

Antibiotic Resistance Pattern in First Year of Novel COVID-19 Era in a Metropolitan City in Bangladesh: A Retrospective Analysis

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Abstract

Background: Often bacterial infections cause illness and death all over the world. Selective pressure and increasing drug resistance are reportedly associated with the indiscriminate use of antibiotics to treat such illnesses. In this study our main goal is to evaluate the antibiotic resistance pattern in first year of novel COVID-19 era in a metropolitan city in Bangladesh.

Materials and methods: This retrospective study was carried out at various pathology laboratories of Chattogram metropolitan city from March, 2020 to March, 2021. Total 5557 data were collected for this study.

Results: During the study, Escherichia coli found to be most commonly isolated bacteria 32.8%. S. Typhi highly resistant to Azithromycin; 54%. Significantly high resistance rates observed of E. coli to azithromycin (68.5%). P. aeruginosa was highly resistant to Vancomycin (78%). Significantly high resistance rates of Klebsiella pneumoniae to Teicoplanin (75%). Staphylococcus was highly resistant to Vancomycin (78.1%). Enterococcus faecalis was highly resistant to Azithromycin (100%). Among the nine antibiotic ciprofloxacin created highest total resistance (31.86%).

Conclusion: This study shows the main scenario of bacterial pathogens in different human specimen and their antibiotic resistance pattern during the COVID-19 epidemic. Gradual increase in number of E .coli and klebsiella organisms and their resistance to common antibiotics such as ampicillin, ciprofloxacin, cefuroxime were concerning issue in COVID-19 pandemic situation.

Key words: Antibiotic resistant pattern; COVID-19; Gram negative and positive bacteria.

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Introduction

Antibiotics fight against infections. Antimicrobial Resistance (AMR) a global health issue, results from antibiotic overuse. One solution is to optimize antibiotic use by using the right antibiotic at the right dose, for the right duration, and in a way that minimizes side effects and AMR. Antimicrobial stewardship programs exhibit these.¹ Since the COVID-19 pandemic began, antibiotic use for COVID-19 patients has increased, raising concerns about AMR. 2 The SARS-CoV-2 pandemic in 2020 disrupted the health care system (SARS-COV-2).²⁻³

In January 2020, a China adult contagionist unit found that 71% of COVID-19 hospitalized patients received antibiotics despite only 1% bacterial co-infection rate.⁴⁻⁵ Antimicrobial medication was a major treatment option in China and the UK, regardless of secondary bacterial co-infection. During covid era, Bangladesh followed the same trend. Since Bangladesh's first case on 8 March 2020, antibiotic overuse has raised much concerns.⁶⁻⁷ Moreover, antimicrobials can be purchased without a prescription in Bangladesh, even in remote areas.⁸

Bacterial resistance is linked to antibiotic use.⁹⁻¹² And, antibiotics are assumed to be used unrestrictedly during pandemics. We have not yet studied antibiotic resistance patterns during the pandemic period. This study examines antibiotic resistance in the first year of novel COVID-19 in a Bangladeshi metropolis. Objective of the study is to assess the antibiotic resistance pattern in first year of novel covid19 era in a metropolitan city in Bangladesh.

Materials and methods

This retrospective observational study was conducted at different laboratories of Chattogram metropolitan city from March, 2020 to March, 2021. Inclusion criterion was all accessible lab reports showing positive results meaning bacteriological proven infection against microorganisms.

Exclusion criterion was duplicate samples with differing sensitivities. As there is no specific information of the clients exposed, written informed consent was not necessary. After getting approval from Ethical and Review Committee of Chittagong Medical College (CMC) and proper permission from the private laboratory authorities, 5557 lab reports relevant to the study were collected from different laboratories and data from these reports are put down in Case Record Form (CRF) by the research associates and research assistant. The CRF included A. Client's age and sex from the record, B. Specimen with growth, C. Name (s) of the bacteria, D. Drug sensitivity profile.

