Antimicrobial Resistance Pattern in Different Age Groups- A Retrospective Study

By

Md. Anwar Ibrahim
20146091

A thesis submitted to the Department of Pharmacy in partial fulfillment of the

requirements for the degree of Bachelor of Pharmacy

School of Pharmacy

Brac University
2024

Declaration

It is hereby declared that

1. The project submitted is my own original work while completing degree at Brac University.
2. The project does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The project does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

Md. Anwar Ibrahim
20146091

Approval

The project titled "Antimicrobial Resistance Pattern in Different Age Groups - A Retrospective Study" submitted by Md. Anwar Ibrahim (20146091) of Spring, 2020 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy on 02-05-2024.

Examining Committee:

Supervised By:

Mushtahsin Ferdousi
Lecturer
School of Pharmacy
Brac University

Approved By:

Program Director:

Professor Dr. Hasina Yasmin
Program Director and Assistant Dean
School of Pharmacy
Brac University

Dean:

Professor Dr. Eva Rahman Kabir
Dean
School of Pharmacy
Brac University

Ethics Statement

There were no trials involving humans or animals in this study.

Abstract

According to WHO, antibiotic resistance has emerged as a serious public health risk in the 21st century. To highlight the situation of antibiotic resistance in Dhaka city, Bangladesh, a retrospective study was conducted using 100 isolates from the Institute of Child and Mother Health (ICMH) Hospital for six months. The isolates obtained from patients' blood and urine involved four bacterial species. The data was stratified according to age of the patient and antibiotic susceptibility and the distribution of pathogens and their resistant pattern was determined. *E.coli* was found to be the most prevalent pathogen responsible for antibiotic resistance. Amoxyclav showed greater resistance in adult patients compared to children. Erythromycin has shown significant resistance in both child and adult patients towards three pathogenic species. Irrational use of antibiotics and lack of proper knowledge and awareness greatly contribute to increasing antimicrobial resistance. It is high time awareness is made and necessary steps should be taken before antibiotic resistance becomes incurable.

Keywords: Antibiotic resistance; Resistant pattern; Amoxyclav; Erythromycin; *E.coli*.

Dedication

Dedicated to my parents, whose unwavering faith, devotion, guidance, and sacrifices made it possible for me and without it I would not be where I am today.

Acknowledgement

At first, I want to express my gratitude to Almighty Allah. Then, I would like to express my gratitude to my supervisor, Mushtahsin Ferdousi, Lecturer, School of Pharmacy, Brac University, for her constant assistance, guidance, support and patience during the entire research process. Her encouraging words and perceptive feedback have greatly influenced the development of my thesis.

In addition, I'm grateful to Dr. Eva Rahman Kabir, the honorable Dean and Chairperson of the school of pharmacy at Brac University, for her involvement and assistance during the study. I'm also grateful to Dr. Hasina Yasmin, the Deputy Chairperson, and Namara Marium Chowdhury, the Program Coordinator for their guidance. Furthermore, I am grateful to all faculty members of the School of Pharmacy at Brac University, for their valuable assistance and guidance.

I'd like to thank all of the lab officers and staff members of school of pharmacy, Brac University, who helped me significantly during the study by offering continuous guidance and assistance. I'd like to express my appreciation to all of the participants who kindly offered their valuable time and cooperation, adding to the overall quality of this study. Finally, my greatest gratitude goes out to my family and friends for their constant support and understanding throughout this journey.

Table of Contents

List of Tables

.

List of Figures

List of Acronyms

WHO	World Health Organization
PK	Pharmacokinetics
PD	Pharmacodynamics
S. Typhi	*Salmonella Typhi*
GLASS	Global Antimicrobial Resistance and Use Surveillance System
DNA	Deoxyribonucleic acid
RNA	Ribonucleic Acid
E.Coli	*Escherichia coli*
AMR	Antimicrobial Resistance

Chapter 1

Introduction

1.1 Antibiotics

An antibiotic is a chemical substance that is obtained from a living microorganism and that is detrimental to other disease-causing microorganisms, such as bacteria. Soil microorganisms are usually responsible for producing antibiotics. Fungi and bacteria are examples of microorganisms that possess the ability to produce antibiotics and that are helpful in treating or preventing illness. In 1941, discovery of penicillin marked the global introduction of antibiotics. Since then, they've improved the treatment of bacterial infections in people and animals. However, they don't work against viruses (The Editors of Encyclopaedia Britannica, 2024).

1.2 History of discovering antibiotics

In 1928, Alexander Fleming, a Scottish bacteriologist, discovered that colonies of bacteria growing on a culture plate had been affected and contaminated by a mold, ***Penicillium notatum***. After ten years, British scientist Ernst Chain, Australian pathologist Howard Florey, and others identified the active element, penicillin, and demonstrated its exceptional efficacy against a variety of dangerous infectious diseases caused by bacteria. Toward the end of the 1950s, scientists experimented with introducing various chemical groups to the core of the penicillin molecule to develop semisynthetic versions. As a result, a wide spectrum of penicillins was accessible to treat infectious diseases caused by many types of bacteria, including staphylococci, streptococci, pneumococci, gonococci, and syphilis spirochaetes. Notably, penicillin had no effect on the tubercle bacteria, also known as *Mycobacterium tuberculosis*. However, it was discovered that this bacterium was extremely susceptible to the antibiotic streptomycin, which was isolated from *Streptomyces griseus* in 1943. Streptomycin was shown to be highly efficient not only against tuberculosis but also against a wide range of other bacteria, such as the bacillus that causes typhoid fever. The compounds gramicidin and

tyrocidine, which are generated by *Bacillus* bacteria, were two further early discoveries. René Dubos, an American microbiologist, made the discovery in 1939. Although they were too toxic to be used internally, they were useful in treating outer layer infections. The mold *Cephalosporium acremonium* produces cephalosporins, which are related to penicillins and were identified by researchers in the 1950s. After ten years, Scientists identified another category of antibiotics called quinolones. Quinolones inhibit DNA replication, a key phase in bacterial reproduction, and have been shown to be effective in treating urinary tract infections, infectious diarrhea, and a variety of other infections affecting bones and white blood cells (The Editors of Encyclopedia Britannica, 2024).

1.3. Classification of antibiotics

Antibiotics work by either inhibiting bacterial cell division or altering a vital cellular process or function inside the bacterial cell. Based on how they affect bacteria in vitro, antimicrobial agents are usually divided into two primary groups. One is "bacteriostatic" and the other is "bactericidal". Bacteriostatic antibiotics "prevent the growth" of bacteria, whereas bactericidal antibiotics "kill" bacteria (Patel et al., 2023).

Moreover, antibiotics can also be classified according to their spectrum of activity—whether they are narrow-, broad-, or extended-spectrum. Narrow-spectrum antibiotics (such as penicillin) primarily affects gram-positive bacteria. Tetracyclines and chloramphenicol are broad-spectrum antibiotics that target both gram-positive and gram-negative bacteria. An extended-spectrum antibiotic is one that, as a consequence of chemical alterations, targets a wider range of bacteria, commonly that are gram-negative.

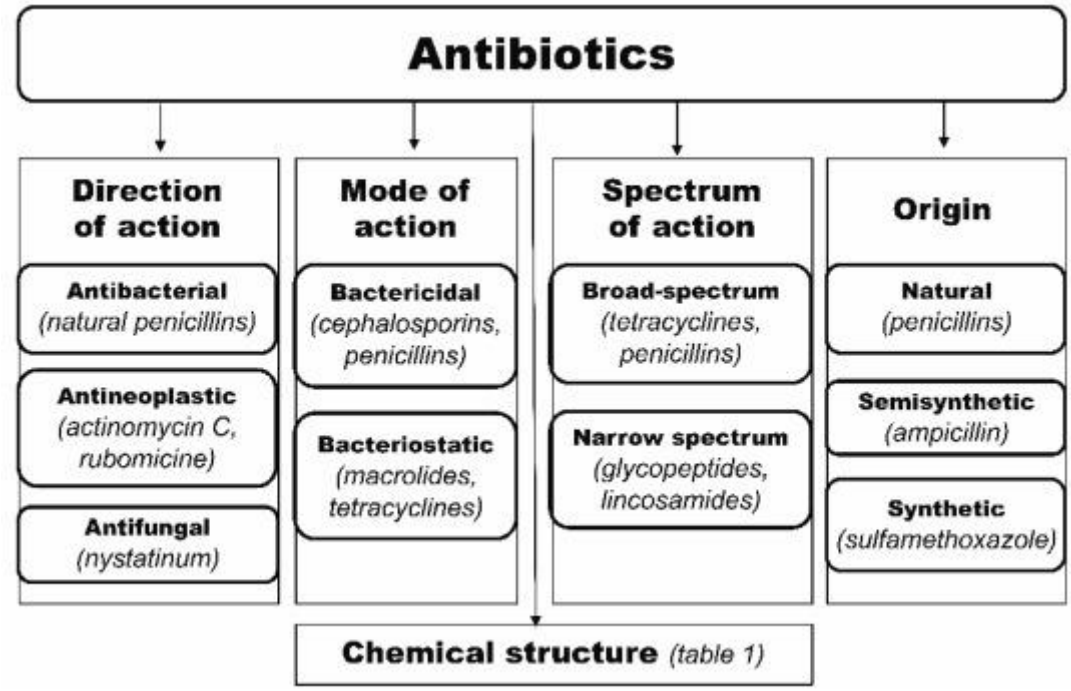

Figure 1: Classification of Antibiotics (Bayan et al., 2021)

