-	-	-	-	-	0.002

Note: R=Resistance; S=Sensitive; I= Intermediate Note: $p \leq 0.05$ (significant)

Table 6: Association of Multidrug resistance with Co-morbidities

Multidrug	Co-morbidities (p value)				
	DM	HTN	IHD	COPD	CVD
COTRIM	0.413	0.538	0.714	0.007	0.694
CHLORAM	0.251	0.026	0.001	-	-
CIPRO	0.027	0.612	0.710	0.457	0.942
AMOXICLAV	0.219	0.176	0.030	0.76	-
CEFIXIME	0.881	0.881	0.871	0.565	0.037
AMIKACIN	0.195	0.479	0.230	0.824	0.00
PIPERCILLIN	0.006	0.482	0.875	0.749	0.031

Discussions

In this research, in Gram negative 55.7% of the patients included Klebsiella bacteria, 16.5% Pseudomonas bacteria, 12.7% Acinetobacter bacteria, 5.1% E. coli bacteria, and 2.5% Enterococcus bacteria in Gram positive 7.60% were Staph Aureus bacteria. Total 73 (92.40%) were Gram negative and 6 (7.60%) were gram positive. Gram-negative bacteria were predominantly resistant which is similar to other study.

According to a prior research, an article reveals that gram-negative bacteria cause 81.97 percent more clinical ailments than gram-positive bacteria cause 18.03 percent.[2] Whereas other study done among emergency admitted patients reported that, on the basis of microbial culture, the most common were Escherichia coli (64 patients, 12%), Staphylococcus aureus (27 patients, 5%), Streptococcus pneumoniae (23 patients, 4%), Klebsiella pneumoniae (12 Patients, 2.2%), Haemophilus influenzae (9 patients, 1.7%) and Pseudomonas aeruginosa (9 patients, 1.7%).[7]

In this study sample collection from, maximum of 64.6% of samples were collected from tracheal and 1.3% of samples were collected from pus culture. On the other hand, only tracheal (1) and urine (3) samples yielded E. coli. In addition to Acinetobacter, it was discovered in seven blood and three tracheal samples. Similar results for the bacterium Enterococcus. In addition, Klebsiella and Pseudomonas were discovered in the majority of patient samples. There is a substantial connection between the sample and the microorganism.

István Vincze et.al in their study "Antibiotic Pharmacokinetics, Molecular Biomarkers and Clinical Status in Critically Ill Adults" Blood and tracheal secretion was collected from subjects.[18]

In one study, 27,069 clinical samples were examined, including 6796 blood samples (25.1%), 16173 urine samples (59.7%), 1961 respiratory secretions (7.2%), and 2139 pus and wound swab samples (7.9%). Growth was observed in
27.3 percent of the total sample. 28% of the urine, 8% of the blood, 66% of the pus and wound swab, and 42% of the lung sample were culture positive.[3]

In our study, levofloxacin antibiotic used in 94.9% cases followed by amikacin used in 93.7% cases, cefuroxime used in 92.4% cases, cefixime and ciprofloxacin used in 86.1% cases.[10]

The antibiotic vancomycin is used to treat a variety of bacterial illnesses. Methicillin-resistant Staphylococcus aureus skin infections, bloodstream infections, endocarditis, bone and joint infections, and meningitis are treated intravenously with this antibiotic.[3,4]

According to study vancomycin-resistant enterococci (VRE) are linked with significant multidrug-resistant infections and chronic colonization, and are of both medical and public health significance. Enterococci are opportunistic environmental dwellers with an exceptional ability for adaptive evolution and transmission of antimicrobial-resistant determinants.[5]

In our study among the 34 antibiotics Klebsiella had highest resistance against 32 (94.11%) antibiotics. This result is slightly higher than other study as this study conducted among critically ill patients in ICU. In the study of Aminul et.al (2021) shows that the majority of *Klebsiella*

pneumonia were multi-drug resistant (82%). The bacteria were found resistant to most β-lactam antibiotics, aminoglycosides, ciprofloxacin, cotrimoxazole, carbapenem, piperacillin, and tazobactam. However, only about 0.7% colistin resistance was observed.[19]