Once data collection was completed, data were compiled and tabulated according to key variables. The analysis of various variables was performed using the standard statistical tool SPSS 23 and calculations were performed using scientific calculators and the MS-excel application on a computer. This study employs both descriptive and differential analysis. Correlation and the chi square test were used to determine the strength of the dependent variables.

Results

In Table-I shows age distribution of the study group where majority of the cases belong to 20-29 years age group, 21.1% followed by 16.2% cases belong to 30-39 years age group, 12.8% belong to 0-9 years age group, 11.9% cases belong to 50-59 years age group, 11.6% cases belong to 60-69 years age group, 7.1% cases belong to 10-19 years age group. Mean age of the study group was 36.98±21.74.

Table I Age distribution of the study group

Age group	Frequency	Percent	Mean	Std.
0 to 9 years	712	12.8	36.98	21.74
10 to 19 years	393	7.1		
20 to 29 years	1175	21.1		
30 to 39 years	901	16.2		
40 to 49 years	609	11.0		
50 to 59 years	662	11.9		
60 to 69 years	642	11.6		
70 to 79 years	344	6.2		
80 to 89 years	91	1.6		
90 and >90 years	29	.5		

In Figure-1 shows gender distribution of the study group where female cases were higher, 62% than male, 38%.

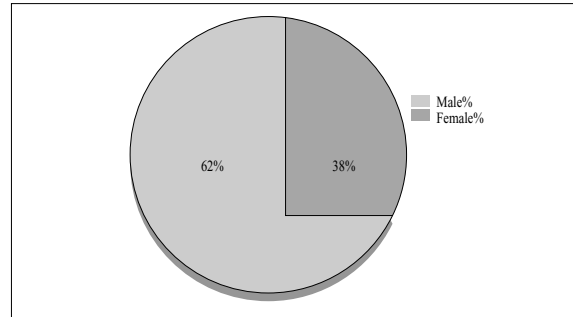


Figure 1 Gender distribution of the study group

In Table II shows distribution of isolated bacteria where Escherichia coli was most commonly found; 32.8% followed by Klebsiella, 10.9%, Staphylococcus, 9.3%, Pseudomonas, 3.4%, Pseudomonas aeruginosa, 2%, klebsiella pneumoniae, 1.1% Enterococcus faecalis, 1.4% and 5.6% others bacteria were commonly isolated.

Table II Distribution of isolated bacteria

Bacteria	n	%
Escherichia coli	1821	32.8
N/A	1809	32.6
Klebsiella	603	10.9
Staphylococcus	515	9.3
Pseudomonas	187	3.4
Pseudomonas aeruginosa	110	2
Enterococcus faecalis	78	1.4
klebsiella pneumoniae	60	1.1
Salamonellaser. Typhi	44	0.8
Others	328	5.6

Figure 2 shows distribution of the patients according to source or specimen of bacteria where 68% specimen were collected from patients urine followed by 8.20% collected from blood, throat swab, 5.8% sputum, 5.80%, wound swab 6.40%.

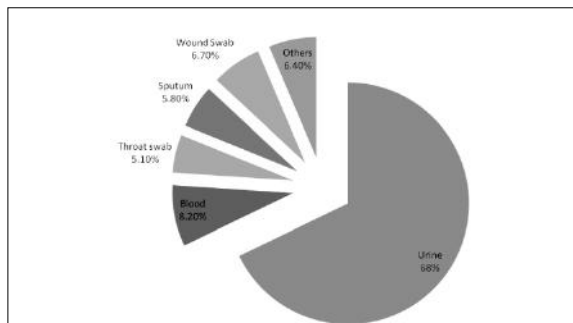


Figure 2 Distribution of the patients according to source or specimen of bacteria