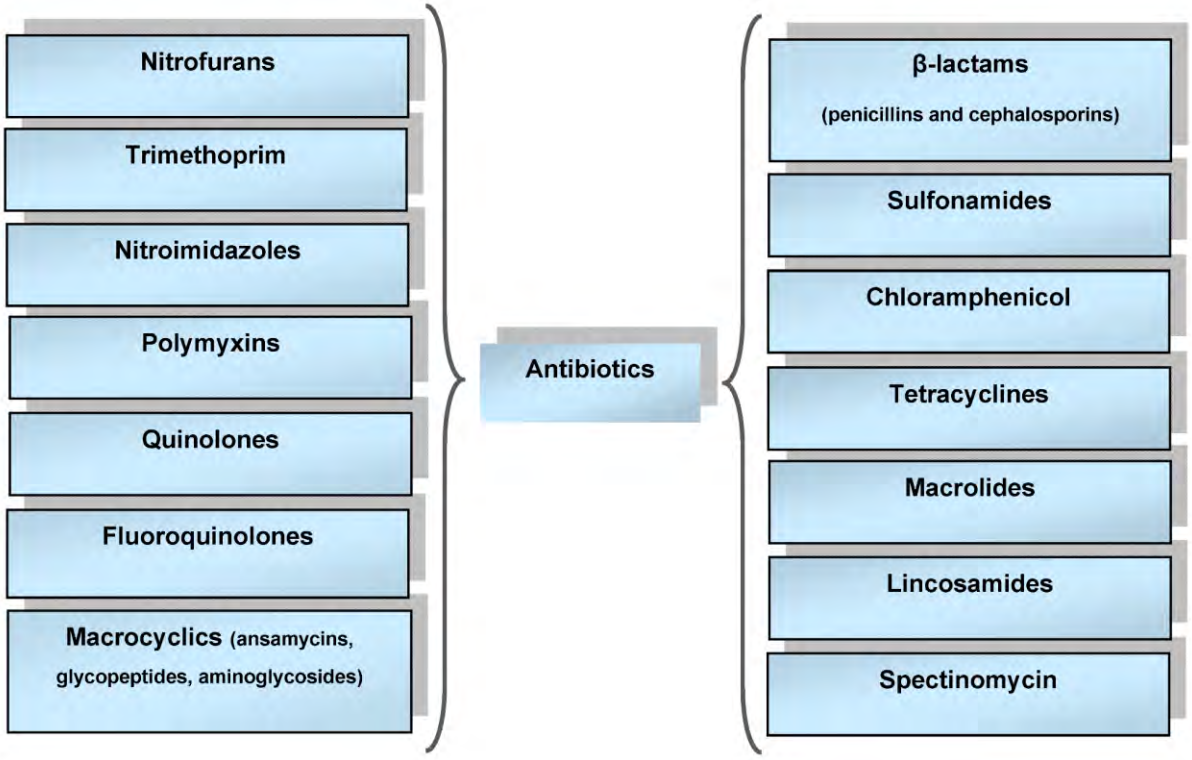

Figure 2: Classification of Antibiotics (Guliy, Zaitsev, & Borodina, 2023)

1.4. Mechanism of action of antibiotics

An antibiotic is a chemical substance that is obtained from a living microorganism and that is detrimental to other disease-causing microorganisms, such as bacteria (The Editors of Encyclopedia Britannica, 2024). Antibiotics exert their effects via a number of mechanisms of action. Antibacterial effect is commonly related to one of four pathways, three of which include the prevention or control of enzymes responsible for cell wall formation, nucleic acid metabolism and repair, or protein synthesis, respectively. The fourth process employs the breakdown of membrane structure. Many antibiotics, known as β-lactams, block bacterial cell wall formation ((Kapoor et al., 2017). Floroquinolones, interrupts the DNA breakage-reunion phase by binding to DNA-gyrase, topoisomerase II, and topoisomerase IV ("Antibiotics: Mode of Action and Mechanisms of Resistance," n.d.). Daptomycin depolarizes calcium-dependent membranes, causing the termination of macromolecular production and breakdown of the cellular membrane in bacteria ("Antibiotics: Classification and Mechanisms of Action With Emphasis on Molecular Perspectives," n.d.). Bacitracin inhibits the transport of precursors necessary for peptidoglycan ("Mechanism of Action of Antibiotics," n.d.). Other antibiotics, including aminoglycosides, chloramphenicol, erythromycin, and clindamycin, block protein synthesis in bacteria. The antibiotics which are selectively toxic disrupt the activity of the bacterium's proteins, inhibiting the production of new proteins and bacterial cells. Antibiotics such as polymyxin B and polymyxin E (colistin) attach to phospholipids in the bacterium's cell membrane and disrupt its function as a selective barrier, allowing vital macromolecules to pass out and causing cell death. These antibiotics are toxic in nature. Some antibiotics, such as sulfonamides, are competitive inhibitors of the production of folic acid (folate), a necessary step in the synthesis of nucleic acids. Sulfonamides can prevent folic acid production because they are identical to an intermediate chemical (para-aminobenzoic acid) that an enzyme converts to folic acid. Because of their structural similarities, para-aminobenzoic acid and the

sulfonamide compete for the enzyme that converts the intermediate to folic acid. This process is reversible by eliminating the chemical, which inhibits but does not kill the microbes. Rifampin, an antibiotic, inhibits ribonucleic acid (RNA) production in bacteria by attaching to a component of the bacterial enzyme that duplicates RNA. Rifampin has a far higher affinity for the bacterial enzyme than for the human enzyme, therefore therapeutic doses have no effect on human cells. Antibiotics mainly target many of the biological activities that are most active when cells proliferate (The Editors of Encyclopaedia Britannica, 2024).

1.5. Pharmacokinetics and Pharmacodynamics of antibiotics

Pharmacokinetic (PK) and pharmacodynamic (PD) factors are used to enhance the effectiveness of antimicrobial treatment in patients by optimizing dose. The four PK components that regulate antibiotic concentration over a period of time include absorption, distribution, metabolism, and excretion. These mechanisms illustrate how an antibiotic passes through the body, from the moment it enters until the parent drug or metabolites are eliminated. The PD of an antibiotic explains the drug's action within the body once it reaches the infection target.

Bactericidal action is either concentration or time dependent. If an antibiotic has concentration-dependent killing, such as fluoroquinolones or daptomycin, the efficiency of bacterial killing improves as the antibiotic concentration increases. Penicillins and tetracyclines are time-dependent, therefore their effectiveness is determined by their duration in the body. After an antibiotic is absorbed, its distribution determines its antibacterial action.

The volume of distribution is calculated by comparing the total amount of medication in the body to the serum concentration. The amount of protein binding determines the availability of the active medication at the site of infection. If an antibiotic is heavily protein-bound, there will

be less free drugs available for antibacterial action, as demonstrated in individuals with hypoalbuminemia. Increased adipose tissue in a patient increases the volume of distribution of a medication with high lipophilicity properties (Patel et al., 2023).