In one Bangladeshi study, which was based on critical patients it was reported that, the frequency of third generation cephalosporin resistant E. coli, Klebsiella and imipenem resistant Pseudomonas and Acinetobacter were >50%. Acinetobacter was remarkably resistant to most antibiotics including imipenem (>70% resistant), but most of the members of the Enterobacteriacae group showed maximum sensitivity to imipenem (50%-94%).[12]

Whereas other study based on ICU reported that, a study conducted in the same ICU reported 82% of Pseudomonas as resistant to third generation cephalosporins.[13]

Where according to one Bangladeshi study, Ceftriaxone used in 98% cases, Ceftazidime used in 95.2% cases, amikacine used in 60% cases. Through in our cases vancomycin used in 16.5% cases. Moreover in other study vancomycin used in 55% cases.[11]

Cephalexin is used to treat a variety of bacterial diseases, including pneumonia and other respiratory tract infections, as well as infections of the bone, skin, ears, genital, and urinary tract. Cephalexin belongs to the family of medicines known as cephalosporins. It functions by destroying microorganisms.[6] Antibiotics like cephalexin are ineffective against colds, influenza, and other viral diseases.

Moreover, one study reported that, in their study patients who admitted on CCU, most frequently prescribed antibiotics were cefotaxime (22.3%), levofloxacin (19%) and ceftazidime(10.8%).[14]

Where according to other study it was reported that 30.1% antibiotics cases were vancomycin, followed by 26.6% were ceftazidime, 25.9% ciprofloxacin, 25.2%gentamicin, 23.8% amikacin. Whereas according to study patients without sepsis/prophylaxis got other antibiotics such as ceftriaxone; 20.2%, cefazolin;12.6%, ceftazidime and cefotaxime; 10.9%, cefoxitin; 8.4%.[15]

Besides that, according to other study, the most commonly used antibiotic for both empirical and adjusted therapy was amoxicillin/clavulanate. In addition, broad-spectrum antibiotics (cefepime, imipenem, meropenem, piperacillin/tazobactam) or vancomycin were initially administered to 95 patients (17.6%).[15]

Using antibiotics when they are not necessary raises your chance of developing a resistant illness in the future. In this study, Chephalexin's resistance to Klebsiella (2.3 %) and Acinetobacter has been shown (10%). Chephalexin exhibits no significant bacterial resistance ($p > 0.05$). Another study reported that, The incidence of urinary tract infections in pediatric patients was determined to be 19.68%, with E. coli (68.5%) being the most prevalent pathogen implicated. 64.9% of 739 E. coli isolates were multidrug resistant (MDR), and 5% were severely drug resistant (XDR). ESBL was found in 288 (38.9%) of the E. coli isolates.[7]

A number of bacterial illnesses, including bronchitis, pneumonia, and sexually transmitted diseases (STDs), as well as infections of the ears, lungs, sinuses, skin, throat, and reproductive organs, may be treated with azithromycin. A form of lung infection that often affects patients with human immunodeficiency virus (HIV), disseminated Mycobacterium avium complex (MAC) infection, may also be treated with azithromycin, and the antibiotic can also be used to prevent MAC infections. The macrolide antibiotics are a kind of drug that includes azithromycin as one of its members. It achieves its effect by inhibiting the development of microorganisms.[8]

Besides in this study shows that, Azithromycin has been resistant to E. Coli (25%), Acinetobacter (20%), Enterococcus (50%), Klebsiella (27.3%), Pseudomonas (15.4%) and Satph A. (66.7%). Azithrodoes not show any significant resistance against bacteria ($p > 0.05$). Another study found that, Between October 2016 and July 2018, we screened 2,519 Salmonella Typhi and 506 Salmonella Paratyphi A isolates for azithromycin

resistance using disc diffusion.