Table III shows the distribution of some of the common bacteria isolated. Overall the bacteria found were high among female in contrast to male. Both E. coli and Klebsiella were comparatively high among female; 38% and 11.8%, than male; 24.5% and 9.8%, respectively. Enterococcus faecalis is slightly high in female, 1.4% than male, 1.2%. However, other bacteria isolated were higher in male than female; Staphylococcus, 7.6%, 5.4%, Staphylococcus aureus, 4.4%, 2.4%, Pseudomonas aeruginosa, 3.2%, 0.6% and Klebsiella pneumoniae, 1.7%, 0.6%, respectively. Ciprofloxacin created highest (31.86%) resistance with selected five micro-organisms. The following Table III shows antibiotic resistance pattern among common isolated bacteria.

Table III Distribution of common bacteria by gender

Gender	Escherichia coli, %	Klebsiella pneumoniae, %	Staphylococcus aureus, %	Staphylococcus aeruginosa, %	Pseudomonas pneumoniae, %	Klebsiella faecalis, %	Enterococcus faecalis, %
Male	24.5	9.8	7.6	4.4	3.2	1.7	1.2
Female	38	11.8	5.4	2.4	1	0.6	1.4

Table IV shows there is significantly high resistance rates E. coli to azithromycin (68.5%), Ciprofloxacin (39.80%), Teicoplanin (40%), Vancomycin (28%), Amoxicillin (66.7%). P. aeruginosa was highly resistant to Vancomycin (78%), Amikacin (32%), Ciprofloxacin (58%), Teicoplanin (54.2%), Tigecycline (39.3%). Significantly high resistance rates of Klebsiella pneumoniae to Teicoplanin (75%), Vancomycin (73%), Linezolid (66%) and Azithromycin (53.8%). Staphylococcus was highly resistant to Vancomycin (78.1%), Teicoplanin (75%), Azithromycin (54%) and Linezolid (66%). Enterococcus faecalis was highly resistant to Azithromycin (100%), Vancomycin (84%), Tigecycline (57.5%), Ciprofloxacin (52.5%). The table also explores that S. Typhi was highly resistant to Azithromycin, 100%, vancomycin 100%, tigecycline; 66% and Ciprofloxacin, 48%. Among the nine antibiotic ciprofloxacin created highest total resistance (31.86%) (Figure 3).

Table IV Distribution of antibiotic sensitivity, intermediate sensitivity and resistance against micro-organism

Antibiotic	Microbe					
	Escherichia coli	Klebsiella pneumoniae	Staphylococcus aeruginosa	Pseudomonas faecalis	Enterococcus typhi	Salmonella
Sensitivity						
Amikacin	75.80%	80.70%	77.90%	66.70%	66.70%	71.10%
Azithromycin	24%	32.8	31.20%	0%	0%	0%
Ciprofloxacin	54.30%	57.50%	58%	39%	45%	48.40%
Teicoplanin	55.20%	22.7	22.70%	40%	30%	50%
Tigecycline	74.80%	68%	66.6	55.70%	37%	31.40%
Vancomycin	60%	21%	20%	20%	16%	0%
Linezolid	77%	31%	32%	80%	60%	100%
Amoxicillin	33.30%	0%	0%	0%	0%	0%
Tazobactam	91%	91%	90%	0%	0%	0%
Intermediate Sensitive						
Amikacin	3.30%	2.60%	3.09%	1.30%	2.20%	0%
Azithromycin	7.5	13.40%	14.80%	0%	0%	0%
Ciprofloxacin	5.90%	2.50%	2%	3%	2.50%	3.20%
Teicoplanin	4.80%	2.30%	2.30%	5.80%	20%	50%
Tigecycline	3.60%	7.60%	8.30%	5%	5.50%	3%
Vancomycin	12%	6%	1.90%	2%	0%	0%
Linezolid	2%	3%	2%	5%	20%	0%
Amoxicillin	0%	0%	0%	0%	0%	0%
Tazobactam	0%	0%	0%	0%	0%	0%
Resistance						
Amikacin	20.90%	16.40%	19.01%	32%	31.10%	28.90%
Azithromycin	68.50%	53.80%	54%	100%	100%	100%
Ciprofloxacin	39.80%	40%	40%	58%	52.50%	48.40%
Teicoplanin	40%	75%	75%	54.20%	50%	0%
Tigecycline	21.60%	24.40%	25.10%	39.30%	57.50%	65.60%
Vancomycin	28%	73%	78.10%	78%	84%	100%
Linezolid	21%	66%	66%	15%	20%	9%
Amoxicillin	66.70%	0%	0%	0%	0%	0%
Tazobactam	9%	9%	10%	0%	0%	0%