1.6. Resistant Bacteria

Every time an antibiotic is taken, bacteria are killed. Sometimes the bacteria that cause infections are already resistant to recommended medications. Bacteria may potentially develop resistance throughout the progression of a disease. Resistant bacteria do not react to drugs and continue to cause infections. These bacteria are called superbugs. "Superbug" is the term used to describe pathogens that are resistant to several antibiotics (Key, 2017). A prevalent myth is that a person's body develops resistance to certain medications. However, microorganisms are the main reason behind this resistance. If an antibiotic is taken unnecessarily or incorrectly, the risk of getting antibiotic-resistant pathogens is increased. As a result, it is vital to only use antibiotics whenever needed. Because of these resistant bacteria, several diseases that were once relatively easy to cure are now difficult to treat.

Bacteria may acquire resistance due to certain reasons. They are:

1. Antibiotic resistance occurs when pathogens evolve ways to withstand the use of drugs designed to kill or weaken them.
2. If a pathogen develops resistance to many medications, treating infections can become difficult.
3. Resistance may occur if a bacterial disease is only partially cured. To avoid this, it is vital to complete the whole antibiotic dose as directed, even if the patient feels better. **(*Antibiotics*, n.d.)**

1.7. Antibiotic Resistance

Antibiotic resistance is a global concern with substantial morbidity and death (Frieri et al., 2017). Bacteria are extremely small inhabitants. They can go into a person's body. Several of them are safe and can be beneficial. However, some of these microorganisms can cause disease. When they proliferate throughout a person's body, they might cause an infection. Antibiotics are medications designed to eliminate pathogens. Particular types of these microorganisms may eventually adapt to these medications. They may mutate in such a manner that antibiotics cannot kill them (Cedars-Sinai, n.d.). A genetic mutation may allow bacteria to develop enzymes that deactivate antibiotics (“Antibiotics and Antibiotic Resistance,” n.d.). As time passes, bacteria mutate and transform into "super bacteria" or "superbugs." "Superbug" is the term used to describe pathogens that are resistant to several antibiotics (Key, 2017). Resistance is more common when the concentration needed to inhibit or kill microorganisms exceeds what a patient can achieve. Microorganisms might be intrinsically resistant to an antibiotic or develop resistance after exposure to it (acquired resistance). Resistance can occur as a result of a mutation or the direct transfer of genes that encode resistance mechanisms. Resistance genes can be transferred by a variety of modes, including conjugation (transmission of genes carried on plasmids), transformation (direct transfer of naked DNA), and transduction (transfer of identical DNA by bacteriophages).

(Antibiotic resistance: what, why, where, when and how? n.d.)

1.8 Mechanism of Antibiotic Resistance

Antibiotic resistance is when bacteria develop resistance to the antibiotics meant to destroy them or stop their growth. Bacteria can have mainly 2 types of resistance. One is Intrinsic resistance and another one is Acquired resistance. If a bacteria lacks an appropriate receptor for a certain antibiotic, it is called intrinsic resistance. For example, some microorganisms are automatically immune to specific antibiotics. There are some antibiotics that destroy the bacteria's cell wall. If a bacterium lacks a cell wall, the antibiotic is ineffective. This is intrinsic resistance. If a bacterium potentially develops resistance by inheriting resistance genes from other bacteria or generates an alteration that reduces or eliminates antibiotic effectiveness, it is called acquired resistance (Patel et al., 2023).

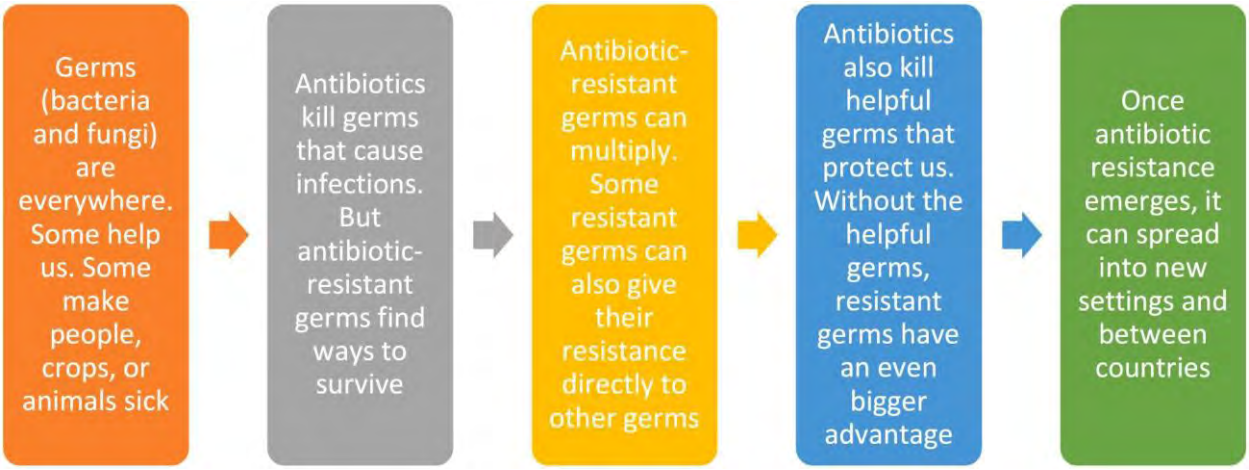

Figure 3: Antibiotic resistance mechanism flowchart (Bonna et al., 2022)

Bacteria can not only spread from one individual to another but also from one species to another because they employ a wide variety of complicated transmission methods. Touching hands,

coming into close contact with an infected person, and coming into contact with contaminated surfaces seem to be the most prevalent ways that germs are spread (Bonna et al., 2022).

A bacteria can develop resistance against antibiotics through several processes. They can:

- Prevent the antibiotic from achieving the target at a sufficient concentration.
- Alter or bypass the target that the antibiotic works on.

Prevent the antibiotic from achieving the target at a sufficient concentration:

1. Pump the antibiotic outside of the bacterial cell: efflux pumps are relatively widespread in bacteria and can transfer a wide range of substances, including signal molecules and nutrients. Some of these pumps can also move antibiotics out from the bacterium, reducing antibiotic concentrations within the bacterial cell.
2. Reduce the permeability of the membrane that covers the bacterial cell: Certain modifications in the bacterial membrane make it harder to pass through. This method ensures that less antibiotic is ingested into the bacterial membrane.
3. Deactivate the antibiotic: There are bacterial enzymes that can deactivate antibiotics. One example is β-lactamase, which degrades the active component (the β-lactam ring) of penicillins.
4. Modify the antibiotic: Sometimes bacteria can develop such enzymes that are capable of adding new chemical groups to antibiotics. This prevents the antibiotic from attaching to its target in the bacterial cell.

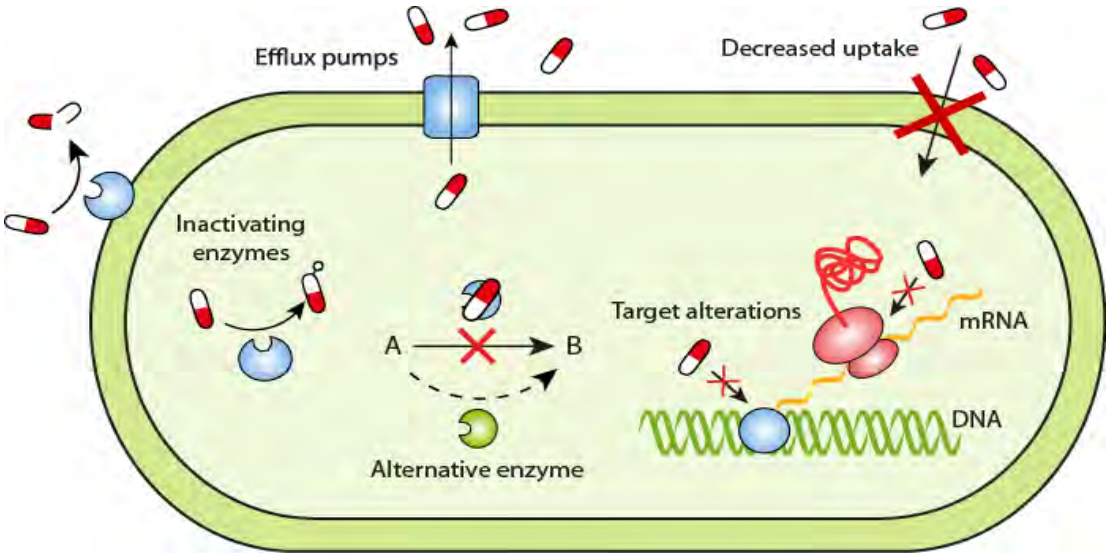

Figure-04: Mechanism of antibiotic resistance (Resistance Mechanisms – Antibiotic Resistance – ReAct, 2021)

Alter or bypass the target that the antibiotic works on:

1. Change the target structure: If changes are done in the structure of the target in the bacterium (caused by mutations in the bacterial DNA), it will prevent the antibiotic from interacting with it. Moreover, bacteria might add alternative chemical groups to the target structure, protecting it from the antibiotic.
2. Generate alternative proteins: Some bacteria can create alternative proteins that can replace those that are blocked by the antibiotic. For example, Staphylococcus aureus can develop the resistance gene and generate a novel penicillin-binding protein. The novel penicillin-binding protein has limited affinity for β-lactam antibiotics, making it resistant to these medicines.
3. Reprogram the target. Bacteria may eventually develop a distinct form of the structure they require. For example, Vancomycin-resistant bacteria produce a different cell wall than susceptible bacteria. The antibiotic fails to interact with this form of cell wall (*Resistance Mechanisms – Antibiotic Resistance – ReAct*, 2021).