Penicillins are a class of antibacterial medications that are effective against a broad spectrum of microorganisms. They were the first medications of this sort utilized by physicians. The discovery and production of penicillins have revolutionized medicine, since these antibiotics have saved millions of lives.[10] Occasionally, bacteria may create penicillinase, an enzyme that destroys penicillins. In a process known as conjugation, this capacity may spread across the bacterial population via a tiny ring of DNA. This is the bacterial counterpart of sexual reproduction, in which different organisms exchange new genetic information. Findings shows that, Penicillin has been resistant to Klebsiella (15.9%), Pseudomonas (15.4%), Staphylo. Aureus (16.7%), Acinetobacter (30%) and E.Coli (25%). Another study reported that, 105 samples (35.0%) were positive for S. pneumoniae, whereas 115 serotypes were idntified (ten specimens yielded two serotypes each). Overall, 78 of 115 (67.8 percent) pneumococci isolates were resistant to penicillin (PNSP). S. pneumoniae exhibited resistance levels of 82.6, 10.4, 6.0, 3.5, and 0% to trimethoprim–sulfamethoxazole, tetracycline, erythromycin, and chloramphenicol, respectively. Multidrug resistance was observed in 19 (16.5%) of the isolate.[12]

Certain bacterial illnesses, such as meningitis (infection of the membranes that protect the brain and spinal cord) and infections of the throat, sinuses, lungs, reproductive organs, urinary system, and gastrointestinal tract, are treated with ampicillin. Ampicillin belongs to the family of drugs known as penicillins.

It functions by destroying microorganisms.[13] Antibiotics like ampicillin are ineffective against colds, influenza, and other viral diseases. Taking antibiotics when they are not required raises your chance of developing a resistant illness in the future. Another study reported that, Disk diffusion revealed the greatest levels of antibiotic resistance in the penicillin antibiotic group (e.g., 67 percent for ampicillin) and macrolides (e.g., 46 percent for erythromycin), although quinolones were effective against all isolates. 9 (56 percent) of the 16 ampicillin-resistant isolates were lactamase positive. None of the-lactamase- negative isolates met the phenotypic BLNAR categorization requirements of an ampicillin minimum inhibitory concentration of >1 g/mL, and only one exhibited an ftsI mutation. Multiple locus sequence typing indicated frequent

H. influenzae strain shift, which was related with alterations in the antibiotic sensitivity pattern.[14] Besides, in our study finds that, Ampicillin has been resistant to E. Coli (75%), Acinetobacter (40%), Enterococcus (50%), Klebsiella (77.3%), Pseudomonas (69.2%) and Satph A. (33.3%). Ampicillin shows significant resistance against bacteria ($p < 0.05$). Through in our case penicillin used in only 19% cases.

In this study significant association observed between antibiotics and co-morbidities. COTRIM vs COPD, CHLORAM vs HTN and IHD, CIPRO vs DM, and HYPOTHY, AMOXICLAV vs IHD, CEFIXIME vs CVD, AMIKACIN vs CVD and PIPERCILLIN vs CVD are significantly associated. CEFEPIME had resistance with (30.8%) patients with hypertension (HTN) and PENICILLIN with (13.2%) patients with Diabetes Mallets (DM). This is slightly higher than other study because this study conducted on critically ill patients in ICU.

S. Cheng et al (2016) in their study showed that Multi-drug resistant tuberculosis (MDRTB) patients with comorbidities have poorer treatment outcomes. There were higher percentages of MDRTB patients presenting with hypertension, 23.1% (N=6), and cancer, 15.4% (N=4). Other comorbidities included diabetes mellitus, 11.5% (N=3), hepatitis B, 7.7% (N=2), anemia, 7.7% (N=2), and miscellaneous-grouped diseases, 38.5% (N=10). Out of the 13 patients with comorbidities, hypertension counts 46.2% (N=6).[17] The overall finding of the study almost similar to previous studies globally, in Asia, in India or in Bangladesh.

Conclusion

The primary scenario of rational anti-microbial medication for critically sick patients is presented in this research. There was a catastrophic scenario due to the gradual rise in the number of E. coli and Klebsiella organisms, as well as their resistance to popular antibiotics like ampicillin, ciprofloxacin, and cefuroxime. This condition was worrying and severe. Despite having a deficient healthcare system at present, Bangladesh has evidently been working to eliminate the improper use of antimicrobial drugs. Antibiotic effectiveness may be preserved by correct administration of antibiotics, containment of resistant bacteria that are spreading, continued monitoring and study of multi-drug resistant bacteria and the use of containment measures.

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