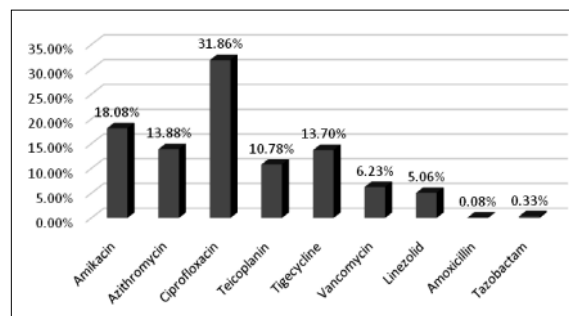


Figure 3 Total antibiotic resistance against micro-organism (n=2765)

Discussion

One study reported that, E. coli strains showed the highest antimicrobial sensitivity to amikacin (94.94%) and ceftazidime (93.67%). E. coli is the most prevalent bacterial pathogen that causes severe illnesses in humans, such as blood stream

infections. The spread of *E. coli* bloodstream infections is complicated, yet the great majority of *E. coli* bloodstream infections begin in the community.¹³ In our study, significantly high resistance rates of *E. coli* to azithromycin (68.5%), Ciprofloxacin (39.8%) and Amoxicillin (66.7%) were documented.

Similar results found in another study where amikacin displayed outstanding action (93.0 % - 94.7 % susceptible) against *Escherichia coli*, including Extended-Spectrum Beta-Lactamase (ESBL)-producing isolates (45.7 %), comparable to tigecycline, piperacillin/tazobactam, and carbapenems.¹⁴ On the other hand, significantly high degree of sensitivity rates to nitrofurantoin (96.4%), norfloxacin (90.6%), gentamicin (79.6%) and ciprofloxacin were detected in another study.¹⁵ Another study also showed that *E. coli* resistance was highest in amoxicillin (85%), followed by cefuroxime (65%) and ceftriaxone (60%).¹⁶

In our study *P. aeruginosa* was highly resistant to Vancomycin, 78%, Amikacin, 32%, Ciprofloxacin, 58%. Other report found the overall drug resistance among 121 strains of *P. aeruginosa* was low to moderate to commonly used anti-pseudomonal drugs (4.9% to 30.6%). Significantly less resistance was exhibited by piperacillin-tazobactam (4.9%) and meropenem showed significantly high resistance (30.6%) as compared to other antibiotics, followed by ticarcillin (22.3%) and imipenem (19%), irrespective of the site of infection. The antibiotics with <10% resistance were cefepime (8.3%), amikacin (7.4%) and piperacillin-tazobactam, which showed lowest resistance (4.9%). *E. faecalis* strains isolated in our study shown to have high resistant to Tetracycline 73.1%, Vancomycin 21.8%, Ciprofloxacin, 50%, Levofloxacin 44.7%. Whereas in other study it is found that the *E. faecalis* strains were resistant to penicillin (9.7%), ampicillin (0%), ampicillin/sulbactam (0%), nitrofurantoin (0%), imipenem (0%), vancomycin (0%), teicoplanin (0%), quinupristin/dalfopristin (100%), ciprofloxacin (9.7%), levofloxacin (4.8%), norfloxacin (26.8%), erythromycin (95%), gentamicin (46.3%), tetracycline (97.5%), and trimethoprim/sulfamethoxazole (31.5%), respectively.¹⁶