1.9. Antibiotic resistance situation in the world

In 2019, 1.27 million deaths were directly related to resistance. It was projected that antibiotic resistance was responsible for 4.95 million deaths globally in 2019 (World Health Organization: WHO, 2023). In 2019, the main six pathogens responsible for resistance-related deaths were *Escherichia coli*, *Staphylococcus aureus, Streptococcus pneumoniae, Acinetobacter baumannii*, and *Pseudomonas aeruginosa*. These pathogens accounted for 929 000 deaths related to antibiotic resistance (Murray et al., 2022). The effectiveness of standard antibiotics against common bacterial infections is being threatened by the global growth of antibiotic resistance. Alarming rates of resistance among common bacterial infections are highlighted in the 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report. A major issue is the median reported rates of 35% for methicillin-resistant Staphylococcus aureus and 42% for third-generation cephalosporin-resistant E. Coli across 76 nations (World Health Organization: WHO, 2023).

1.10. Antibiotic Resistance situation in Bangladesh

The antibiotic resistance situation in Bangladesh is also getting worse nowadays. As per information from the World Health Organization, almost 90% of patients in Bangladesh become resistant to ciprofloxacin, compared to the United Kingdom where only 11.5% of patients are resistant to Ciprofloxacin. According to a professor at Bangabandhu Sheikh Mujib Medical University, 70 percent of ICU deaths are caused by AMR (Islam, 2023b). According to a study, there has been a 11% rise in antibiotic resistance rate in Bangladesh over the last five years. In 2023, the efficiency of many frequently taken antibiotics has decreased by up to 82%, compared to 71% which was five years ago. Drugs such as carbapenem possess an

alarming resistance rate of 84%. Laboratory testing also identified drug-resistant bacteria in 70% of urine samples whereas 10% in blood samples (IEDCR, 2023). Aside from people, Antibiotic residue compounds are also clearly present in animals and water surfaces (Islam, 2023b).

Chapter 2

Aims and objectives

The aims & objectives of this study are to highlight the alarming situation of antibiotic resistance in Bangladesh, especially in Dhaka city, highlighting the possible causes of antibiotic resistance and making people aware of this issue. According to WHO, antibiotic resistance has emerged as a serious public health risk in the 21st century. In developing countries like Bangladesh, the rate of antibiotic resistance is increasing day by day. It's a matter of irony that people are not so much aware of this issue. Even now, there are children being born who are suffering from incurable diseases due to resistance to antibiotic therapy. There will come a time when it will be impossible to cure any bacterial disease. If this issue is left uncontrolled, bacteria will slowly develop resistance against all antibiotics. This means that no antibiotics will work against any bacterial infection in the near future. It is therefore crucial to raise awareness about this issue.

Chapter 3

Methodology

A retrospective study was conducted using 100 isolates from Institute of Child and Mother Health (ICMH) Hospital between 17/08/2023 and 14/02/2024. Data of the antibiotic sensitivity test of the isolates for different diagnostic purposes were used. The results of the antibiotic sensitivity test contained patient information, including their age group. The isolates obtained from patients' blood and urine involved bacterial species, namely *Escherichia coli*, *Salmonella typhi*, *Acinetobacter sp.* and *Enterobacter sp.* After data collection, an excel sheet was created with the patient's name, age, sample collection date and antibiotics susceptible or resistant to. The data was stratified by age and antibiotic susceptibility. Patients were divided into three groups based on their age: A (0-13 years old), B (14-30 years old), and C (31-52 years old). Then the distribution of pathogens and their resistant pattern were studied in the different age groups. The resistant pattern of these four pathogens in percentage was also prepared. Then the common resistant pattern of were analyzed from the Excel Sheet

Chapter 4

Results and Observations

4.1 Distribution of Pathogens

Table 1: Percentage distribution of pathogens

Name of bacterial species	Number	Percentage
E.Coli	71	71%
Salmonella typhi	21	21%
Acinetobacter sp.	05	05%
Enterobacter sp.	03	03%
	Total= 100	

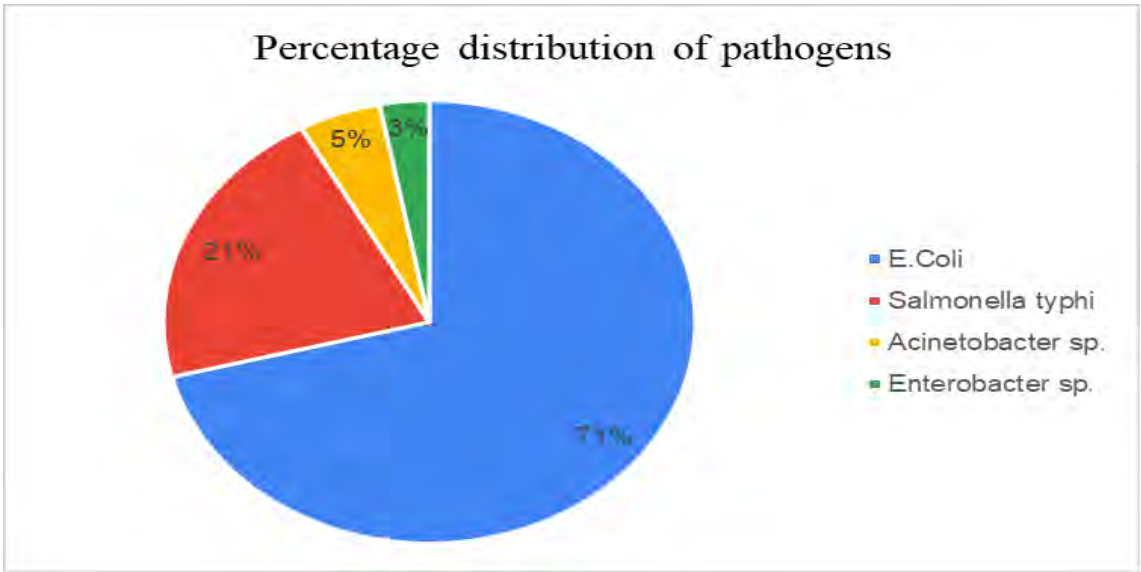

Figure 5: Percentage distribution of pathogens

In this study, a total of 100 data of pathogens were included. Among them, *E.coli* is the most common, which is 71%. This means, the maximum number of patients are infected by E.coli.

Then, the second most common pathogen is *Salmonella typhi* which is 21%. After that, *Acinetobacter sp.* (5%) and *Enterobacter sp.* (3%) are also found.

4.2 Distribution of Pathogens according to age

Table 2: Pathogens distribution according to age

Name of bacterial species	**Age**			**Total**
	0-13 years	**14-30 years**	**31-52 years**	
E. Coli	17 (22.53%)	38 (53.52%)	16 (23.94%)	71
Salmonella typhi	09 (42.86%)	10 (47.62%)	02 (09.52%)	21
Acinetobacter sp.	05 (100%)	00 (0.00%)	00 (0.00%)	05
Enterobacter sp.	00 (0.00%)	03	00	03

In case of patients infected by *E.coli*,*Salmonella typhi* and *Enterobacter sp.,* patients aged (14-30y) are most in number. Only exception is in patients infected by *Acinetobacter sp.* where child patients who aged (0-13y) are most in number.

4.3 Resistance pattern of different classes of antibiotics against *E.coli*

Table 3: Resistance pattern of different classes of antibiotics against E.coli

Antibiotic Name	Percentage of resistance
Amoxyclav	76%
Erythromycin	62%
Azithromycin	13%
Nitrofurantoin	08%
Cefixime	44%
Ceftazidime	14%
Ceftriaxone	4%
Ciprofloxacin	Not shown

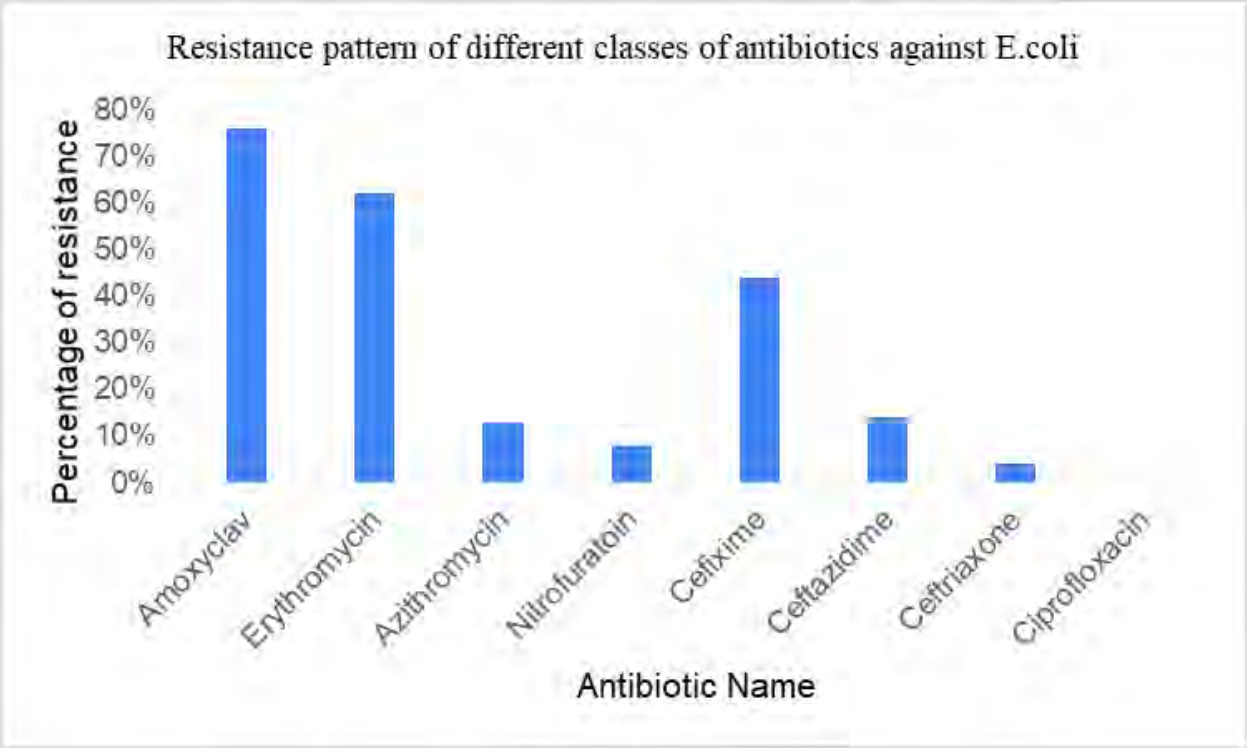

Figure 6: Resistance pattern of different classes of antibiotics against E.coli

Amoxyclav(76%) is the most resistant antibiotic against *E.coli*. The second most resistant antibiotic is Erythromycin(62%). Followed by Cefixime(44%), Ceftazidime(14%), Azithromycin(13%), Nitrofurantoin(8%) and Ceftriaxone(4%). Ciprofloxacin showed no resistance towards *E.coli*.

4.4 Resistance pattern of different classes of antibiotics against *S. typhi*

Table-04: Resistance pattern of different classes of antibiotics against S. typhi

Antibiotic Name	Percentage of resistance
Amoxyclav	38%
Erythromycin	95%
Azithromycin	Not shown
Nitrofurantoin	5%
Cefixime	43%
Ceftriaxone	Not shown
Ciprofloxacin	5%
Metronidazole	52%
Imipenem	Not shown
Amikacin	52%
Gentamicin	Not shown

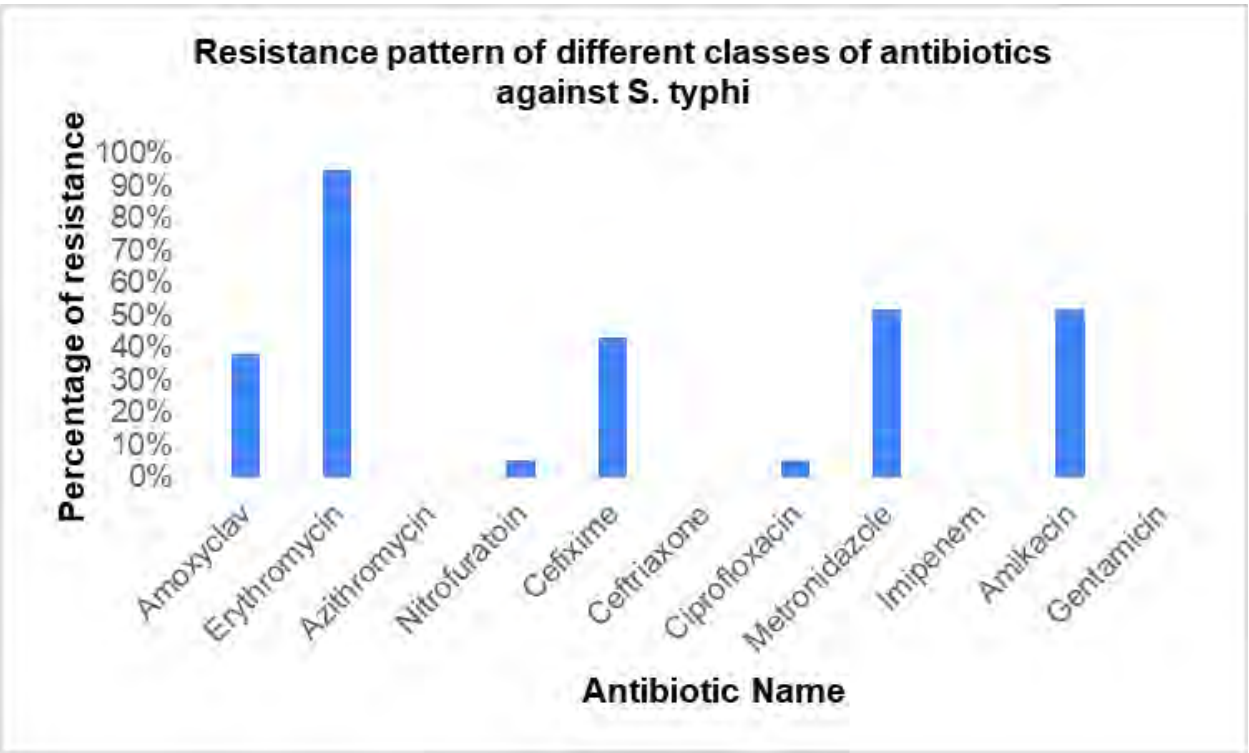

Figure 7: Resistance pattern of different classes of antibiotics against S. typhi

Erythromycin(95%) is the most resistant antibiotic against *Salmonella typhi*. The second most resistant antibiotics are Metronidazole(52%) and Amikacin(52%). Followed by Cefixime(43%), Amoxyclav(38%), Nitrofurantoin(8%) and Ciprofloxacin(5%). Azithromycin, Ceftriaxone, Imipenem and Gentamicin showed no resistance towards *S. typhi.*

4.5 Resistance pattern of different classes of antibiotics against *Acinetobacter sp.*

Table-05: Resistance pattern of different classes of antibiotics against Acinetobacter sp.