We found that, again *E. coli* is highest to be isolated 32.8% followed by *Klebsiella* (10.9%), *Staphylococcus* (6.1%), *Staphylococci* (3.4%), *Staphylococcus aureus* (3.2%), *Pseudomonas aeruginosa* (2%), *Klebsiella* (1.1%) and *Enterococcus faecalis* (1.4%). In a previous study, prior to Covid pandemic, *E. coli* has been the most frequently reported (53%), followed by *P. aeruginosa* (23%), then *K. pneumonia* (15%) and *Proteus spp* (9%). Another study observed a significant increase in antibiotic resistance (>40%) to the following antibiotics: cefazolin, amoxicillin-clavulanic acid, cefuroxime, cefepime, ceftriaxone and ceftazidime. Unfortunately, the majority of these antibiotics were commonly prescribed for the treatment of *K. pneumoniae* infections.⁴ Whereas in our study *Klebsiella pneumoniae* to Teicoplanin (75%), Vancomycin (73%), Linezolid (66%), and Azithromycin (53.8%). One research showed that the prevalence rate of drug-resistance in *K. pneumoniae* were highest in cefotaxime (79.2%) followed by ceftazidime (75.7%), aztreonam (73.3%) and amikacin (40.8%).¹⁷⁻¹⁸

In our study *Staphylococcus* was highly resistant to Vancomycin (78.10%), Teicoplanin (75%), Azithromycin (54%) and Linezolid (66%). Although 54% of patients in intensive care units (ICUs) in 88 countries had suspected or confirmed bacterial co-infection, 70% of them had received at least one antibiotic therapy or antimicrobial prophylaxis, according to a recent research.¹⁹ In the study of Selim et al. shows that from 292 urine samples, 103 bacterial strains (35.3%) were identified as *S. aureus*. Various antibiotics were used to test the isolates' antibacterial resistance profiles. Antibiotic resistance to erythromycin was found in most bacterial isolates, whereas tobramycin antibiotic sensitivity was found in most of them. Vancomycin resistance was found in 23 of all *S. aureus* isolates in this study. Analysis for β -lactamase found that 71% of *S. aureus* isolates were positive in all isolates. From 292 urine samples, 103 bacterial strains (35.3%) were identified as *S. aureus*.^{19,20}

In our study *Salmonella typhi* was highly resistant to Azithromycin (100%). Similar result observed in MasabUmair and Shajee Ahmad Siddiqui study in Pakistan where *Salmonella typhi* was highly resistant to Azithromycin (63.4%).²¹

Limitations

A limitation of this study is that presence of plentiful missing data in the information sheet. During the study we didn't calculate statistical value of the changing trends of all microbes, couldn't attempt to investigate underlying disease condition of patients and couldn't correlate with COVID patients.

Conclusion

After the COVID-19 pandemic, AMR will continue to pose a worldwide concern. The paper shows the main scenario of rational anti-microbial prescription during the COVID-19 epidemic. Gradual increase in number of *E. coli* and *Klebsiella* organisms and their resistance to common antibiotics such as Ampicillin, ciprofloxacin, cefuroxime were concerning issue in COVID-19 pandemic situation.

Recommendations

Bangladesh has obviously been trying to prevent misuse of antimicrobial medication with a weak health infrastructure at the moment. Proper use of antibiotics, containment of resistant spreading bacteria and ongoing monitoring and research of multi-drug resistant bacteria will help preserve antibiotic efficacy.

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Contribution of authors

MHA-Conception, design, data collection, data analysis, manuscript writing & final approval.

RA-Data collection, data compilation, manuscript writing & final approval.

TT-Data collection, interpretation of data, critical revision & final approval.

EEU-Interpretation of data, critical revision & final approval.

AS-Study design, manuscript writing & final approval.

Disclosure

All the authors declared no conflict of interest.

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