Antibiotic Name	Percentage of resistance
Ampicillin	20%
Erythromycin	20%
Amikacin	60%
Gentamicin	Not shown
Cefixime	80%
Ceftriaxone	20%
Ciprofloxacin	Not shown
Metronidazole	20%
Imipenem	Not shown

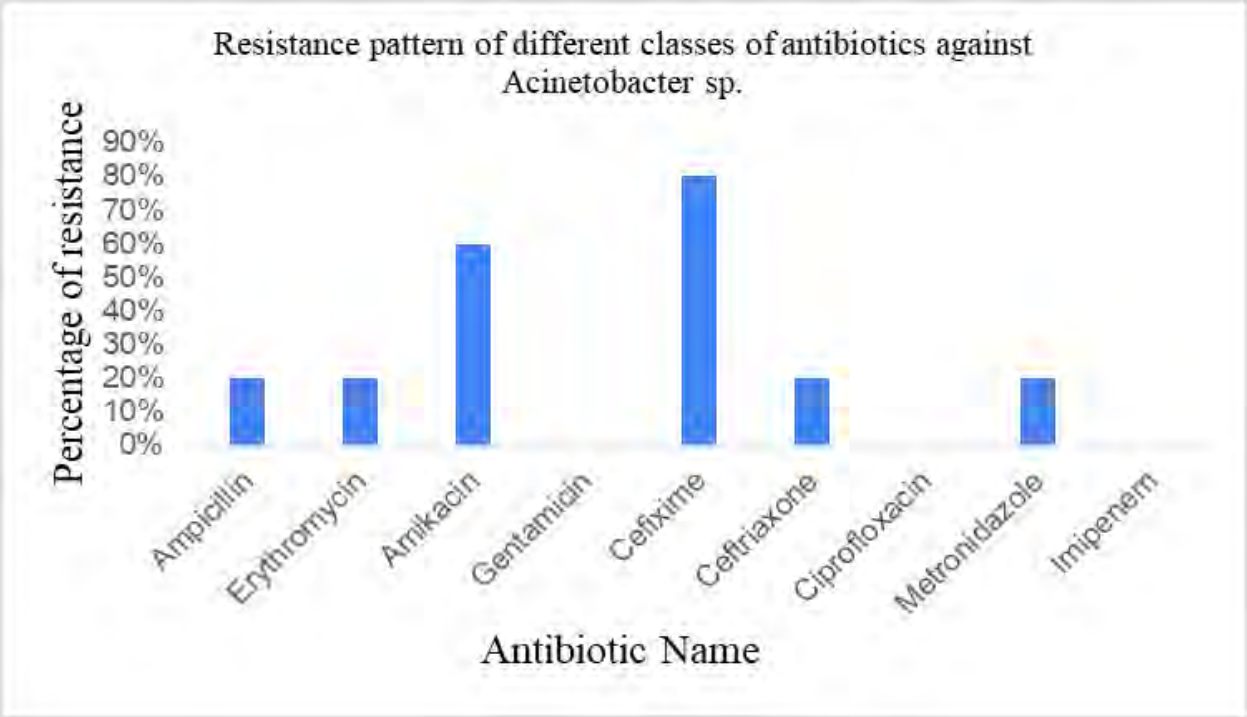

Figure 8: Resistance pattern of different classes of antibiotics against Acinetobacter sp.

Cefixime (80%) is the most resistant antibiotic against *Acinetobacter sp*. The second most resistant antibiotic is Amikacin(52%), followed by ampicillin (20%), erythromycin (20%), ceftriaxone (20%) and metronidazole (20%). Ciprofloxacin, imipenem and gentamicin showed no resistance towards *Acinetobacter sp.*

4.6 Resistance pattern of different classes of antibiotics against *Enterobacter sp.*

Table 6: Resistance pattern of different classes of antibiotics against Enterobacter sp.

Antibiotic Name	**Percentage of resistance**
Ampicillin	67%
Erythromycin	67%
Amikacin	Not shown
Gentamicin	Not shown
Cefixime	Not shown
Ceftriaxone	Not shown
Ciprofloxacin	33%
Metronidazole	Not shown
Imipenem	Not shown

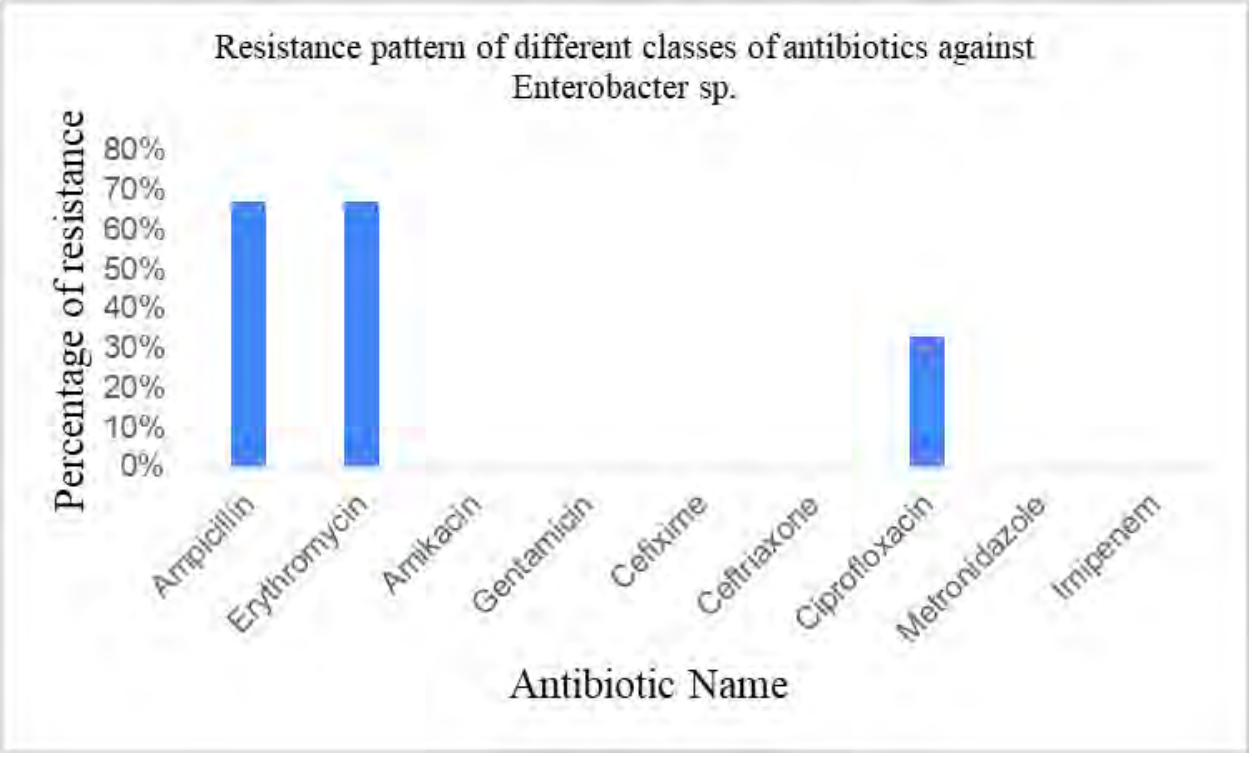

Figure-09: Resistance pattern of different classes of antibiotics against Enterobacter sp.

Ampicillin (67%) and Erythromycin (67%) are the most resistant antibiotic against *Enterobacter sp.* The second most resistant antibiotic is Ciprofloxacin (33%). amikacin, gentamicin, cefixime, ceftriaxone, metronidazole and imipenem showed no resistance towards *Enterobacter sp.*

4.7 Resistance pattern of different classes of antibiotics against *E.coli* according to age

Table-07: Resistance pattern of different classes of antibiotics against E.coli according to age

Antibiotic Name	**Age (0-13 years)**	**Age (14-30 years)**	**Age (31-52 years)**
Amoxyclav	00	38	16
Erythromycin	12	19	15
Azithromycin	04	04	01
Nitrofurantoin	01	04	01
Cefixime	06	19	07
Ceftazidime	04	05	01
Ceftriaxone	03	00	00
Ciprofloxacin	00	00	00

Table 8: Significance difference in resistance pattern of different classes of antibiotics against E.coli according to age in percentage

Antibiotic Name	**Child** **Age (0-13)**	**Adult** **Age (14-52)**
Amoxyclav	Not shown	76.06%
Erythromycin	16.90%	47.89%
Azithromycin	5.63%	7.04%
Nitrofurantoin	1.41%	7.04%
Cefixime	8.45%	36.62%
Ceftazidime	5.63%	8.45%
Ceftriaxone	4.22%	Not shown
Ciprofloxacin	Not shown	Not shown

Amoxyclav showed no significant resistance in child patients against E.coli but it showed 76.06% resistance in adult patients. From table-08, we can observe that almost all antibiotics showed maximum resistance in adult patients. This means antibiotics are less susceptible to E.coli in child patients. Ceftriaxone showed no significant resistance against E.coli in adult patients but it showed 4.22% resistance against E.coli in child patients. Ciprofloxacin didn't show any significant resistance in both child and adult patients.

4.8 Resistance pattern of different classes of antibiotics against S. typhi according to age

Table-09: Resistance pattern of different classes of antibiotics against S. typhi according to age

Antibiotic Name	Age (0-13)	Age (14-30)	Age (31-52)
Amoxyclav	00	06	02
Erythromycin	09	09	02
Azithromycin	00	00	00
Nitrofurantoin	01	00	00
Cefixime	07	02	00
Ceftriaxone	00	00	00
Ciprofloxacin	01	00	00
Metronidazole	07	04	00
Imipenem	00	00	00
Amikacin	08	03	00
Gentamicin	00	00	00

Table-10: Significance difference in resistance pattern of different classes of antibiotics against S.typhi according to age in percentage

Antibiotic Name	**Child** **Age (0-13)**	**Adult** **Age (14-52)**
Amoxyclav	Not shown	38.10%
Erythromycin	42.86%	52.38%
Azithromycin	Not shown	Not shown
Nitrofurantoin	4.76%	Not shown
Cefixime	33.33%	9.52%
Ceftriaxone	Not shown	Not shown
Ciprofloxacin	4.76%	Not shown
Metronidazole	33.33%	19.05%
Imipenem	Not shown	Not shown
Amikacin	38.10%	14.29%
Gentamicin	Not shown	Not shown

Azithromycin,Ceftriaxone,Imipenem and Gentamicin showed no significant resistance towards *S. typhi* in both child and adult patients. Erythromycin showed maximum resistance (52.38%) towards *S. typhi* in adult patients. Other antibiotics such as Amikacin (38.10%), Cefixime (33.33%), Metronidazole (33.33%), Nitrofurantoin (4.76%) and Ciprofloxacin (4.76%) also showed significant resistance towards *S. typhi* in child patients. That means children are getting more prone to antibiotic resistance against *S. typhi*. Lastly, Amoxyclav

showed no significant resistance in child patients whereas it showed 38.10% resistance in Adult patients.

4.9 Resistance pattern of different classes of antibiotics against *Acinetobacter sp.* according to age

Table-11: Resistance pattern of different classes of antibiotics against Acinetobacter sp. According to age

Antibiotic Name	Age (0-13)	Age (14-30)	Age (31-52)
Ampicillin	01	00	00
Erythromycin	04	00	00
Amikacin	03	00	00
Gentamicin	00	00	00
Cefixime	04	00	00
Ceftriaxone	01	00	00
Ciprofloxacin	00	00	00
Metronidazole	04	00	00
Imipenem	00	00	00

Table-12: Significance difference in resistance pattern of different classes of antibiotics against Acinetobacter sp. according to age in percentage

Antibiotic Name	**Child** **Age (0-13)**	**Adult** **Age (14-52)**
Ampicillin	20%	0%
Erythromycin	80%	0%
Amikacin	60%	0%
Gentamicin	0%	0%
Cefixime	80%	0%
Ceftriaxone	20%	0%
Ciprofloxacin	0%	0%
Metronidazole	80%	0%
Imipenem	0%	0%

No antibiotic showed any significant resistance towards Acinetobacter sp. in adult patients but almost all antibiotics showed significant resistance in child patients. Among them, Erythromycin, Cefixime and Metronidazole showed maximum resistance (80%) towards Acinetobacter sp. Amikacin showed 60% resistance. Ampicillin and Ceftriaxone showed 20% resistance. Gentamicin, Ciprofloxacin and Imipenem showed no resistance towards Acinetobacter sp. in child patients.

4.10 Resistance pattern of different classes of antibiotics against Enterobacter sp. According to age

Table-13: Resistance pattern of different classes of antibiotics against Enterobacter sp. According to age

Antibiotic Name	Age (0-13)	Age (14-30)	Age (31-52)
Ampicillin	00	02	00
Erythromycin	00	02	00
Amikacin	00	00	00
Gentamicin	00	00	00
Cefixime	00	00	00
Ceftriaxone	00	00	00
Ciprofloxacin	00	01	00
Metronidazole	00	00	00
Imipenem	00	00	00

Table-14: Significance difference in resistance pattern of different classes of antibiotics against Enterobacter sp. according to age in percentage

Antibiotic Name	**Child** **Age (0-13)**	**Adult** **Age (14-52)**
Ampicillin	0%	66.67%
Erythromycin	0%	66.67%
Amikacin	0%	0%
Gentamicin	0%	0%
Cefixime	0%	0%
Ceftriaxone	0%	0%
Ciprofloxacin	0%	33.33%
Metronidazole	0%	0%
Imipenem	0%	0%

No antibiotics showed any significant resistance towards Enterobacter sp. in child patients. Among them, Amikacin, Gentamicin, Cefixime, Ceftriaxone, Metronidazole and Imipenem showed no significant resistance in both child and adult patients. Both Ampicillin and Erythromycin showed 66.67 % resistance towards Enterobacter sp. in adult patients. Lastly, Ciprofloxacin showed 33.33% resistance towards Enterobacter sp. in adult patients.

Chapter 5

Discussions

We observed that maximum patients are susceptible to *E.coli.* In table 4.1, we can see that 71 patients among 100 isolates are susceptible to *E.coli* which is the highest. About 21 patients among the rest are susceptible to *Salmonella typhi* which is the second highest. That means these two microorganisms are now top leading resistance causing pathogens nowadays (Akter et al., 2020 & Polash et al., 2021). From table 4.2, we can observe that adult patients are most infected by *E.coli*,*Salmonella typhi* and *Enterobacter sp.* Child patients are less susceptible towards these pathogens. Child patients are mostly infected by *Acinetobacter sp.* If we thoroughly observe the resistance pattern of different classes of antibiotics, we can observe that Amoxyclav, Erythromycin, cefixime and amikacin are the top leading antibiotics that have showed significant resistance towards *E.coli, S. typhi* and *Enterobacter sp.* One reason behind this can be these antibiotics are very common and easily available. As a result, irrational and misuse of antibiotics can lead to antibiotic resistance. Amoxyclav showed significant resistance in adult patients rather than child patients (from table-10). The reasons behind this can be people's food habits, misuse and overuse of antibiotics, lack of proper knowledge, irrational use of antibiotics by health care providers and over the counter sales of antibiotics. Maximum patients want symptomatic relief. As soon as they get relief from these symptoms, they stop taking antibiotics and do not complete the dosage. This can be another reason why adult patients are more susceptible to antibiotic resistance compared to child patients. Another finding is that both child and adult patients are becoming more Erythromycin resistant towards pathogens (from table- 08, 10, 12, 14). This is also a matter to be concerned about. If no awareness is made as soon as possible and left uncontrolled, this resistance rate will increase and will be impossible to cure in near future. So, this is high time awareness is made and necessary steps should be taken before antibiotic resistance becomes incurable.

Chapter 6
Conclusion

In this study it is found that E.coli is the most prevalent pathogen responsible for antibiotic resistance (Akter et al., 2020 & Polash et al., 2021). Amoxyclav shows more resistance towards pathogenic bacteria in adult patients compared to child patients. Moreover, Erythromycin has shown significant resistance in both child and adult patients towards *E.coli, S. typhi, Acinetobacter sp.* and *Enterobacter sp.* This is also an alarming issue. The reasons behind increased antibiotic resistance rate in Bangladesh can be people's food habits, misuse and overuse of antibiotics, lack of proper knowledge, lack of awareness, irrational use of antibiotics by health care providers, over the counter sales of antibiotics and easy availability of antibiotics etc (Cars & Nordberg, 2005). It is high time awareness is made and necessary steps should be taken before antibiotic resistance becomes incurable.

References

Akter, T., Fatema, K., Nahar, S., Sultana, H., Sumon Khan, M., Shahidul Alam, M., Afrin, S., & Jakir Hossain, M. (2020). Spectrum of Antimicrobial Susceptibility of Escherichia coli Isolated from Urine Samples of a Tertiary Care Hospital of Bangladesh (Vol. 24, Issue 03). https://nib.portal.gov.bd/sites/default/files/files/nib.portal.gov.bd/page/2c82b665_09b4_4cbb_b6a6_266f5c390c4c/2022-03-14-06-20-fe35104d8364df645805f326ade65cf5.pdf

Antibiotic resistance in Bangladesh rises 11% in 5 years: IEDCR. (2023, November 22). Antibiotic resistance in Bangladesh rises 11% in 5 years: IEDCR. *The Business Standard*. https://www.tbsnews.net/bangladesh/health/antibiotic-resistance-bangladesh-rises-11-5-years-iedcr-744522

Antibiotic resistance: what, why, where, when and how? (n.d.). Antibiotic Resistance: What, Why, Where, When and How? https://www.researchgate.net/publication/283211266_Antibiotic_resistance_What_why_where_when_and_how?enrichId=rgreq-d6e9ee6909e31a4b67484ff1e8b5a35a-XXX&enrichSource=Y292ZXJQYWdlOzI4MzIxMTI2NjtBUzo0ODA1MjUwNTI4NDYwODFAMTQ5MTU3NzUwODkwMQ%3D%3D&el=1_x_3&_esc=publicationCoverPdf

Antibiotics and antibiotic resistance. (n.d.). *Antibiotics and Antibiotic Resistance*. https://d1wqtxts1xzle7.cloudfront.net/61711779/BJSTR.MS.ID.00011720200107-34616-jfmu0e-libre.pdf?1578464435=&response-content-disposition=inline%3B+filename%3DAntibiotics_and_Antibiotic_Resistance_In.pdf&Expires=1713889357&Signature=Y5z1XUq8mcai6HOMIm~V2pm8JwzuXsw4kserfqj7Ij6MM6FAmGy1NR87C4~fkdkWsYLzFAclJV7OAV9HCt3Vy-

X7~ArSt1Ku7XiFBFheQ0fs8QyXaVT9jsLzzPcJc71e~Xq49slBckY4OSQEMJIxPfHmNiKcuokf~lFY-PsfhDi3ToGNmEsaQzYwauwY7mxF~Bz~n~h6iAng9894QxjtAZmm3Bf8ma6Jotj-yTxhq9yKRGregcsRD60uAlrelBN90~NWvBtifh8lEgr~mXA-sn7OXjn59PEj3UsZOev5gus~ClZNaxPcBlRNjYR0Xp3xIEohR9RN8fU8CO4ahEW3w__&Key-Pair-Id=APKAJLOHF5GGSLRBV4ZA

Antibiotics. (n.d.). Johns Hopkins Medicine. https://www.hopkinsmedicine.org/health/wellness-and-prevention/antibiotics

Antibiotics: Classification and mechanisms of action with emphasis on molecular perspectives. (n.d.). Antibiotics: Classification and Mechanisms of Action With Emphasis on Molecular Perspectives. https://www.researchgate.net/publication/319881509_Antibiotics_Classification_and_mechanisms_of_action_with_emphasis_on_molecular_perspectives?enrichId=rgreq-b7ece474bbbd7ae457621420af2e5c83-XXX&enrichSource=Y292ZXJQYWdlOzMxOTg4MTUwOTtBUzo1NDAwNTg4MzU4MDAwNjRAMTUwNTc3MTQ2ODgxOQ%3D%3D&el=1_x_3&_esc=publicationCoverPdf

Antibiotics: mode of action and mechanisms of resistance. (n.d.). Antibiotics: Mode of Action and Mechanisms of Resistance. https://www.researchgate.net/publication/317381477_Antibiotics_Mode_of_action_and_mechanisms_of_resistance?enrichId=rgreq-5b54a58d6964988f8308b645832fdc22-XXX&enrichSource=Y292ZXJQYWdlOzMxNzM4MTQ3NztBUzo1MjcyMTg2MDc2O

TM4MjRAMTUwMjcxMDExOTkyMg%3D%3D&el=1_x_3&_esc=publicationCoverPdf

Aslam, B., Wang, W., Arshad, M., Khurshid, M., Muzammil, S., Rasool, M. H., Nisar, M. A., Alvi, R. F., Aslam, M., Qamar, M. U., Salamat, M. K. F., & Baloch, Z. (2018). Antibiotic resistance: a rundown of a global crisis. *Infection and Drug Resistance*, *Volume 11*, 1645–1658. https://www.tandfonline.com/doi/full/10.2147/IDR.S173867

Bayan, E. M., Pustovaya, L. E., & Volkova, M. G. (2021). Recent advances in TiO2-based materials for photocatalytic degradation of antibiotics in aqueous systems. *Environmental Technology & Innovation*, *24*, 101822. https://doi.org/10.1016/j.eti.2021.101822 https://www.sciencedirect.com/science/article/abs/pii/S2352186421004703

Bonna, A. S., Pavel, S. R., Ferdous, J., Khan, S. A., & Ali, M. (2022). Antibiotic resistance: An increasingly threatening but neglected public health challenge in Bangladesh. *International Journal of Surgery Open*, *49*, 100581. https://www.sciencedirect.com/science/article/pii/S2405857222001449

Cars, O., & Nordberg, P. (2005). Antibiotic resistance-The faceless threat. In International Journal of Risk & Safety in Medicine (Vol. 17). IOS Press. https://reactgroup.org/uploads/publications/react-publications/antibiotic-resistance-the-faceless-threat.pdf

Cedars-Sinai. (n.d.). Antibiotic resistance. https://www.cedars-sinai.org/health-library/diseases-and-conditions/a/antibiotic-resistance.html

Frieri, M., Kumar, K., & Boutin, A. (2017). Antibiotic resistance. *Journal of Infection and Public Health*, *10*(4), 369–378. https://doi.org/10.1016/j.jiph.2016.08.007

Guliy, O. I., Zaitsev, B. D., & Borodina, I. A. (2023). Electroacoustic biosensor systems for evaluating antibiotic action on microbial cells. *Sensors*, *23*(14), 6292. https://www.mdpi.com/1424-8220/23/14/6292

Islam, K. M. M. (2023b, February 11). Antimicrobial resistance: The overlooked pandemic. *The Daily Star*. https://www.thedailystar.net/opinion/views/news/antimicrobial-resistance-the-overlooked-pandemic-3244996

Kapoor, G., Saigal, S., & Elongavan, A. (2017). Action and resistance mechanisms of antibiotics: A guide for clinicians. *Journal of Anaesthesiology-Clinical Pharmacology/Journal of Anaesthesiology Clinical Pharmacology*, *33*(3), 300. https://doi.org/10.4103/joacp.joacp_349_15

Key, A. P. (2017, February 23). *Antibiotics: Everything You should know*. WebMD. https://www.webmd.com/a-to-z-guides/what-are-antibiotics

Mechanism of action of antibiotics. (n.d.). *Mechanism of Action of Antibiotics*. https://krishi.icar.gov.in/jspui/bitstream/123456789/31823/1/10_Mechanism%20of%20action%20of%20antibiotics.pdf

Murray, C. J. L., Ikuta, K. S., Sharara, F., Swetschinski, L. R., Aguilar, G. R., Gray, A. P., Han, C., Bisignano, C., Rao, P. C., Wool, E., Johnson, S., Browne, A. J., Chipeta, M. G., Fell, F., Hackett, S., Haines–Woodhouse, G., Hamadani, B. H. K., Kumaran, E. a. P., McManigal, B., . . . Naghavi, M. (2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*, *399*(10325), 629–655. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext

Patel, P., Wermuth, H. R., Calhoun, C., & Hall, G. A. (2023, May 26). *Antibiotics*. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK535443/

Polash, Md. J. I., Agarwala, R., Simran, K. T., Tisha, T. T., & Sarkar, A. P. (2021). Antibiotic resistance in Bangladesh: A current epilogue, and a systematic review. Asian Journal of Pharmacy and Pharmacology, 7(5), 222–239. https://doi.org/10.31024/ajpp.2021.7.5.3

Mode of actions and targets for antibacterial drugs. Mode of Actions and Targets for Antibacterial Drugs - Creative Biolabs. (n.d.). https://www.creative-biolabs.com/drug-discovery/therapeutics/mode-of-actions-and-targets-for-antibacterial-drugs.htm#:~:text=There%20are%20six%20major%20modes,inhibition%20of%20ATP%20Synthase%20

Resistance mechanisms – Antibiotic resistance – ReAct. (2021, December 9). ReAct. https://www.reactgroup.org/toolbox/understand/antibiotic-resistance/resistance-mechanisms-in-bacteria/

Survey on Antimicrobial Resistance: Reason behind the Misuse of Antibiotics in Bangladesh - Lib Research Guardians. (n.d.). http://journal.edit4journal.com/id/eprint/1061/

The Editors of Encyclopaedia Britannica. (2024, March 29). *Antibiotic | Definition, types, side effects, resistance, Classification, & facts*. Encyclopedia Britannica. https://www.britannica.com/science/antibiotic

World Health Organization: WHO. (2023, November 21). *Antimicrobial resistance*. https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance