Antibiotic Resistance Pattern of *Escherichia coli*: A Cross-sectional Study of Antibiograms

A project submitted

by

Md. Samiul Hussain

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Dedicated to my parents, who sacrificed their every desire since my birth to make me a good person and inspire me in every steps of my life.

Certification Statement

This is to certify that this project title 'Antibiotic Resistance Pattern of *Escherichia coli*: A Cross-sectional Study of Antibiograms' submitted for the partial fulfillments of the requirements for the degree of Bachelor of Pharmacy from the Department of Pharmacy, BRAC University constitutes by my own work under the supervision of Md Tanvir Kabir, Senior Lecturer, Department of Pharmacy, BRAC University and that appropriate credit is given where I have used the language, ideas or writing of another.To the best of my knowledge, this project paper contains no information previously published or written by another person except where due references are given in the paper itself.

Signed,

_____

Countersigned by the supervisor,

_____

Acknowledgement

The blessings and mercy of the Almighty Allah who is the source of our life and strength of our knowledge and wisdom, have helped me to continue my study in full diligence which I hope will reflect in my project.

I would like to express my gratitude towards my supervisor Md. Tanvir Kabir, Senior lecturer, Department of Pharmacy, BRAC University for his continuous provision, guidance and patience since the first day of the project work. He has continuously inspired and motivated me with his knowledge and expertise which made me more passionate about the project since it began.

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Abstract

Antibiotic resistance is one of the serious issues nowadays. This is a global problem and more problematic in developing and underdeveloped countries. It develops due to various reasons, like food habit, poor sanitization, improper prescribing method, taking antibiotics without prescription or any kind of consultation with doctor, and uncontrolled antibiotic use for fisheries, poultry and veterinary and for the lack of knowledge of antibiotic use. In case of resistance mechanism, it follows several ways such as change of cell wall, target modification, antibiotic inactivation, efflux pump out, ribosome protection and biofilm formation. In this research, culture and sensitivity test reports were collected from the microbiology department of a renowned diagnostic center, and all the antibiogram is about *Escherichia coli* sensitivity. In case data of analysis, the reports were analyzed by gender, age group, and divisions. Out of 543 antibiogram reports, most sensitive antibiotics were amikacin, ampicillin, amoxyclav, cefotaxim, cefexime, ceftriaxone, ciprofloxacin, colisitin, gentamycin, imipenem, meropenem, nitrofuration and tigecycline up to 95%. Most resistant antibiotics were azithromycin, aztreonam, cefuroxime, ceftriaxone, cephradine, nalidixic acid, levofloxacin, cefoxitin and tetracycline (60-90%). Here, mostly susceptible age grouped peoples are under 30 years and elderly peoples in some cases. Among the 28 antibiotics, 9 were analyzed with significance where no mortality was found but the statistical significancefor 31-45 years age group was evident with an odds ratio (OR) 3.42 (95%CI; 1.60±7.32; p= 0.002) and for ≥46 years (OR22.47, 95%CI; 1063±47.47; p= <0.001) for amoxyclav. Cefexime is more significant in case of resistance compared to sensitivefor 31-45 years age group (OR1.08, 5%CI; 0.40±2.89; p= 0.883) and for ≥46 years (OR1.41; 95%CI; 0.40±2.89; p= .554). In case of doxycycline 31-45 year age group (OR1.43; 95%CI; 0.59±3.53) and for more than 46 years age group (OR1.41; 95%CI; 0.57±3.53; p= 4.63). Lastly, for tigecycline 31-45 years age group (OR 0.45; 95%CI; 0.29±0.68; p= <0.001) and for more than 46 years age group (OR0.27; 95%CI; 0.17±0.44; p= <0.001) which is less significant. *Escherichia coli* is very common and can be contaminated very easily so people of all ages and divisions should be more careful regarding antibiotics intake to control the increasing antibiotic resistance.

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Abbreviations

AMR- Antimicrobial Resistance

BSMMU- Bangladesh Sheikh Mujib Medical University

CI- Confidence Interval

c.s. - Culture and Sensitivity

DDD- Defined Daily Dose

DNA- Deoxyribonucleic Acid

E. coli – *Escherichia coli*

ICU- Intensive Care Unit

MIC- Minimum Inhibitory Concentration

n.s.- Not Significant

OR- Odd Ratio

R/M- Resistance Mechanism

UTI- Urinary Tract Infection

USA- United State of America

WHO- World Health Organization

Background studies

The reason behind working on this area for research is, antibiotic resistance is one of the crucial threats for the human beings. Especially in the third world or in developing countries chances of getting resistant to antibiotics is very high. This is because of the availability of antibiotics and taking antibiotics without consulting with physician are elevating every day, and contamination of bacteria in the environment adds up to it. Adding to the fact, this contamination causes other bacteria of the same species to create resistance (Grenni, Ancona, & Barra Caracciolo, 2018). Worryingly, consumption of antibiotics has increased up to 70% all over the world, and In every 2 minutes 2 tons of antibiotics are used all over the world (Harbarth et al., 2015). In our sub-continent, Escherichia coli is a very common bacteria which can cause infections so many means and in any condition (Munita, Arias, Unit, & Santiago, 2016). At the same time, this common bacteria getting resistantvery fast throughout Bangladesh. Very few researchers researched on this area where this is a very vast and important area to be researched about. We thought about the necessity to conduct a research study in this field by keeping the upcoming threats in mind and hoped for new related scope to be uncovered.

Chapter 1: Introduction

1. Introduction

1.1 Antibiotic

Antibiotic is defined as a drug which kills or slows the growth of bacteria and other microorganisms. Antibiotics are a class of antimicrobials that includes anti-fungal, anti-viral, and anti-parasitic drug. Antibiotics are the kind of drug which are derived or produced from other microorganisms (Bayarski, 1928). Antibiotics are the most prescribed medicines in modern healthcare facilities. There are mainly two types of antibiotics, one of them is known as “bactericidal”, which has the ability to kill the bacteria, and another one is “bacteriostatic”, which is capable of slowing down the multiplication of bacterial cell (Bayarski, 1928).

In other words, antibiotics are the drug which is used to treat bacterial infection. Viral effects are not affected by antibiotics. Originally, antibiotics are the kinds of substances that are produced from other microorganisms or can be synthetic which slows down the growth or kill selective bacteria (“Definition of Antibiotic,” n.d.). Synthetic antibiotics are compared to natural antibiotics in a variable of chemical properties that accomplish comparable tasks. So, antibiotics could be natural or synthetic, but the effect is the same, it would be either a bactericidal or a bacteriostatic in nature (“Definition of Antibiotic,” n.d.).

1.2 Antibiotic resistance

According to World Health Organization, -“Anti-microbial resistance happens when microorganisms such as virus, bacteria, fungi, and parasites change when they are exposed to microbial antimicrobial drugs such as antibiotics, antifungals, antivirals, etc. In other words, antimicrobial or antibiotic resistance is the ability of a particular micro-organism to secure themselves from the medicines previously they were sensitive” (“WHO | Antibiotic resistance,” 2017).

As soon as the penicillin was discovered after two years of it penicillinase, an enzyme was discovered which can inactive the bacteria produce the antibiotic and this. This is the initiation of antibiotic resistance. The main feature of any antibiotic to lose their effectiveness is time. Moreover, here bacteria are getting mutant faster. This feature is not common like the drugs that work in the cardiovascular system or nervous system. For example, they get inactivated by genetical modification, changing of the site of action in the

bacterial cell, increase production of target enzyme and avoidance of inhibiting effect, etc. Recent phenomenon suggests that targeted studies of ancient DNA have identified genes with resistance to β-Lactams, tetracycline, and glycopeptide antibiotics. Though antibiotic resistance is a natural process of occurrence preceding medicinal antibiotic use (Dickes L, L, & A, 2015).

However, with increased use of antibiotics more and more bacteria developing resistance to their inhibitory effect. As antibiotics have a limited life when they are used on a pathogen for the first time, the bacterial cell may variously develop resistance. Currently, antimicrobial resistance threatens (AMR) the effective prevention or treatment of an ever-expanding range of infections. In recent years, researchers got a good understanding of intra and extracellular mechanism of getting resistance from the bacterial cell (Penesyan, Gillings, & Paulsen, 2015).

1.3Development of antibiotic resistance

We all know that Alexander Fleming invented penicillin as an antibiotic, he himself discovered that antibiotic could be resistant. Later on, some other scientists also proved that antibiotic could be resistant for a number of reasons. The situation of antibiotic resistance is worse than Alexander Fleming predicted. Though antibiotic resistance will be developed naturally, but some factors can accelerate the antibiotic resistance ("Alexander Fleming Discovery and Development of Penicillin - Landmark - American Chemical Society," n.d.). Some key factors are:

- In many places around the world, people misuse or overuse antibiotics for humans and animals at the same time which is given without the professionals' guidance very often. For example, people use antibiotics for viral fever and cold. This is because of improper guidance of medicines and improper regulations. That is why people easily get antibiotics, in some cases, doctors even prescribe antibiotics on the basis of guess. At the same time animals are given antibiotics forcefully which can spread-out to the humans (Carbon, Bax, & Bernard, 1998).
- Antibiotics are given to animals with growth promoters as a result bacterium will develop antibiotic resistance and there are huge possibilities of spread-out of this resistance among human being(L. L. Founou, Founou, & Essack, 2016). These are

given to the poultry and fisheries so that the life rate and growth of those animal ensure conformity and the food demand is full filled. Again, some people think these medicines will enhance the growth of the animals and we will get more meat(L. L. Founou et al., 2016).

- Inadequate food handling like improper cooking of animal meats, fishes or unsafe packaging of these food items can easily accelerate the increasing rate of antibiotic resistance as bacteria can remain all over the places and get resistance by mutation(Press, 2015). When those animal meats which are given antibiotics, we collect to eat if those animals are effected by any bacteria those could be spread in us. Though, it is not necessary that animal bacteria will affect us but the problem is bacteria can exchange or collect new genes among themselves. Thus, improper cooking or improper handling of those meat can spread-out antibiotic resistance("Antibiotics in Livestock: Frequently Asked Questions - Animal Health Institute," 2018).

- Poor sanitation system and poor control of infection treatment also accelerate the rate of antibiotic resistance. If the bacteria cause infectious disease to us, sanitation system should be given more importance. Because we excrete drugs bacteria through our stool and urine. So, if we are not conscious about sanitation system these will attack us so easily. Again, control in the infectious disease is more important therefore, everyone should take precaution to save themselves(Carr, 2001).

- Inappropriate prescribing of antibiotics is one of the most important factors of increasing rate of resistance. Studies have showed that, choosing of antibiotics, treatment indication and choosing the duration of therapy is wrongly prescribed in case of 30% to 50 % patients in developing countries(Ventola, 2015).This happens mostly in developing countries, it is because of mainly doctors prescribe antibiotics on the basis of guess and at the same time patient do not complete the course of antibiotics. These are the reason of rapid increasing of antibiotic resistance. Doctors should be more concern about prescribing antibiotics. For the same symptoms everyone should not prescribed same drugs each time. There should be a proper way of lab testing to

find out the bacteria or pathogen that infected the patient and then they should be given appropriate medicine(S. Kumar, 2003).

- The environmental micro biomeis affected by the agricultural use of antibiotics. About 90% of the antibiotics are excreted through urine and stool. After this, it get mixed with the soil and up taken by plants. At the same time, in some countries, antibiotics like tetracycline are used as a pesticide(Ventola, 2015).This is again for the lacking of proper sanitation system. With a proper system of sanitation these contamination could be stopped. Specially, toilets and cleaning rooms should be made at appropriate distance from farm land and water sources. Use of antibiotics as pesticides is not a wise decision. Antibiotic should be used only for treatment of bacterial diseases(Cairncross., et al 2010).

- Availability of new antibiotics is another important fact.Because of this,use of antibiotics are happening for a short duration. At the same time practitioners change the antibiotics for various reasons. So, at first doctor should prescribe old antibiotics on the basis of lab test, if they are sensitive to those bacteria. The practice should not be like they will prescribe newest drug always(Llor & Bjerrum, 2014).

1.3.1 Process of antibiotic resistance

As it is the bacteria which becomes resistant, it does not occur all on a sudden. At first, there will be some pathogenic bacteria in a host body (figure-1). There they will proliferate and will divide the cells. During cell division, some bacterial cell may get mutant (figure-1). At the same time, if antibiotics are applied, it will kill the bacteria, but during getting mutation in the presence of antibiotic, bacteria can produce resistance against that antibiotic (Alberts et al., 2002). It will kill pathogenic bacteria as well as good bacteria, but some bacteria will achieve resistance in their plasmid (figure1). That antibiotic will not affect that resistant bacteria, and these resistant bacteria can proliferate very easily. While dividing the cells or in proliferating time bacteria can easily transfer the resistant plasmid to the new cells as their genetic property. In this way, a particular population of bacteria can emerge, which will be resistant to that antibiotic. This emerged resistant bacteria could effect on other host so quickly as they are mutant and different than previous. So, the resistant plasmid will create

resistance against antibiotics for those bacteria. Thus, in this process, all the bacteria getresistant against a particular antibiotic (Cairncross et al., 2010).

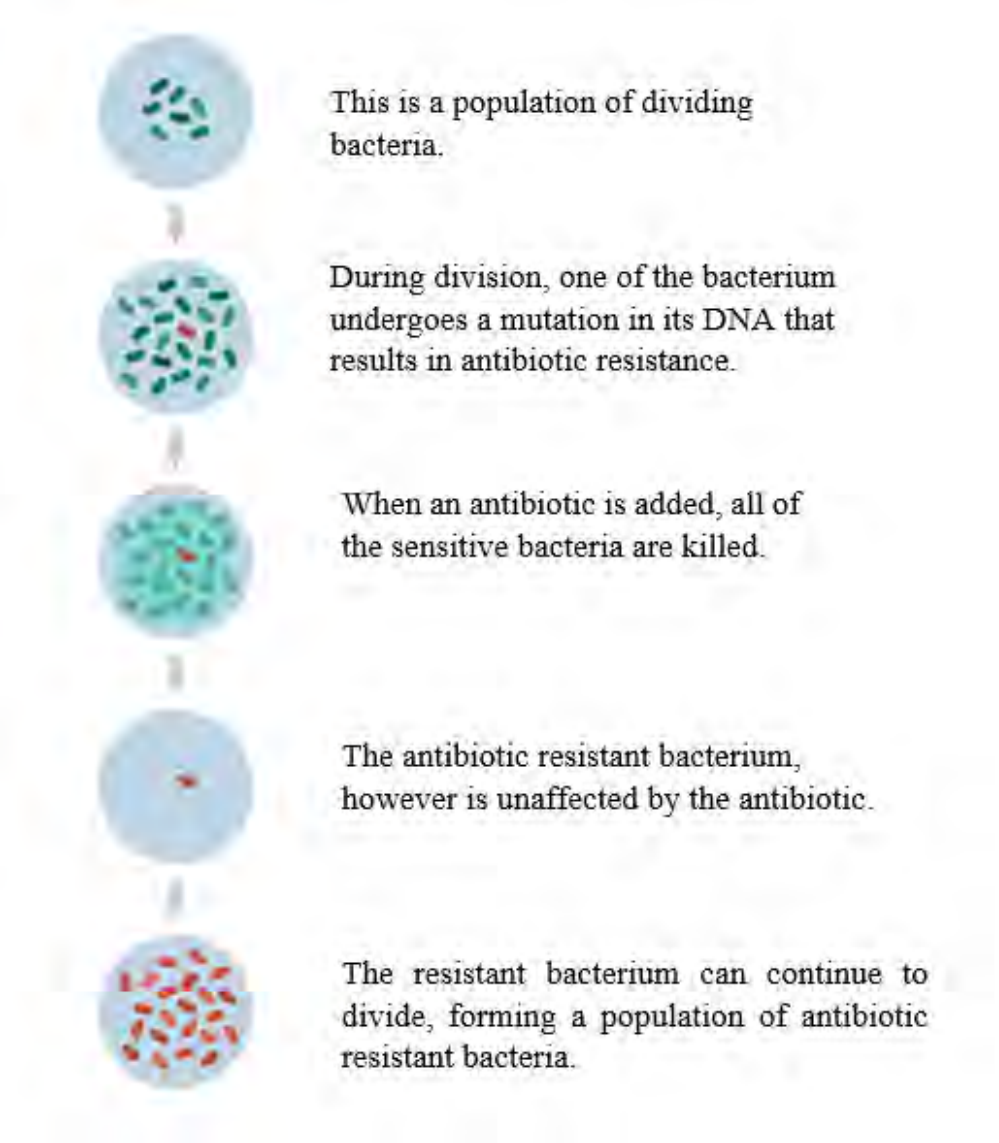


Figure 1.1: Process of antibiotic resistance (Adopted from: "What is antibiotic resistance? | Facts | yourgenome.org," 2016.).

1.3.2Spread-out of antibiotic resistance

How antibiotic resistance spread out, it could be described by a flowchart:

In the flowchart (Figure-2) it is shown that antibiotics are taken by either humans or animals and they produce resistance in their gut. In case of human, he might get care at home or in hospital, if he stays in hospital resistant bacteria may spread- out by him on the surface of

healthcare facilities and into other people. At the same time, he may spreads the resistant bacteria among the family member and on the meeting with mass population resistance could be spreads in society members. In case of the patient stays in hospital resistant bacteria can spread-out by the nurses, doctors or other patients staying in the hospital for (figure-2).

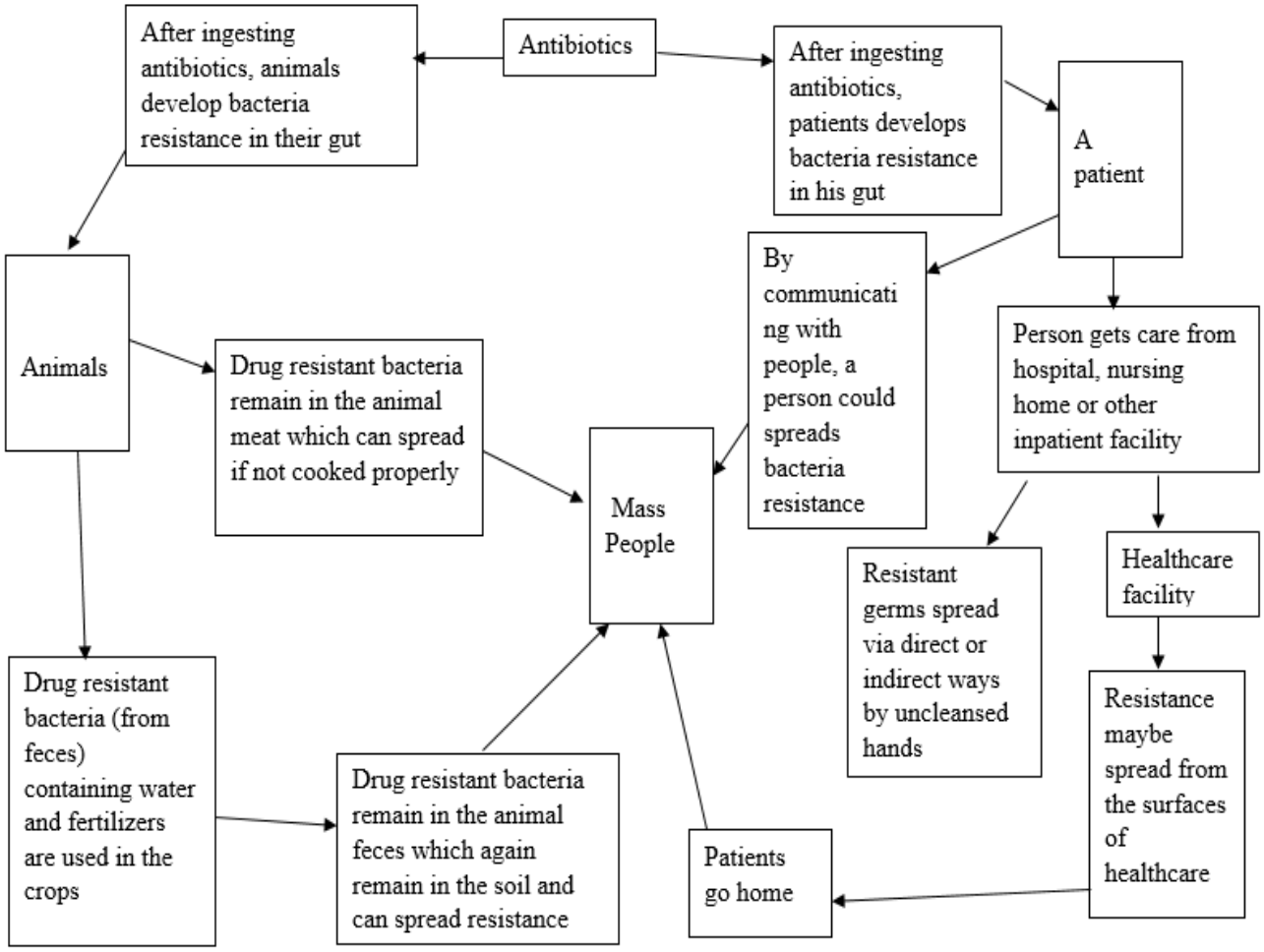


Figure1.2 : Flowchart of how antibiotic resistance spreads among mass people.(Adopted from: CDC, 2013)

Resistant bacteria can also spread by the surface of the health care facilities and equipment which will be used on other patients later on. In the flowchart (Figure-2), antibiotics are taken by animals they can also generate antibiotic resistance. Firstly, in case of eating those animals if we do not cook them properly resistant bacteria can spreads into us. Secondly,

those resistant bacteria could be spread into the soil, water and air from the feces and urine of those animals. By this way, these bacteria also could attack the normal animals and humans at the same time and thus antibiotic resistance spreads among the mass people(CDC, 2013).

1.4 Classification of antibiotic resistance

Antibiotic resistance in bacteria could be classified in two types:

1. Intrinsic resistance
2. Acquired resistance

Intrinsic resistance: Intrinsic resistance is a kind of natural development of resistance and it is the structural and functional features of particular bacteria. Some bacteria remain resistant without prior exposure to some antibiotics. As instance, vanomycin is an antibiotic which is a large molecule and it crosses the outer cell membrane, however gram negative bacteria are resistant to this. Aerobic bacteria are resistant to the antibiotics which act on anaerobic environment(Bhattacharjee, 2016).

Acquired resistance: In a population which bacteria are sensitive may acquire the ability to be resistant to some antibiotic, this is acquired resistance. Unlike intrinsic resistance, which is effective to some particular species, acquired resistance could be observed in a bacterial species subpopulation. Mainly it occurs in two ways: (1) By point mutation and (2) by resistance gene acquisition("about resistance — alliance for the prudent use of antibiotics," 2017).

Resistance developed by point mutation mainly occurs in two ways, first one is natural method and another one is induced method. In case of natural method, it is a natural change of bacteria, most of the time bacteria has the proliferation time around 20 min. So, they could be colonized in a billion number within a very short time. Before every cell division there is a chromosomal change where chromosomal DNA duplicates by a process DNA replication with the help of an enzyme named DNA polymerase which bind to the template DNA. As it is a very first process enzyme makes some mistakes during replication, though 99% mistakes are corrected by DNA polymerase but 1% may remain and each of the error may lead the bacteria to point mutation in addition with developing resistance. On the other

hand, in case of induced method point mutation occurs due to harsh environmental condition like, effect of chemicals, effect of radiations etc. This may not be related with antibiotic resistance in a host body, but recently it has been invented that antibiotic in a host body may generate point mutation among the infective bacteria. As it will induce the harsh environment for those bacteria(Bhattacharjee, 2016).

Resistance developed by gene acquisition is another way to get resistant. In this way the bacteria mainly spread out resistance to other, as already resistant bacteria transfers the genes to other bacteria. For example, penicillin the first antibiotic is already resistant to many bacteria because of a enzyme calledβ-lactamase which is produced by some bacteria and this gene could be transferred to other bacteria. There are three organisms can control the gene acquisition named plasmid, transposon and integrons. Plasmid which is a small extra chromosomal DNA piece remains in multiple copies and helps in replication by their protein. A plasmid could have multiple gene of resistance, though they does not carry any important function but they can easily transfer the genes during replication. After this, transposons which is another small part of a DNA that could insert into the chromosome which are mainly known as jumping genes. Transposons contains direct or inverted sequence which could transferred during DNA replication. Similar like plasmids transposons could have multiple genes of resistance to several antibiotics(Resistance, 1997).

Integron is another type of mobile genetic element which have additional ability to capture various genes such as, antibiotic resistant genes for multiple antibiotics. They do not have direct or indirect repeats rather they contain integrate gene that is important for insertion process. In addition, transfer of resistant genes between bacteria is a way of gene acquisition(Bennett, 2008). In genes transfer this could occur in several ways like bacterial conjugation, bacterial transformation and transduction. In 1946, Joshua Lederberg invented that in case of bacterial conjugationthe factor helps is known as conjugative plasmid which is capable to transfer resistant gene to other bacteria. In case of bacterial transformation, living bacteria collect DNA from outer place which is actually released by dead bacteria. Some bacteria can made artificially transformable resistant gene in the presence of chemical or radioactive frequency(Griffiths, Miller, Suzuki, Lewontin, & Gelbart, 2000). Lastly, transduction is the process where DNA transfers using bacteriophages as intermediate.

Bacteriophage is a kind of virus that infect bacteria and use their cellular properties, at this moment some bacterial gene can interfere with this and may become resistant through acquisition(Bhattacharjee, 2016).

1.5 Mechanism of antibiotic resistance

Prior to the mechanism of an antibiotic to a bacterium, mode of antibiotic action should be discussed, it is very clear that every medicine must met a environment or criteria to the specific place for action. Like this, an antibiotic has to meet common 3 criteria. They are- (1) a susceptible target in the cell for antibiotics, (2) antibiotics must reach in enough amount to the susceptible target, (3) antibiotics must be active(Chopra & Roberts, 2001).

Where the antibiotics exert their effect in bacteria can indicate the proper mechanism of that how resistance can occur. Generally, there are five major modes of mechanism of antibiotics. The mechanisms are: - (1) Interference with cell wall synthesis (2) Target modification (3) Antibiotic inactivation (4) Resistance by active efflux or pumping out (5) Resistance by ribosome protection (6) Resistance by biofilm formation(Munita et al., 2016).

1.5.1 Interference with cell wall synthesis

In case of β-lactam antibiotics such as penicillin and cephalosporins they act on the bacteria through cell wall synthesis.B-lactam antibiotics act with peptidoglycan which is an enzyme for cell wall synthesis. Glycopeptides, such as vanomycin, oritavancin etc target the bacterial cell wall by binding with D-alanyl-D-alanine termini of the peptidoglycan chain preventing cross linking chain steps. In case of these kind of antibiotics, bacteria make themselves resistant through inactivation of antibiotics by hydrolysis. This is a process of inactivation, basically bacteria can prevent the antibiotic to enter into the cell to save themselves. In case of gram negative bacteria, the cytoplasmic barrier of cell wall is a hydrophilic compound, to cross this kind of cell wall a firm channel is needed. Which is catalyzed by porins, so due to lack of porins many of antibiotics cannot enter into some bacteria (Bockstael & Van Aerschot, 2009).Gram positive bacteria form cell wall with the help of peptidoglycan by binding C-terminal-acyl-D-alanyl-D-alanine (acyl-D-Ala-D-Ala)-containing residues in peptidoglycan precursors. Here, resistance is achieved by altering the target site by changing the peptidoglycan and C-terminal(Dzidic, Suskovic, & Kos, 2008). This is indicated by cell wall impermeability (Figure-3). If the antibiotics are not able to

cross the barrier that means bacteria have achieved resistance to those antibiotics. This is most common resistance mechanism in case of gram positive and gram-negative bacteria(Dzidic et al., 2008).

1.5.2 Target modification

Target modification is one of the way to alter the attacking target of anti-microbial agent. For example, DNA gyrase which is a target site for quinolones, RNA polymerase which is a

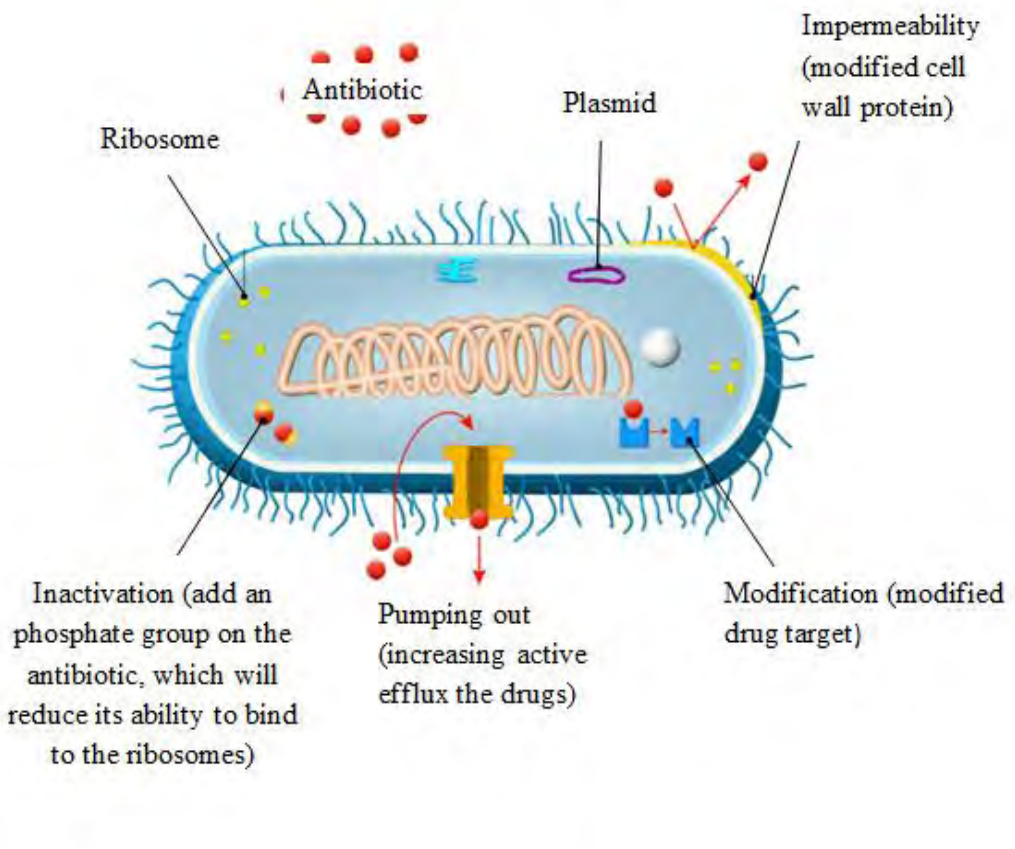


Figure 1.3: Mechanism of resistance to different antibiotics in different ways(Adopted from: "Antimicrobial resistance. Uit hospital - 66421906," n.d.)

target site for rifampin, prokaryotic ribosome- target site for tetracyclines and so on could altered any time if bacteria achieve the ability to do so. In case of β-lactam antibiotics bacteria also can alter the target site for the chemical agent such as *Staphylococcus aureus*, a serious agent forvarious kind of infective disease can achieve resistance through the modification of target site(Sanath Kumar & Varela, 2013).This is the second most common

mechanism to get resistance because the antibiotics cannot dispense its full activity without the proper target.Thus, mutant bacteria change their target site to save themselves. However, this is possible to change or get mutation without effecting the regular cellular function in a bacterium to achieve the susceptibility. This mechanism is indicated as modification (Figure-3), which means drug cannot reach to the actual target site in a bacterial cell due to the alteration or modification of the specific target(Sanath Kumar & Varela, 2013).

1.5.3 Antibiotic inactivation

The defense mechanism of bacteria is also initiated by antibiotic inactivation including the production of enzymes which degrade the antibiotic or change the drug itself. These biochemical strategies are hydrolysis, redox mechanism, and group transfer (Dzidic et al., 2008).

Several antibiotics get destroyed by hydrolysis or by the effect of some enzyme; they get destroyed before reaching to the acting site. B-lactamase one of the one of the hydrolytic amidase breaks down the β-lactam ring in case penicillin and cephalosporin antibiotics. Many gram-positive and gram-negative bacteria can produce this enzyme, till now more than 200 different β-lactamase enzymes have been found. So, they will break down the β-lactam ring according to the mechanism. If this occurs, the antibiotic will not be able to cross the cell wall (Dzidic et al., 2008).

Group transfer, which is another mechanism of antibiotic inactivation. This is done by the enzyme group of transferases. Transferases are the most diverse and largest enzyme for resistance; these enzymes modify the structure of antibiotic that impairs the target binding. Chemical strategies include O-acylation and N-acylation, O-phosphorylation, O-nucleotidylation, O-ribosylation, O-glycosylation, and thiol transfer. These modification strategies all required for activity, including ATP, acetyl-CoA, NAD+, UDP glucose, or glutathione.Consequently, these enzymes are only active in the cytosol. In this case, these enzyme mainly transfer or alter the functional group from the structure of the antibiotic. Bacteria most commonly apply acetyltransferases for inactivation of the antibiotics. Aminoglycoside acetyltransferases is a kind of acetyltransferases that is implied on the antibiotics (Wright, 2005).

There is another way for inactivation of the antibiotic and that is redox mechanism. In case of redox mechanism, reduction or oxidation process is infrequently exploited by pathogenic bacteria. For example, tetracycline could be inactivated by oxidation process. *Streptomyces virginiae,* which is a producer of *virginiamycin M1*protect itself from its antibiotic by reducing a ketone group from the antibiotic(Dzidic et al., 2008). The whole mechanism is indicated as inactivation of antibioticsby adding of a phosphate group but basically there are several ways of inactivating the drug (Figure-3).

1.5.4 Resistance by active efflux or pumping out

Mc Murry and colleagues, in 1980 first discovered that bacteria could acquire resistance through extruding antibiotics. Bacteria have plasmid-encoded proteins capable of extruding or efflux drug like tetracycline. Though the mechanism is novel, it is acquired by horizontal resistant gene transfer. Nevertheless, later on, it was invented that bacteria can also achieve multidrug efflux mechanism and several species can conserve this kind of resistance (Blanco et al., 2016). There are two kinds of the active efflux pump, one is primary active transport, and another one is secondary active transport. Primary active transport uses the mechanism of hydrolysis of ATP to pump out the drug from the cell while secondary active transport is followed to the mechanism of ion gradient for active efflux drug from the cell. In addition, in the case of single drug pumping bacteria can also express the character of pumping out multiple drugs, these multiple drugs are structurally different antimicrobial agent which is referred to multidrug efflux pump. Efflux pumping out is not shown separately rather it is marked as pumping out (Figure-3). Bacterial cell gets energy from the cation gradient by cellular respiration, and this process is known as “antiport” where cations move in one direction over the membrane and drugs move on the opposite direction. Since the secondary active transport or multidrug are achieved eventually after the primary active transport, this is the primary mechanism of active efflux or pumping out (Sanath Kumar & Varela, 2013).

1.5.5 Resistance by ribosome protection

In figure-3 ribosomes are shown, by protecting these ribosomes in the bacterial cell some of the species get resistance. There are several bacteria have developed resistance through protecting the ribosomal protein. Such as, to be safe from tetracycline bacteria can have the ability to generate ribosome protection protein that bind to the ribosomal target and can

prevent the binding of tetracycline to the ribosome. Such bacteria could be disease causing bacteria in the presence of tetracycline(Nguyen et al., 2014).

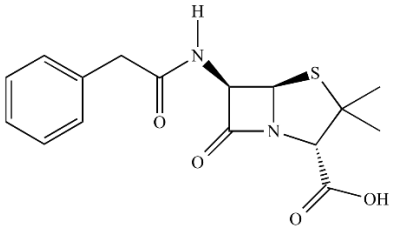
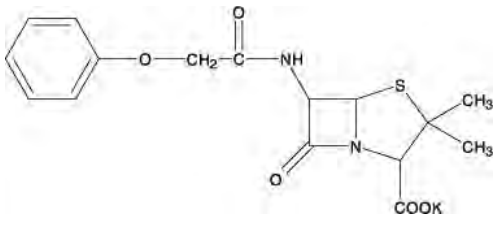
1.5.6 Resistance by biofilm formation

Biofilm is complex structure that continuously remains in touch of water, and this is formed when microorganism secrets some mucilaginous protective coating. This occurs in the colony of microorganisms such as bacteria or fungi. Basically, biofilm production occurs in different loci, like teeth plaque, water environments, medical catheters, trauma wounds, etc. Normally biofilms are formed on a liquid or solid surface in addition to living tissue, and thus it shows, so aspects of having a category named "viscoelastic." They are extremely heterogeneous in nature, and they have several observation like, they have diversity in every colonies, they have different chemical properties and structures. Thus, forming biofilm bacteria could be ineffective by any drug and gain antibiotic resistance (Butt & Khan, 2015).

1.6 Classification of antibiotics

Antibiotics could be classified in so many ways but the common scheme is based on their molecular structure. Here, antibiotic would be classified according to their structure and mode of action. Here, R/M means resistance mechanism of antibiotics how it works on the bacterial cell.

Table 1.1: Classification of penicillin with resistance mechanism(Allen et al., 2013).

Type	Name	Structure	R/M
Natural	Penicillin G		Enzymatic destruction/ Altered target
	Penicillin VK		Enzymatic destruction/ Altered target

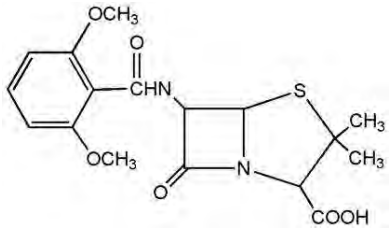
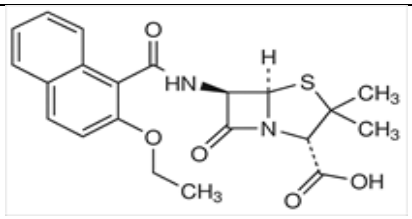
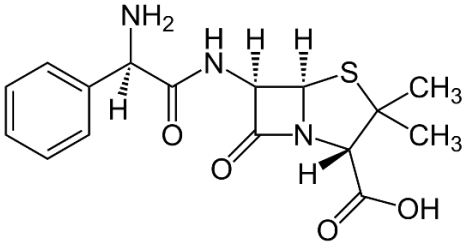
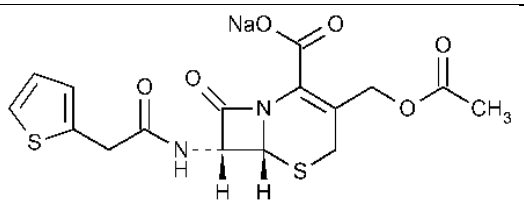
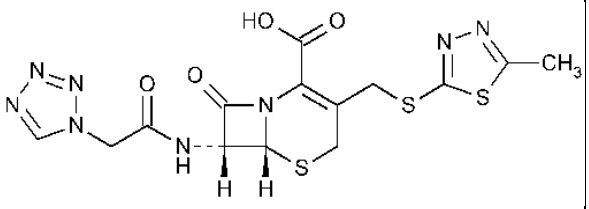
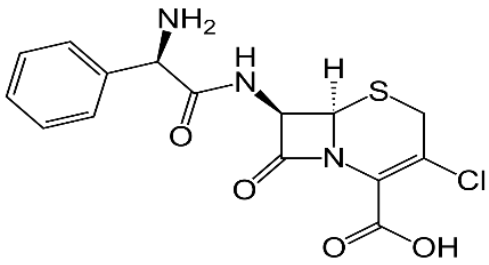
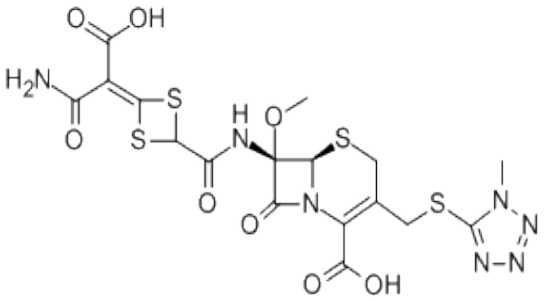
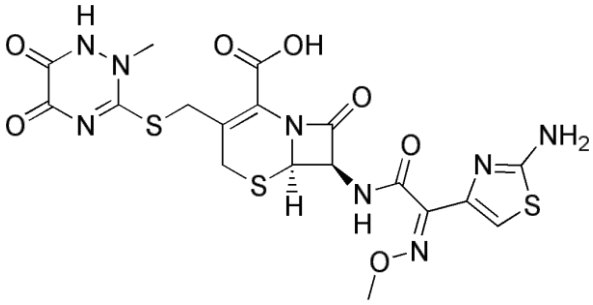
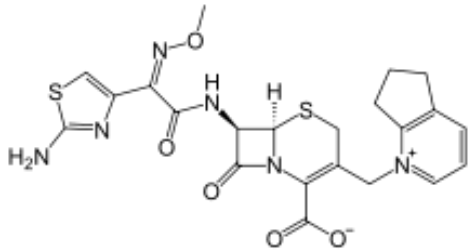
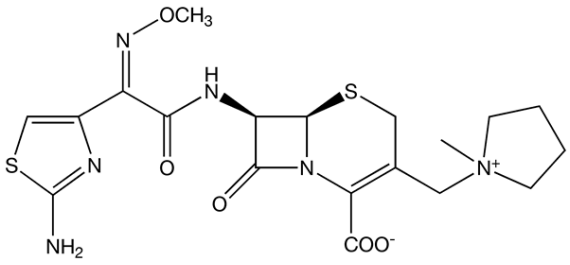
Type	Name	Structure	R/M
Penicillinase resistant	Methicillin		Enzymatic destruction/ Altered target
	Nafcillin		Enzymatic destruction/ Altered target
Amino ampicillins	Ampicillins		β-lactamase inhibitor/ Altered target

Table 1.2: Classification of cephalosporins with resistance mechanism(Mehta, 2015).

Type	Name	Structure	R/M
1st generation	Cephalothin		Impermiability / β-lactamase inhibitor
	Cefazolin		Impermiability / β-lactamase inhibitor

Type	Name	Structure	R/M
2nd generation	Cefacor		Impermiability / β-lactamase inhibitor
	Cefotetan		Impermiability / β-lactamase inhibitor
3rd generation	Ceftriaxone		Impermiability / β-lactamase inhibitor
4th generation	Cefpirome		β-lactamase inhibitor (not significantly found yet)
	Cefepime		Impermiability / β-lactamase inhibitor

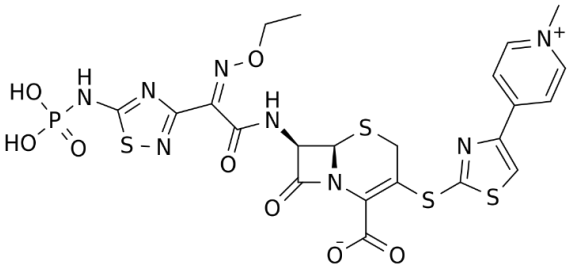
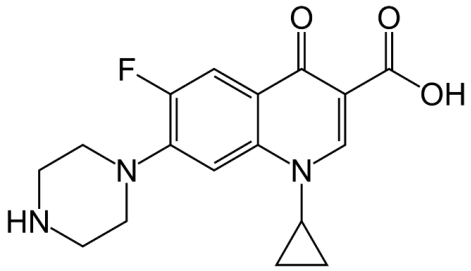
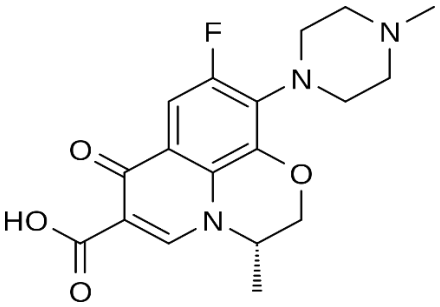
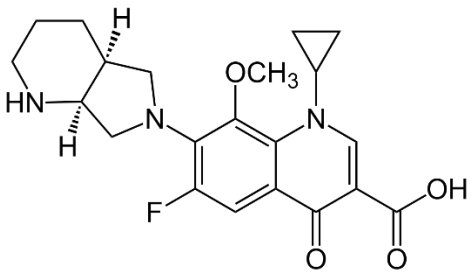
Type	Name	Structure	R/M
5th generation	Ceftaroline		β-lactamase inhibitor (not significantly found yet)

Table 1.3: Classification of fluoroquinolones with resistance mechanism(Allen et al., 2013).

Name	Structure	R/M
Ciprofloxacin		Decreased uptake
Levofloxacin		Decreased uptake
Moxifloxacin		Decreased uptake

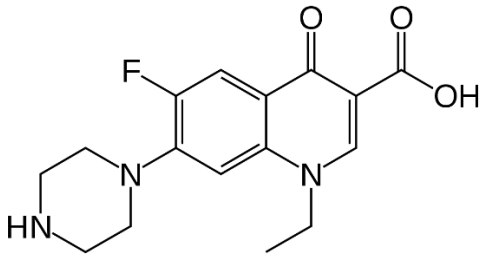
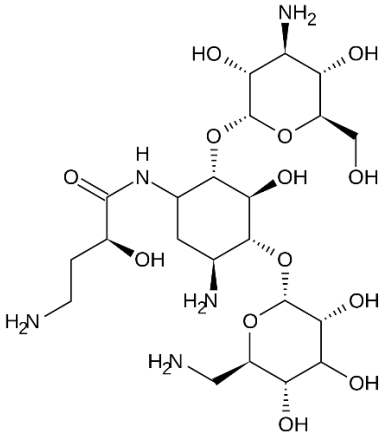
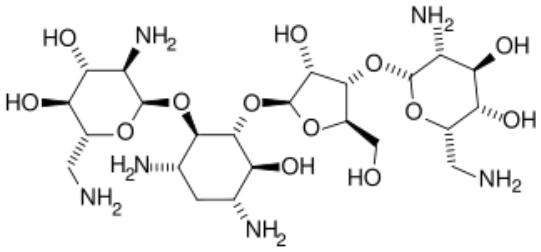
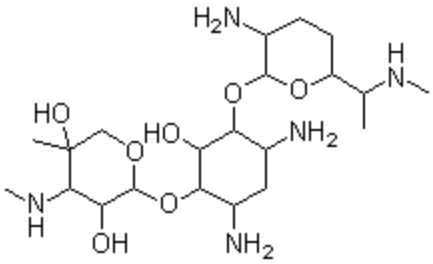
Name	Structure	R/M
Norfloxacin		Decreased uptake

Table 1.4: Classification of aminoglycosides with resistance mechanism(Zhdanovich & Nasonova, 1997):

Name	Structure	R/M
Amikacin		Enzymatic modification/ Altered target
Neomycin		Enzymatic modification/ Altered target
Gentamycin		Enzymatic modification/ Altered target

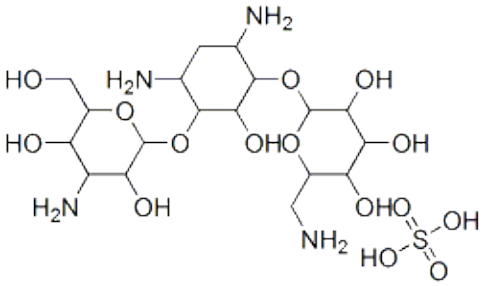
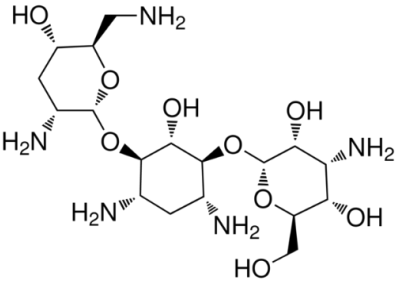
Name	Structure	R/M
Kanamycin		Enzymatic modification
Tobramycin		Enzymatic modification

Table 1.5: Classification of monobactams with resistance mechanism(Allen et al., 2013).

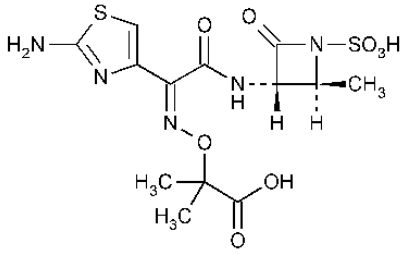
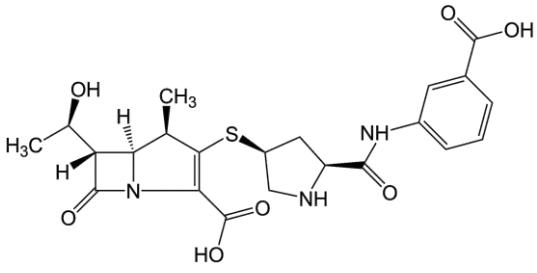
Name	Structure	R/M
Aztreonam		β-lactamase inhibitor

Table 1.6: Classification of carbapenems with resistance mechanism(Allen et al., 2013).

Name	Structure	R/M
Ertapenem		β-lactamase inhibitor

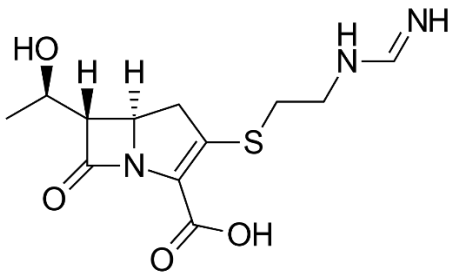
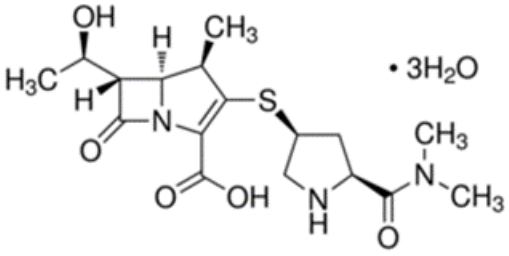
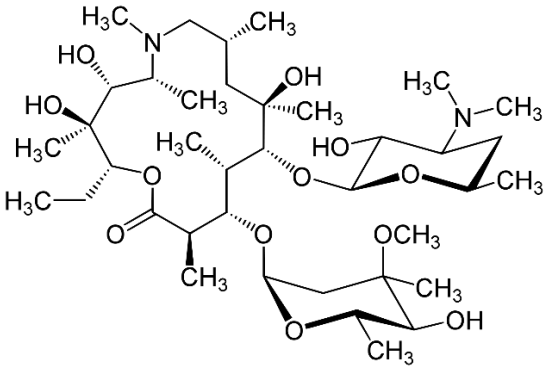
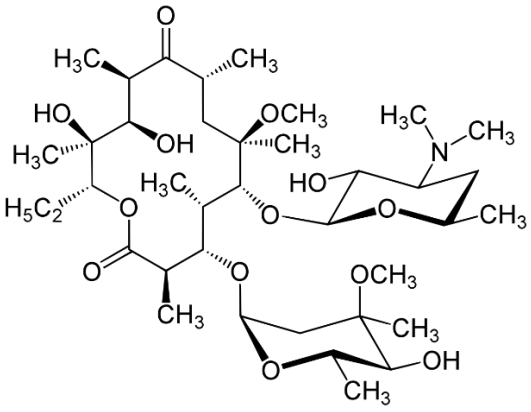
Name	Structure	R/M
Imipenem		β-lactamase inhibitor
Meropenem		β-lactamase inhibitor

Table 1.7: Classification of macrolides with resistance mechanism(Allen et al., 2013).

Name	Structure	R/M
Azithromycin		Enzymatic modification/ Altered target
Clarithromycin		Enzymatic modification/ Altered target
Name	Structure	R/M

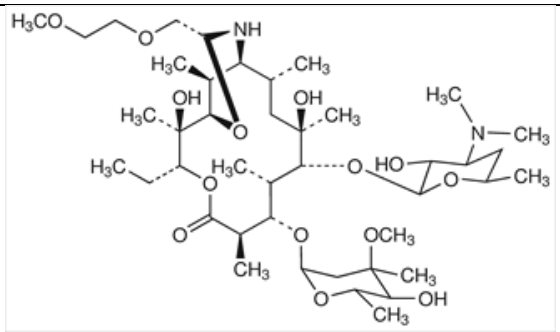
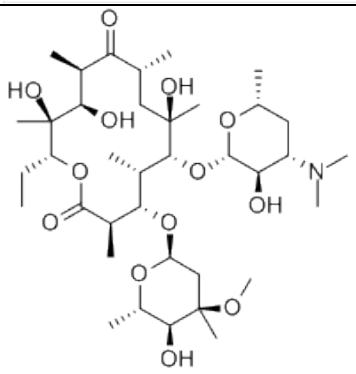
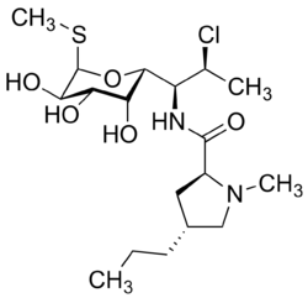
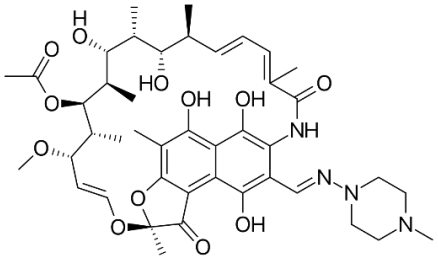
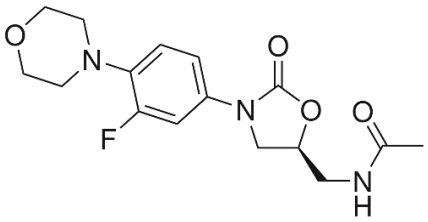
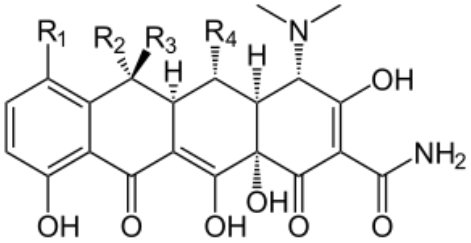
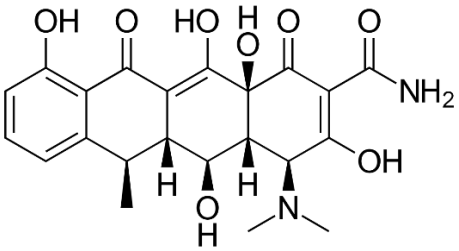
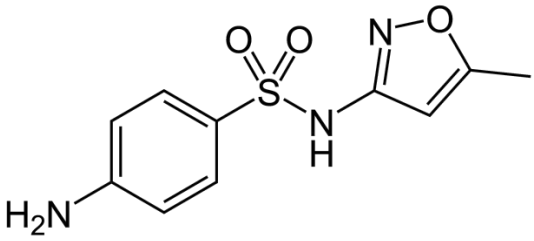
Dirithromycin		Enzymatic modification/ Altered target
Erythromycin		Enzymatic modification/ Altered target
Clindamycin		Enzymatic modification/ Altered target

Table 1.8: Some other antibiotics with resistance mechanism(Allen et al., 2013).

Name	Structure	R/M
Rifampin		Antibiotic inactivation/ Efflux pump out
Name	Structure	R/M

Linezolid		Antibiotic inactivation/ Efflux pump out
Tetracycline		Antibiotic inactivation
Doxycycline		Antibiotic inactivation
Sulfamethoxazole		Antibiotic inactivation

1.7 Regulations of antibiotic

As antibiotics are cytotoxic or cytostatic for the bacteria and it allows body defense such as immune system to eliminate the bacteria from the body it has some mechanisms and processes with the system of the body. Which can affect the body, that's why there are some need of regulations of antibiotics. Millions of metric ton antibiotics of different classes are produced over last 60 years. Across to many sectors and fields which are in need of antibiotics, these are allowed in very cheap price and on a simple drug label. That's why there are some need of regulations and rules (Llor & Bjerrum, 2014).

Congruent international management guidelines for daily antibiotic practices are yet unavailable. Hence, with various country regulations of antibiotic vary everywhere. Some countries acted for this very swiftly such as, United Kingdom (UK) on the other hand some countries do not have any kind of guidance. WHO (World Health Organization) offered some recommendations internationally such as, for developing countries, there antibiotic should not be used for children, it could be used only in severe or bloody diarrhea and cholera. Since, the evolution of drug industry several millions of wastages mixesinto streams, rivers, oceans, lands, and air. There are antibiotics and its wastages too. So, there are guidance for the industries to safely dispose of the materials and others. Yet it is not done and maintained strictly. At the same time some cleansing product like home hygiene product and others are more likely to dangerous to cause resistance for the microorganisms(Zaman et al., 2017a).

With enough evidence, there are no scopes to overlook antibiotic resistance and need of a regulations regarding using these drugs. Antibiotic resistance is higher where the consumption of antibiotics are more prominent and high. Due to lack of regulations, in the developing countries these problems are higher. In those countries people take antibiotics without any prescription and medicine shop sell antibiotics without any guide line. It is more uncontrolled where the universal health coverage for its citizen is not done. In United Kingdom 11.3% patient reported that they did not completed the medication course, among them 65% said that when they felt better they stopped to taking medicine(Zaman et al., 2017a). So, this percentage is pretty much higher in developing countries. We are altogether influenced by this multi-faceted general medical problem. A widely inclusive issue that doesn't simply relate to clinical faculty and microbiologists, industry partners, authorities and the overall population. A way should be find out to handle this problem. Social mindfulness, inspiration, duty in dependable areas, stringent standards and control must be organized. Furthermore, coupled activity may require for the best possible use of antibiotic agents, best administration should be rehearsed (Zaman et al., 2017b).

Notably, irrationality is observed in using antibiotics in livestock. Animals are given antibiotics for faster growth and disease prophylaxis. Strict and enforced regulations in the agricultural industry are needed to curb the harmful ripple effects. The situation is getting

worst day by day. Hence, multi-drug resistance is common so, treatment failure is increasing in rate. Newer and updated antibiotics which are in high demand as they are unknown to the bacteria should use in controlled way and properly regulated. Alternative treatment procedure should be brought under consideration such as passive immunization and administration of immunizing agent have been found fruitful. Most importantly, combination therapy should be highlighted with couple antibiotic to face antibiotic resistance(Chang et al., 2015).

1.8 Antibiotic resistance threats impact

Impact of antibiotic resistance is very important and it is various kind of to describe. This can cause impact on us by physically, mentally, socially, economically and so on. The main impacts are(Dickes L et al., 2015): 1. Poor patient outcomes 2. More potent disease states 3. Higher rates of mortality 4. Greater need for combination therapy 5. Increase in the rate of treatment failure 6. Increased cost of treatment(Dickes L et al., 2015).

1.8.1 People who are at more risk

In general there are certain group of people who are always at high risk of infection. Which means, they are also at a very high risk of antibiotic resistance. People who are at more risks includes("Effects of antibiotic resistance - Canada.ca," 2015):

- Children, specially pre-mature babies who are in lack of a good immunization power.
- Senior citizens, particularly those who are living in long term health-care facilities.

  Because of:
  - they are exposed to more infectious area.
  - they remain close to other patient or infected people.
  - may have very weak immune system due to long term illness or infection.
- People who are homeless or lives in a very crowd place like slums they are more likely to get infection from others.
- People with weak immune system due to illness or injury("Effects of antibiotic resistance - Canada.ca," 2015).

Based on behaviors and social position group of people includes ("Effects of antibiotic resistance - Canada.ca," 2015):

- People who works in healthcare facilities and in day care centers
- People who do not practice good infection prevention and control behaviors like hand hygiene,
- People who do not store, handle or prepare food safely,
- People who have occupations that put them at a greater risk for exposure to bacteria or infectious diseases such as:physicians,veterinarians,nurses,slaughter house and meat processing plants workers, andFarmers("Effects of antibiotic resistance - Canada.ca," 2015).

1.9 Scale of antibiotic use

1.9.1 Scale of human antibiotic use

It is human who uses antibiotics most. As, antibiotics were invented to cure the infection of humans, later on, it was introduced for other animals and other uses. In a statistic, it was found that In 2013, the total measured consumption of antibiotics in England was 27.4 DDD per 1000 inhabitants per day [general practice 79%, hospital 15% and other community consumption (predominantly dentists) 6%], in line with the median across Europe in 2011 of 21.3 median DDD per 1000 inhabitants per day (Singer, Shaw, Rhodes, & Hart, 2016).

In 2010, India was the largest consumer of antibiotics assessing total tonnage. However, their per capita usage was low by comparison to Australia and New Zealand which recorded among the highest usage rates of 87 and 70 units per capita(Singer et al., 2016). In these studies, an antibiotic unit is considered as a dose of the antibiotic. China was the second largest consumer of antibiotics in the world. Heterogeneity in anti-microbial utilize is recreated at apparently every topographical scale. For instance, settled inside the more significant worldwide contrasts are contrasts between nations inside littler locales. In addition, to there being substantial contrasts between nations inside locales, there are huge contrasts in antibiotic use inside nations (Singer et al., 2016).

1.9.2 Scale of animal antibiotic use

With the human now a days uses of antibiotic increased at a very high rate for the animals. In a statistic it was found that each year two-third of antibiotics are used for animals from total production. The changeability between nations in veterinary antimicrobial use in nourishment creating creatures just inside the high pay nations can be noteworthy(Singer et

al., 2016). So, it is notable that in developed countries they use more antibiotics rather than the developing countries. It is true that antibiotic is mandatory for the good health and welfare of the animals as they could not take any precaution by themselves. Antibiotics are often given to animals for prevention of the infection. It is mixed with the water or food that are given to the animals as it is difficult to isolate the infected one and treat that. In addition, isolating of animals could be dangerous and stressful for the animal also(Cheng et al., 2014).

The use of antibiotic as a growth promoter is banned in Europe but it is increasing day by day in developing countries due to lack of regulation(Carbon et al., 1998). It is dilemma that should people use antibiotic for animals or not. As, if it is used antibiotic resistance will increase with a high speed on the other hand if it is not used animals will die and enough food production won't be possible. So, it would be better if use of antibiotic could be control in case of veterinary use with rules and regulations to save the human and animal at the same time(Singer et al., 2016)

1.10 Global scenario of antibiotic resistance

In a statistic researchers have found that more than 2 million people get infected by antibiotic resistance and around 23,000 people die each year because of the results of antibiotic resistance in USA("Antibiotic Resistance Threats in the United States, Antibiotic/Antimicrobial Resistance | CDC," 2013.). Now a day, antibiotic resistance is increasing on a dangerous rate. Before discussing about antibiotic resistance, we should know about antibiotics. Bacteria are found in soil, air, water and even on animal bodies. It is bacteria not the humans who get resistance, and many of the bacteria harm the human body by infections where antibiotics fight against them. Thus, to save themselves microbes acquire antimicrobial resistance("Infections – bacterial and viral - Better Health Channel," 2013).

Threat of antibiotic resistance is not only for developing countries, in developed countries it causes national loss with the suffering of general patients. From a study over prescribing pattern it were found that 50% prescription for outpatient in USA and 57-73% prescription for upper respiratory infectious patient in Australia were inappropriate which causes resistance with a loss of 75 million- 7.5 billion US dollar each year(M. Rahman & Atma, 1998). This is the scenario of developed country what would be in developing country? In

Bangladesh widespread and inappropriate use of antibiotics results development of antimicrobial resistance in microbial ecosystem of this region. For example, 98% from 243 *Shigelladysenterae* type 1 are already resistant (Rahman & Atma, 1998). From this kind of information, this is suggested that people of developing countries are at more risk than others due to the healthcare facilities (M. Rahman & Atma, 1998).

Because of evolutionary natural selection process of antibiotic resistance will go on, but misuse and overuse of antibiotic accelerate the resistance. Resistance of microbes are acquired by them through different ways. Though the mechanism of getting resistance is more or less similar but the reason behind this different. However, in developing countries it occurs mostly for random prescribing for antibiotics which may lead to wrong antibiotic resistance, random use or purchasing of antibiotics, uncontrolled use of antibiotics in poultry and fisheries feeds etc.(Abdelhalim & Ibrahim, 2013).

1.11 Scenario of antibiotic resistance in Bangladesh

Antimicrobial resistance one of the major threat to human being. Though antibiotic resistance is a global problem all over the world but the spread out rate of antibiotic resistance can be assumed by the behavioral antecedents and socioeconomic complex in a particular place such as developing countries like Bangladesh. In this case, the contributing factors easily access to effective drug, truncated use of antibiotics, unregulated manufacturing and dispensing of antimicrobial drugs and overall poverty (Faiz & Basher, 2011). In hospitals and clinics most commonly prescribed medicine groups are antibiotics. Despite the developed healthcare facilities, infectious diseases are the prior problem in developing countries, where practitioners along with the patients prefer widespread use of antimicrobials to treat fungal, viral, bacterial and parasitic infections. This indicates the rising threats to the people to develop resistance. Though prescribers now a day try to diagnose the symptoms by clinical assessment to suspect a microbial etiology to prescribe medicine rather than prescribing based on best-guess. Here, the factors associated with resistance are over-population, lack of hygiene in healthcare facilities, lack of resources and lack of knowledge and training to control infections in hospitals and other places (Faiz & Basher, 2011).

Researchers have found that, in Bangladesh, antibiotics are prescribed mostly in cases of acute watery diarrhea,acute respiratory tract infections, acute trauma and gastrointestinal symptoms. But the serious issue is 67% of hospitalized patients in Bangladesh receive antibiotics, even though at least 50 % cases they were not required, researchers ofJohns Hopkins University stated this ("Bangladesh and its struggle with antibiotic resistance - SNIH," 2016.).

Almost 80% people of Bangladesh lives in rural area therefore, there is huge chances these people are consulted by quack or fake doctors. So, they prescribe antibiotics without having any kind of knowledge of it ("Bangladesh and its struggle with antibiotic resistance - SNIH," 2016.). Another have shown that *E. coli* is more common bacteria for infection (almost 40%) and the reasons behind increasing antibiotic resistance are uncertain diagnosis and emergence of highly resistant bacteria (M. S. Rahman & Huda, 2014).

1.12 Literature review

Review of literature is associate part of doing research, as there may some guideline and parameters which shows the significance of the area of the research. There are not so many research related to antibiotic resistance of *E. coli*.

In Bangladesh, BSMMU's researchers conducted some research but most of them are for hospitalized patient or from non-living object. Sanjee, Karim and others in a research have mentioned about the UTI infection which is because bacteria and in that study *E. coli* is a common bacterium. They have mentioned females are more prone to this kind of infection(Sanjee et al., 2017).

In another study Afroz, Sultana and othershave found that non-living object such as foods may contain *E. coli* and thus may create resistance in human body. As, they are from various source and are of various pattern. They researched in dry milk to find the ratio of *E. coli* resistance(Afroz, Khan, & Datta, 2014).

In case of international researches that contains a vast area like several countries, Stelling, Travers and others have a research on *E. coli* resistance in the areaof North America, Latin America, North Europe, Africa and West Pacific. There they have found different result on different areas such as cefepime is more resistant toin Argentina and

Brazilwhereasdecreasing susceptibility to the area of Belgium, Canada, Colombia, and the United States(Stelling et al., 2005).

The importance of the study regarding antibiotic resistance is a must as it is now becoming an alarming threat to the modern era. Antibiotic resistance nowadays becomes a global threat in the field of health security (Utt, Wells, 2016). In the era of modern medicines, the issue of antibiotic resistance threatens all of our positive outcomes (Utt, Wells, 2016).

The term antibiotic resistance develops when any microorganism is not destroyed by the use of any specific drug thus it becomes sensitive. The leading causes behind this are the misuse or overuse of drugs (Utt, Wells, 2016). In that case, if the rate goes high of the antibiotic resistance, then it will turn into a devastating situation for us. So, there is a real need for analyzing all the issues and give importance and try to solve the issues regarding antibiotic resistance (Utt, Wells, 2016). Leading to a serious infection antibiotic resistance can be a life-threatening issue (Anderson, 2017). A core reason behind bacteria becoming resistant is because of inappropriate use of the antibiotic for an illness caused by any viruses. Some of the diseases that can be caused by the virus are pharyngitis, colds, coughs, infection of sinus, infection in the respiratory tract, influenza virus, etc., and these illnesses are basically, and there is no need to take any particular medications. Use of antibiotic without concerning doctor is a dangerous threat for us, and thus antibiotic resistance occurs (Anderson, 2017).

There is a lack of the development of antibiotic in different classes, thus creates a significant problem also. A drug which shows resistance to any drug, there is a very high possibility that it might be resistant to some other drugs of the same class. Though there are many factors responsible for this, primarily – economic burden and the long process of regulatory issues are the main reason responsible for antibiotic resistance (Utt & Wells, 2016).

Staying up to date regarding vaccination is also a primary concern. Vaccines may sometimes treat bacterial diseases that might sometimes be treated with the antibiotic. A patient while receiving antibiotic must know fully about resistance and effective drug use. These issues are fundamental to know for limiting antibiotic from becoming resistant (Anderson, 2017).

Surveillance studies regarding antibiotic resistance can be beneficial as it can provide information that can be used to cause behind pathogen incident and antimicrobial resistance.

It also helps to identify pathogens that are emerging nationally and globally (Masterton, 2018). Knowledge regarding the mechanisms of antibiotic resistance are very crucial for understanding that how we use these drugs to treat patients, how effective the resistances control strategies and how to reduce resistance emergency (Bonomo & Maria, 2008). The practical approach to stop misuse of antibiotic drugs can be monitoring of antimicrobial drugs and its uses that further help us to identify specific trends concerning dosing, thus preventing the development of antibiotic resistance (Masterton, 2018).

To stop the antibiotic becoming resistant, healthcare professionals, as well as patients, need to take some necessary steps. The illness that causes by a virus such as a cough, cold or flu, the patient should not take any medication without any concern of the doctor.The patient should not take antibiotic by own or antibiotic that is prescribed for some other patient. Patient also should not share their specific antibiotic with others, and the leftover antibiotics should be discarded. Patient should not use one prescribed antibiotic for other diseases because of some reasons (Anderson, 2017). These are discussed below:

- This may not be the right antibiotic for treating the specific infection.
- This may turn into an ineffective condition.
- It may be expired concerning the date, and thus the quality is already degraded.
- Antibiotic must be given in a course wise, and there may be not enough medication available for completing a course.
- If the infection is not treated entirely then, it can cause harm to other people as well.
- The new sickness that the patient has that may be because of a viral attack and antibiotic, in that case, is for no use (Anderson, 2017).

The patients should always abide by all the information and rules that the doctors instructs to follow such as the antibiotics are always given in a course wise, and one must be fulfilled the course to proper diagnosis of the disease. If a disease can be treated by taking some of the medications, the patient must have to take all the drugs that doctor prescribed so that the microbes that are responsible for that specific disease can be wholly destroyed (Anderson, 2017).

Chapter 2: Objectives and Methodology

2. Objectives and methodology

2.1Objectives

The primary objective of this research is to identify the *E. coli* developing resistance, to know the classes of antibiotics against which, resistance has emerged and to assess the possible factors that can favor the development of antibiotic resistance. In addition, to know about which population have more resistance, to know about the age group that are more susceptible to antibiotic resistance and to compare among the different age group about antibiotic resistance.

2.2 Methodology

2.2.1 Research design and methods

Sensitivity pattern of the microbe (*E. coli*) was isolated in the microbiology department in the lab of a renowned diagnostic center in Dhaka, Bangladesh. All these specimen were isolated during March-June month, 2017 in the lab. There were no questionnaires for the patient to conduct this research. All these data are secondary, which means these are the test reports of the laboratory. These data contain the information of number of patient identified, number of age group, number of antibiotic tested against the specimen collected in the laboratory, pattern of sensitivity of the medicines against microbe.

Data were randomly collected from the laboratory and later on it was classified according to the pattern of medicine tested for sensitivity. Beside this data were divided according to the place that were collected. In the laboratory from where these data were collected they receive sample from various place of the country within 12-16 hours after sampling and performed the necessary tests.

The laboratory from where data were collected they follow disc diffusion method for convenience, efficiency and cost. A growth medium is introduced (usually agar) throughout the plate with a standard concentration. Commercially impregnated discs of particular antibiotic are evenly dispensed and pressed against the agar plate and the test immediately starts. After the overnight incubation, bacterial growth around each disc is observed. The zone has no growth is referred as the zone of inhibition. These zone are then measured and compared to a standard interpretation chart used to categorize the sample as susceptible or

sensitive, intermediately susceptible and resistant. MIC measurement is not determined from this test as it is a qualitative test.

Before collecting the data, all the required permissions were taken from the appropriate authority of the diagnostic center. The study protocol was approved by the authority of the diagnostic center. In addition, all kind of privacy and protection were ensured about the patient and diagnostic center.

2.2.2 Data collection

In case of data collection, firstly all the required permission were taken. As these data contain some personal information, these data were collected with care and confidentially from the diagnostic center. There the authorized officer co-operated to get the appropriate data and to print in their printer. Finally, all data were printed in paper within several days.

2.2.3 Data analysis

Metastatic data analysis is done by SEM method reporting significance in comprised of analyzing of data using Microsoft office excel (2016) and Graphpad Prism software (version 7.0), STRATA(version 8.0) and SPSS (version 23).

Chapter 3: Result

3. Result

Here, the analysis was done on different perspective. Firstly the population was divided in male and female in all the divisions and into different ages. Again, sensitivity of antibiotics in different divisions are observed and sensitivity of individual medicines are shown in all the divisions. Lastly, resistance and sensitivity of antibiotics in stratified age groups have been analyzed. In this research all the data analysis is done on *E. coli* isolates from patients.

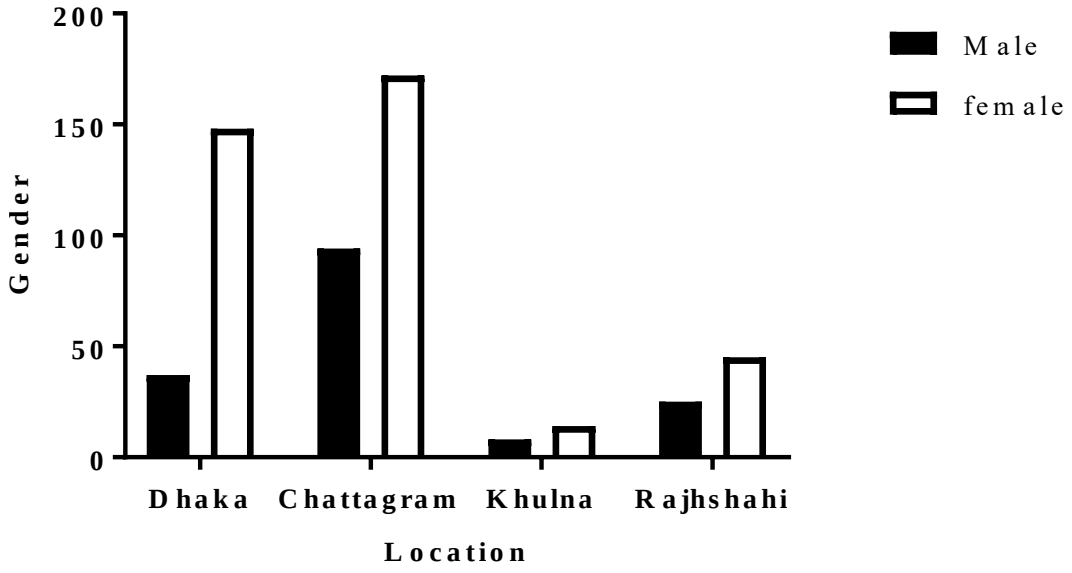


Figure 3.1: Number of patients according to gender in different divisions.

Above figure (figure-3.1) is about male and female population of this research, where in total 164 male and 379 female patients found. Where, 37 male (20.0%) and 148 female (80.0%) patients are in Dhaka division, 94 male (35.3%) and 172 female (64.7%) patients ar in Chattagram division, 8 male (36.4%) and 14 female (63.6%) patients are in Khulna division, 25 male (35.7%) and 45 female (64.3%) patients are in Rajshahi division.

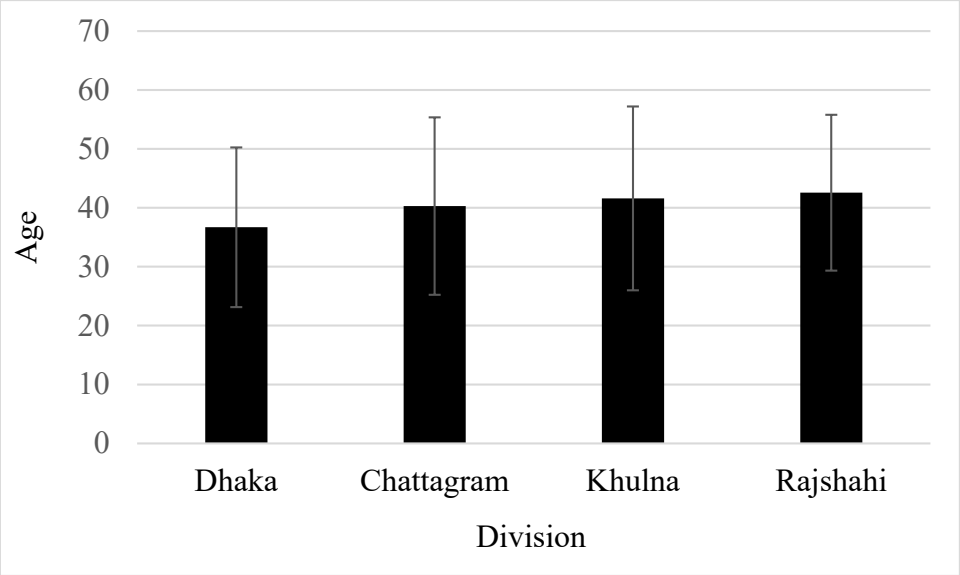


Figure 3.2: Patients of different age in different divisions.

Figure-3.2 is about different age versus division where average age in Dhaka division is 36.69 (±13.56), in Chattagran division stratified age group is 40.29(±15.06), in Khulna division stratified age group is 41.59(±15.60), in Rajshahi stratified age group is 42.56(±13.23).

Figure 3.3 to figure 3.6 shows antibiotic sensitivity of different antibiotics among the patients (%) in four divisions.

Figure 6, describes about the percentage of sensitivity of isolates obtained from patients to different antibiotics in Dhaka division. Here, it was found in total 27 antibiotics were tested with the sample of patients. Where, amikacin, ampicillin and cefotaxime are 100% sensitive, amoxyclav is 80.6% sensitive and 19.4% resistant. Azithromycin is 0.8% sensitive and 99.2% resistant, aztreonam is 1.5 % sensitive and 98.5% resistant and cefexime is 77.8% sensitive with 11.9% intermediate and 10.3% resistant. Ceftazidime is 55.7% sensitive and 44.3% resistant. Ceftriaxone is 93.4% sensitive and 6.6% resistant, cefuroxime and cephradine have become more than 95% resistant. Cefepime is 67.8% sensitive and 32.2% resistant, chloramphenicol is 0.9% sensitive and 99.1% resistant. Ciprofloxacin is 89.8 % sensitive and 10.2% resistant, cotrimoxazole is 49.3% sensitive and 50.7% resistant. Cefoxitinand and colisitin are respectively 27.6% and 38.4% sensitive, 72.4% and 61.1%

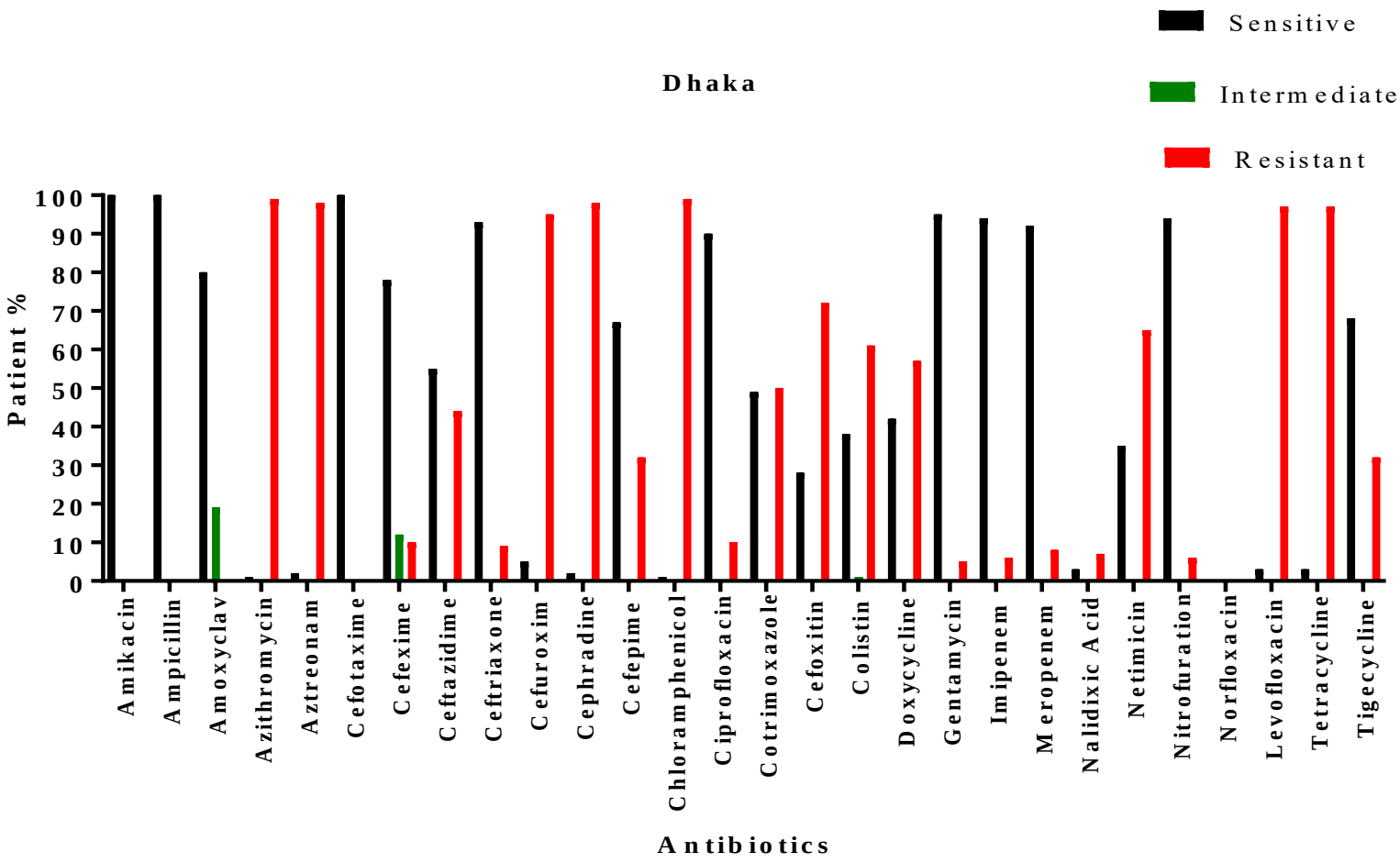


Figure 3.3: Antibiotics sensitivity of *E. coli* isolated from patients (%) in Dhaka division.

resistant and colisitin is 0.5% intermediate. Doxycycline and gentamycin are respectively 42.4% and 95.1% sensitive and 4.9% and 6.0% resistant. Imipenem is 94.0% sensitive and 6.0% resistant and meropenem 92.4% sensitive and 7.6% resistant. Nalidixic acid is about 3.0% sensitive and 97.0% resistant, netimicin is 34.8% sensitive and 65.2% resistant. Nitrofuration is about 94.0 % sensitive and 6.0% resitant and levofloxacin is 3.0% sensitive and 97.0% resistant. Tetracycline and tigecycline are respectively 3.0% and 68.1% sensitive, 97.0% and 31.9% resistant.

Figure 3.4, describes about the percentage of sensitivity of *E. coli* that is isolated from patients to different antibiotics in Chattagram division. Here, in total 24 antibiotics have been found and tested within the sample of patients. Where, amikacin and ampicillin are 100% sensitive, amoxyclav is 72.6% sensitive and 27.4% resistant. Aztreonam is 100% resistant, cefexime is 63.95% sensitive, 35.7% intermediate and 0.4% resistant. Cefotaxime is 99.2% sensitive and 0.8% resistant, ceftazidime is 55.7% sensitive and 44.3% resistant. Ceftriaxone is 97.4% sensitive and 2.6% resistant, cefuroxime and cephradine have become more than 95% resistant. Cefepime is 50% sensitive and 50% resistant. No patient found tested for chloramphenicol and ciprofloxacin, cotrimoxazole is 58.6% sensitive, 41.0% resistant and 0.4% intermediate. Cefoxitin and and colisitin is respectively 5% and 97.0% sensitive, 95.0% and 3.0% resistant and. Gentamycin are respectively 98.9% sensitive and 1.1% resistant. Imipenem is 92.5% sensitive and 7.1% resistant and meropenem 96.6% sensitive and 3.4% resistant. Nalidixic acid is about 2.6% sensitive and 97.4% resistant, netimicin is 82.0% sensitive and 18.0% resistant. Nitrofuration is about 88.7% sensitive and 11.3% resitant and levofloxacin is 0.4% sensitive and 99.6% resistant. Norfloxacin is about 50% sensitive and 50% resistant. Tetracycline and tigecycline are respectively 3.0% and 68.1% sensitive, 97.0% and 31.9% resistant.

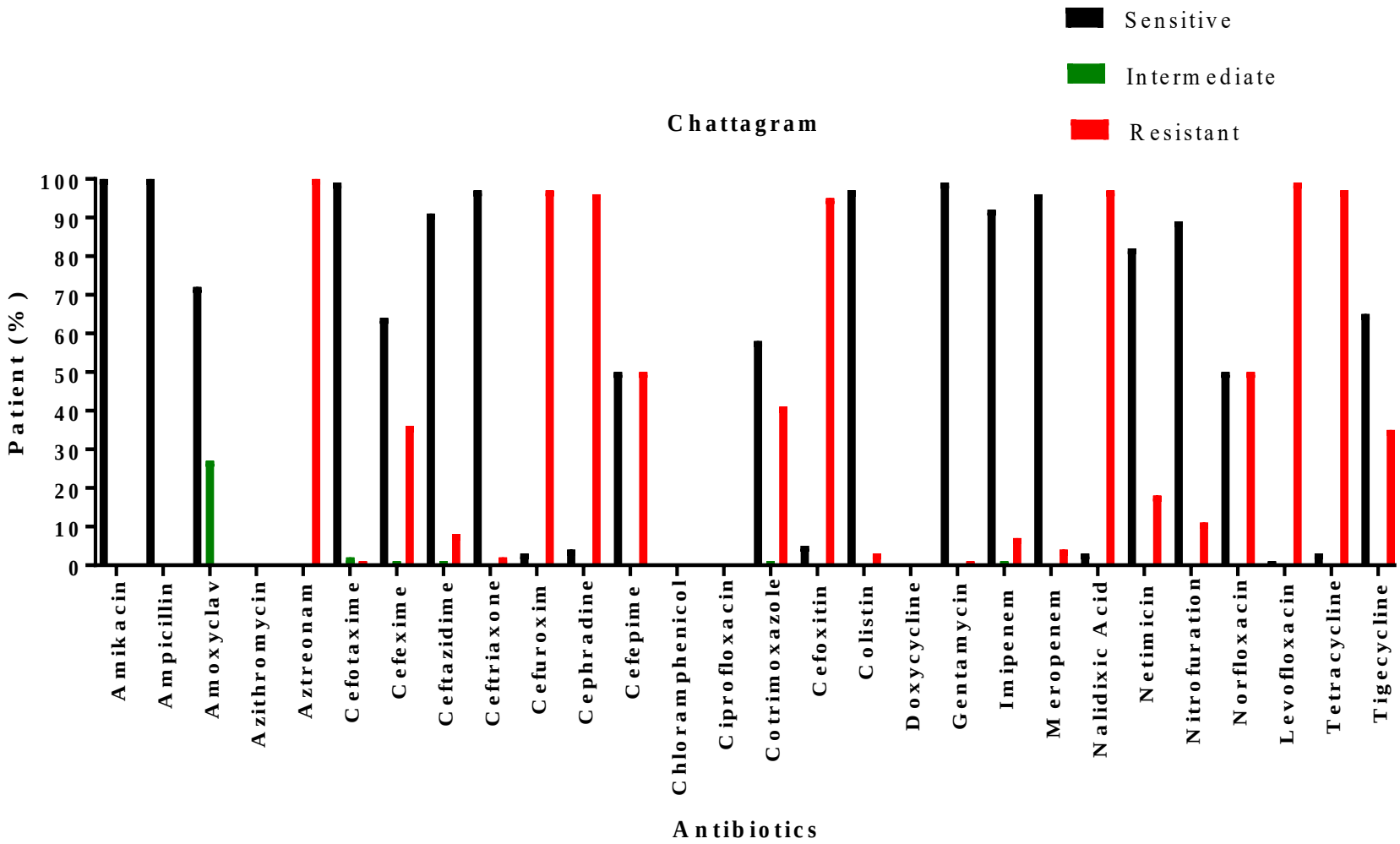


Figure 3.4: Antibiotics sensitivity of *E. coli* isolated from patients (%) in Chattagram division.

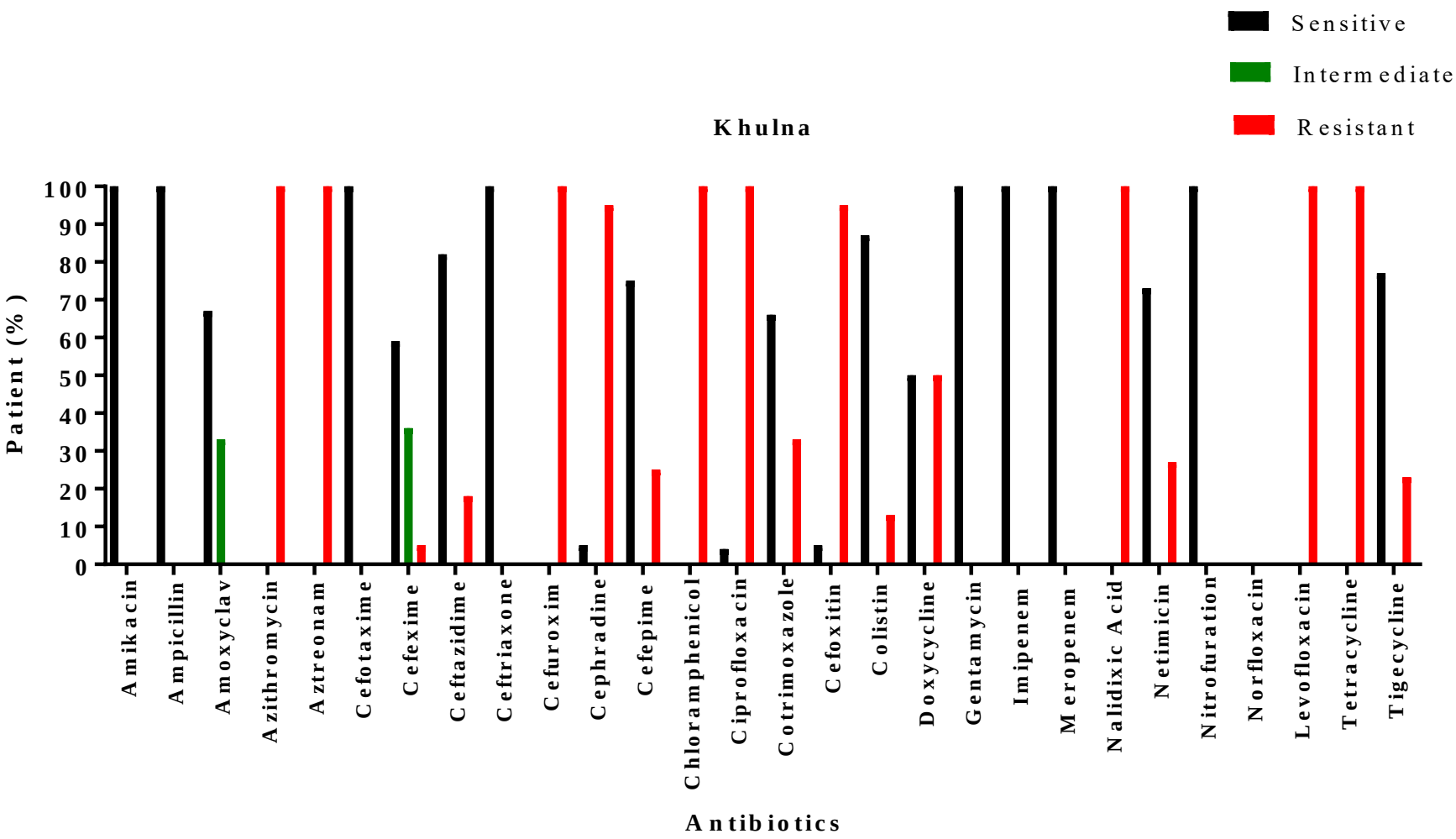


Figure 3.5: Antibiotics sensitivity of *E. coli* isolated from patients (%) in Khulna division.

Figure 3.5, describes about the percentage of sensitivity of *E. coli* that is islotaed from patients to different antibiotics in Khulna division. Here, it was found in total 27 antibiotics have been tested for the samples collected from patients. Where, amikacin, ampicillin, cefotaxime, ceftriaxone, ciprofloxacin, gentamycin, imipenem, meropenem and nitrofuration are 100% sensitive, amoxyclav is 66.7% sensitive and 33.3% resistant. Azithromycin and aztreonam, is 100% resistant in this division, cefexime is 59.1% sensitive, 36.4% intermediate and 0.4% resistant. Ceftazidime is 81.8% sensitive and 18.2% resistant. Cefuroxime and cephradine have become more than 95% resistant. Cefepime is 75.0% sensitive and 25.0% resistant, chloramphenicol is 100% resistant. Cotrimoxazole is 66.7% sensitive and 33.3% resistant. Cefoxitin and and colisitin are respectively 4.5% and 86.4% sensitive, 95.5% and 13.6% resistant. Doxycycline is 50% sensitive and 50% resistant. Nalidixic acid is about 100% resistant, netimicin is 72.7% sensitive and 27.3% resistant. Levofloxacin and tetracycline is about 100% resistant. Tigecycline is 68.6% sensitive and 22.7% resistant.

Figure 3.6, describes about the percentage of sensitivity of *E. coli* that is isolated from patients to different antibiotic in Khulna division. Here, in total 21 antibiotics have been found and tested for the sample collected from patients. Where, amikacin, ampicillin and meropenem are 100% sensitive, amoxyclav is 61.4% sensitive and 38.6% resistant. Aztreonam is 1.4 % sensitive and 98.6% resistant, cefexime is 40% sensitive with 57.1% intermediate face and 2.9% resistant. Ceftazidime is 97.1% sensitive and 2.9% resistant. Cefotaxime is 98.6% sensitive and 1.4% resistant. Ceftriaxone is 92.6% sensitive, 3.7 intermediate and 3.7% resistant, cefuroxime and cephradine have become more than 95% resistant. Cotrimoxazole is 64.3% sensitive and 35.7% resistant. Cefoxitin and and colisitin are respectively 7.1% and 92.8 % sensitive, 92.9% and 7.2% resistant and colisitin is 0.5% intermediate. Gentamycin is respectively 98.6% sensitive and 1.4% resistant. Imipenem is 94.3% sensitive and 5.7% resistant. Nalidixic acid is about 4.3% sensitive and 95.7% resistant, netimicin is 84.3% sensitive and 15.7% resistant. Nitrofuration is about 92.9 % sensitive and 7.1% resitant and levofloxacin is 1.4% sensitive and 98.6% resistant. Tetracycline and tigecycline are respectively 1.4% and 68.6% sensitive, 98.6% and 31.4% resistant.

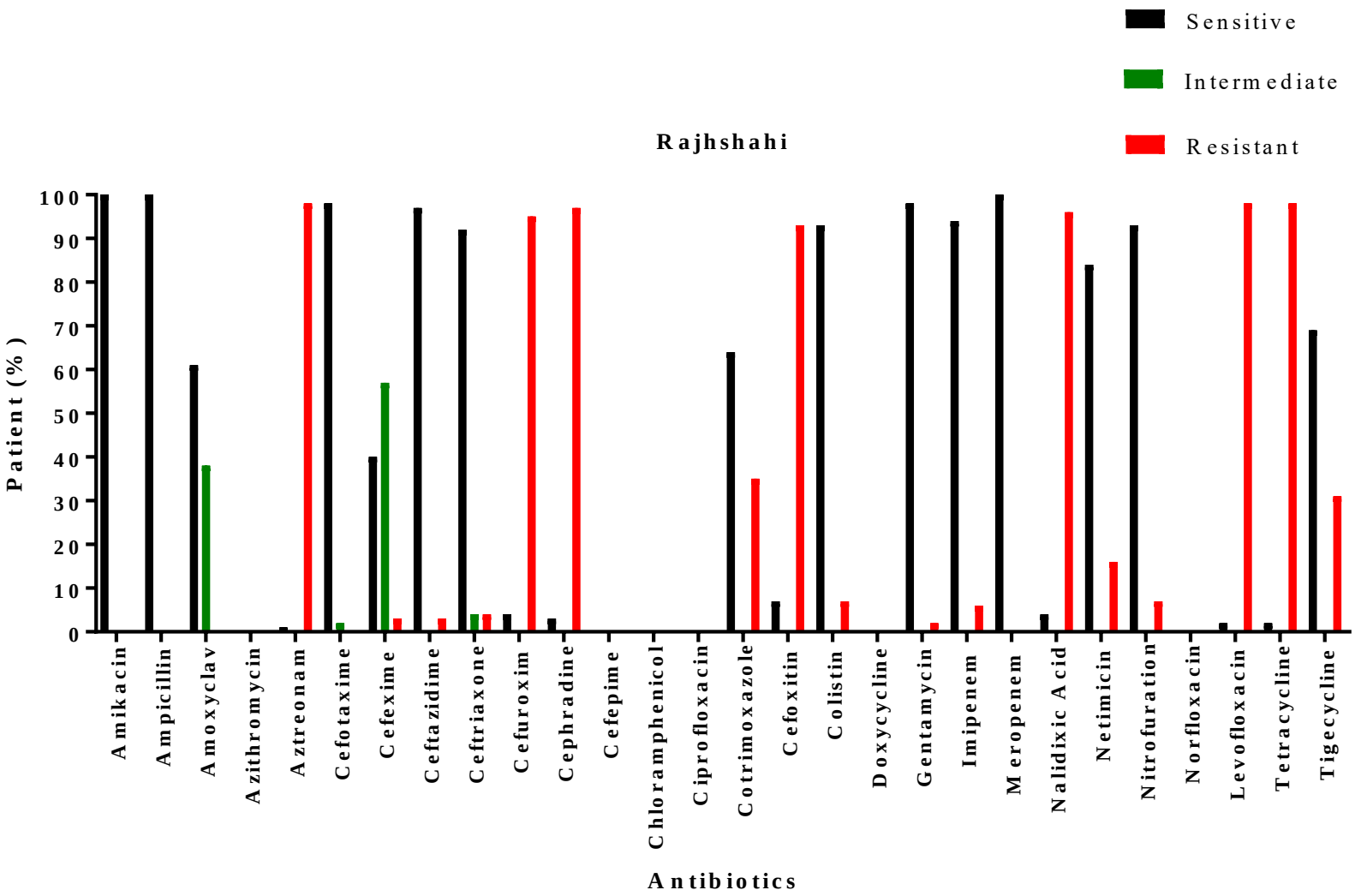


Figure 3.6: Antibiotics sensitivity of *E. coli* isolated from patients (%) in Rajshahi division.

From figure 3.7 to figure 3.33 shows patients (%) sensitivity towards individual antibiotic in four divisions.

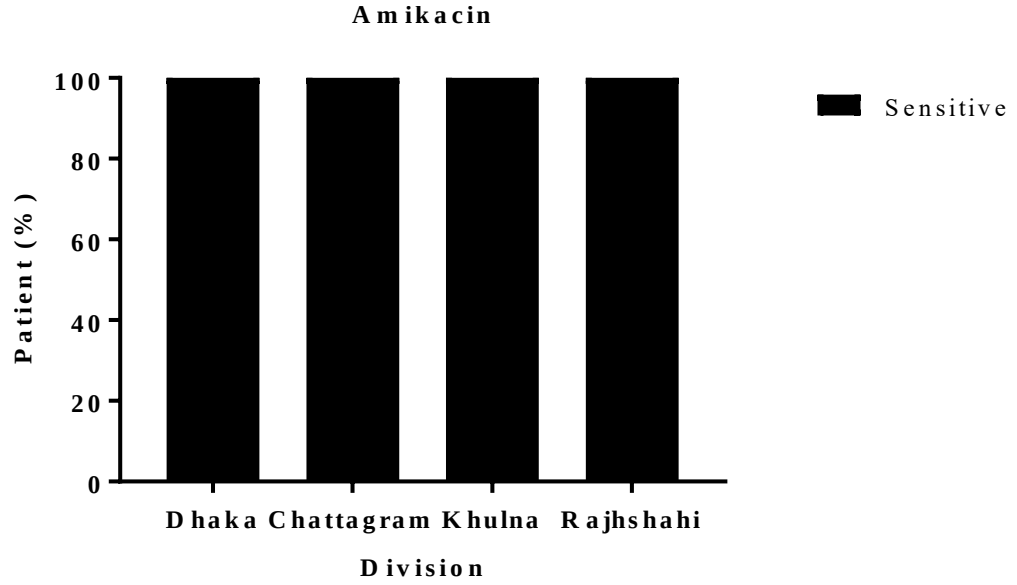


Figure 3.7: Antibiotic sensitivity of*E. coli* to amikacin among the pateints (%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to amikacin in different divisions are described here (Figure-3.7). Where, all the isolates have been found sensitive for this antibiotic, there 67(100%) are sensitive for this antibioticin Dhaka division, in Chattagram 266(100%) are sensitive, in Khulna 22(100%) are sensitive and 70(100%) are sensitivein Rajshahi division.

Figure 3.8 is similar like figure 3.7, it describes about antibiotic sensitivity of the isolates to ampicillin in different divisions. Where, all the isolates have been found sensitive for this antibiotic, in Dhaka division 6(100%) are sensitive, in Chattagram 46(100%) are sensitive, in Khulna 5(100%) are sensitive and in Rajhshahi division 17(100%) are sensitive.

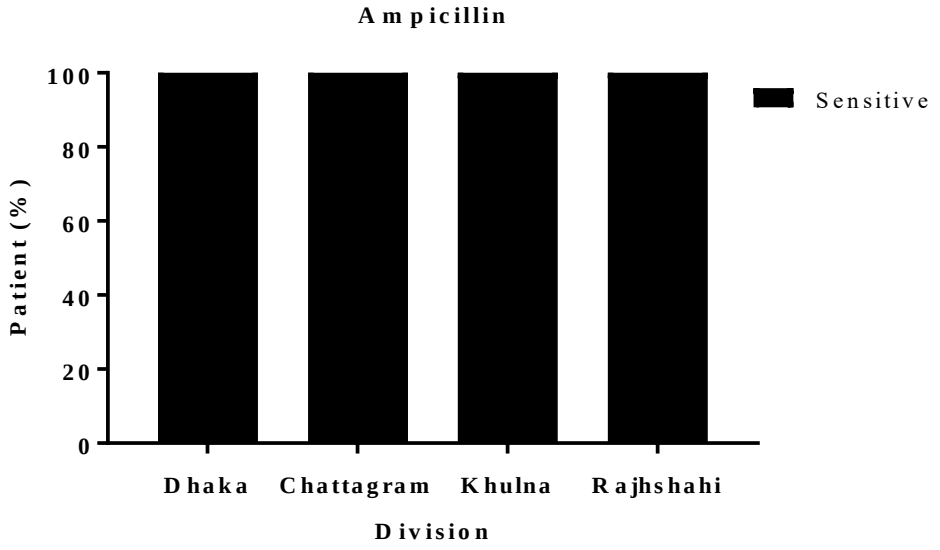


Figure 3.8: Antibiotic sensitivity of *E. coli*to ampicillin among patients (%) in different divisions.

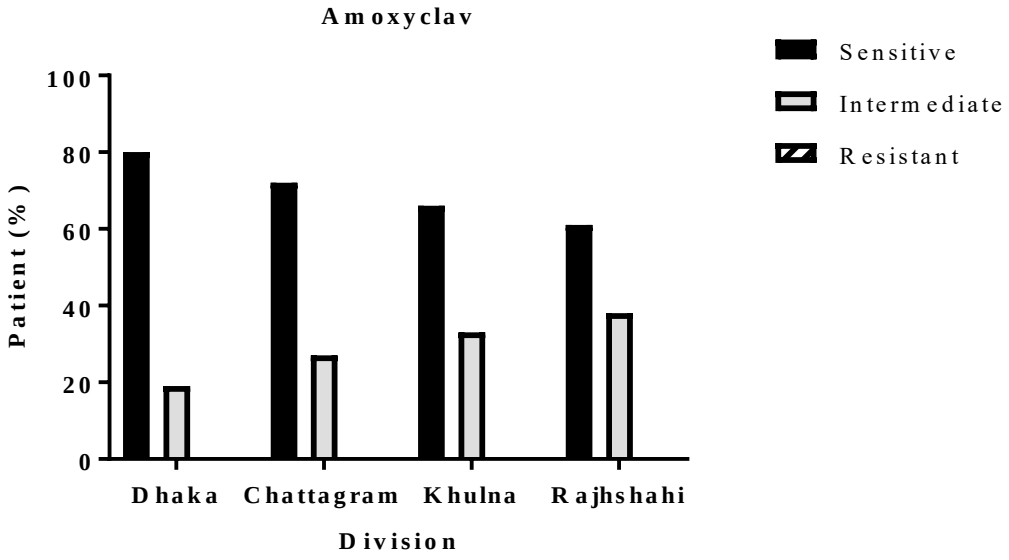


Figure 3.9: Antibiotic sensitivity of *E. coli* to amoxyclave among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to amoxyxlav in different divisions are described here (Figure-3.9). Where, out of 67 isolates 54(80.6%) are sensitive and 13(19.4%) are at intermediate stagein Dhaka division. Out of 266 isolates, 193(72.6%) are sensitive and 73(27.4%) are intermediate in Chattagram division. Out of 18 isolates 12(66.7%) are

sensitive and 6(33.3%) are at intermediate stagein Khulna division.Out of 70 isolates, 43(61.4%) are sensitive and 27(38.6%) are intermediate in Rajshahi division.

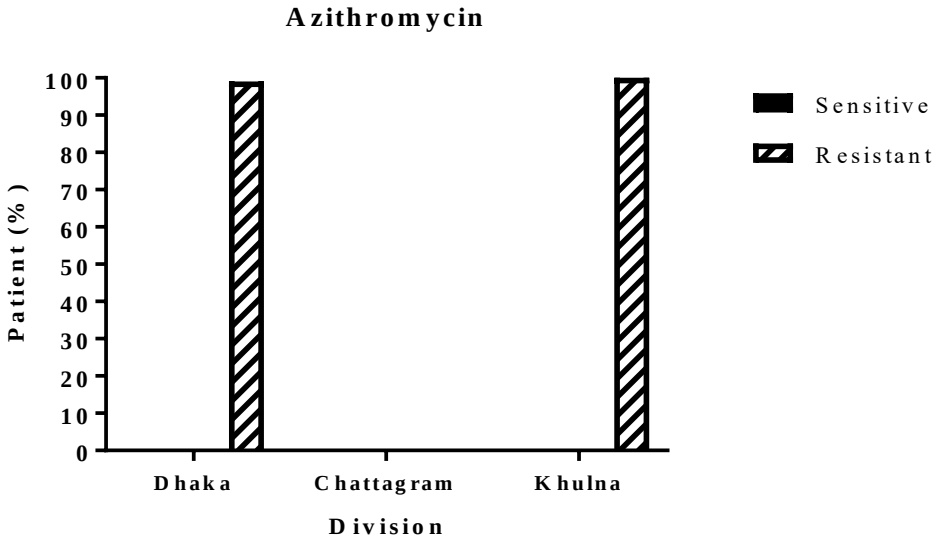


Figure 3.10: Antibiotic sensitivity of *E. coli* to azithromycin among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to azithromycin in different divisions are described here (Figure-3.10). Where, out of 118 isolates 1(0.8%) is sensitive and 11(99.2%) are intermediate in Dhaka division. In Khulna division out of 4 isolates 4 (100%) of them are resistant.

Antibiotic sensitivity of the isolated *E. coli* to aztreonam in different divisions are described here (Figure-3.11). Where, in Dhaka division, out of 67 isolates 1(1.5%) is sensitive and 66(98.5%) are at resistant stage. In Chattagram division, out of 265 isolates, 265(100%) are at resistant stage, in Khulna division out of 18 isolates, 18(100%) are at resistant stage. In Rajshahi divisionout of 70 isolates 1(1.4%) is sensitive and 69(98.6%) are at resistant stage.

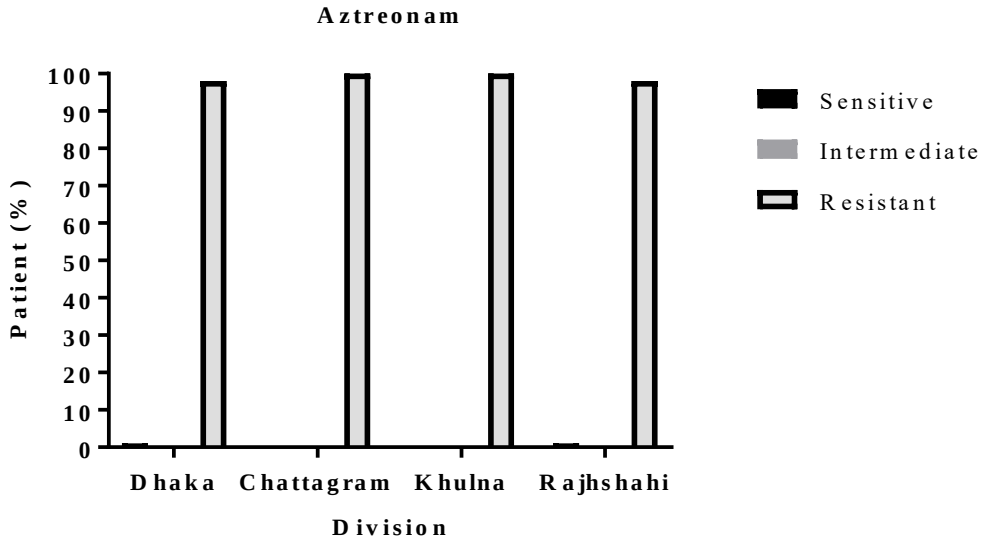


Figure 3.11: Antibiotic sensitivity of *E. coli* to aztreonam among patients(%) in different divisions.

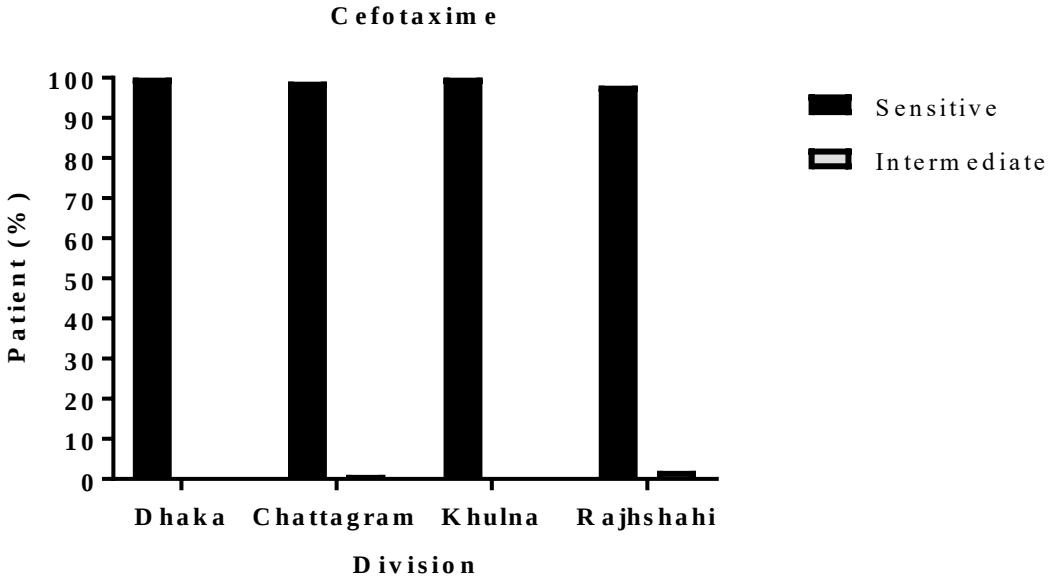


Figure 3.12: Antibiotic sensitivity of *E. coli* to cefotaxime among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to cefotaxime in different divisions are described here (Figure-3.12).Where, out of 67 isolates 67(100%) are sensitivein Dhaka division. In Chattagram division out of266 isolates, 264(99.2%) are sensitive and 2(0.8%) are at intermediate stage, in Khulna division out of 18 isolates, 18(100%) are sensitive and in

Rajshahi division out of 70 isolates 69(98.6%) are sensitive and 1(1.4%) is at intermediate stage.

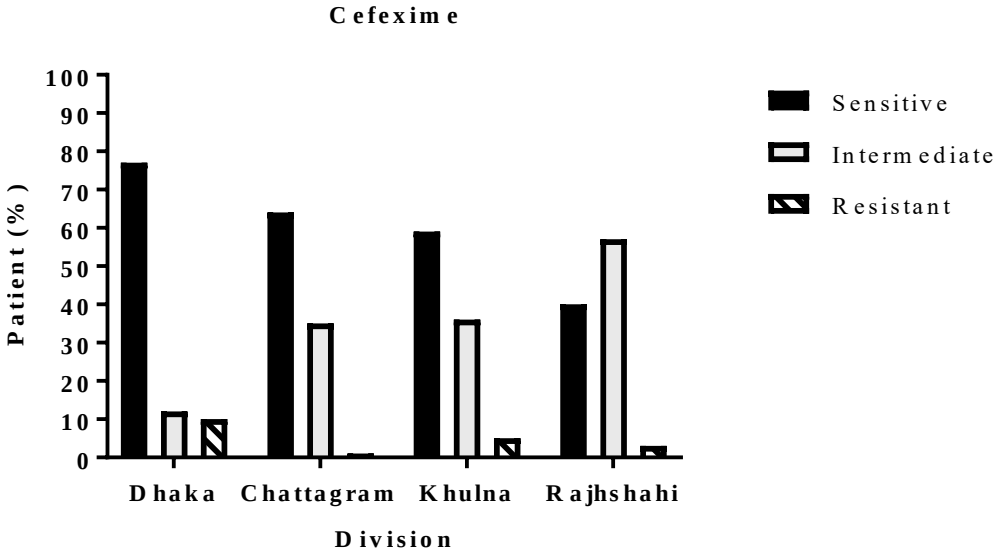


Figure 3.13: Antibiotic sensitivity of *E. coli* to cefexime among patients(%) in different divisions.

Figure 3.13 shows antibiotic sensitivity of isoltes to cefexime in different divisions. Where, out of 185 isolates, 144 (77.8%) are sensitive, 22 (11.9%) are at intermediate and 19 (10.3%) are resistant in Dhaka division. In Chattagram division, out of 266 isolates, 170 (63.95%) are sensitive, 95 (35.7%) are intermediate and 1 (0.4%) is resistant. In Khulna division out of 22 isolates, 13 (59.1%) are sensitive 8 (36.4%) are intermediate and 1 (4.5%) is resistant.In Rajshahi divisionout of 70 isolates, 28(40%) are sensitive, 40(57.1%) are at intermediate and 2(2.9%) are resistant.

Antibiotic sensitivity of the isolated *E. coli* to ceftazidime in different divisions are described here (Figure-3.14).Where, out of 185 isolates 103 (55.7%) are sensitive and 82 (44.3%) are resistant in Dhaka division. Out of 266 isolates, 243 (91.4%) are sensitive, 2 (0.8%) are at intermediate and 21 (7.9%) are resistant in Chattagram division. Out of 22 isolates 18 (81.8%) are sensitive and 4 (18.2%) are resistant in Khulna division. Out of 70 isolates 68 (97.1%) are sensitive and 2 (2.9%) are resistant in Rajshahi division.

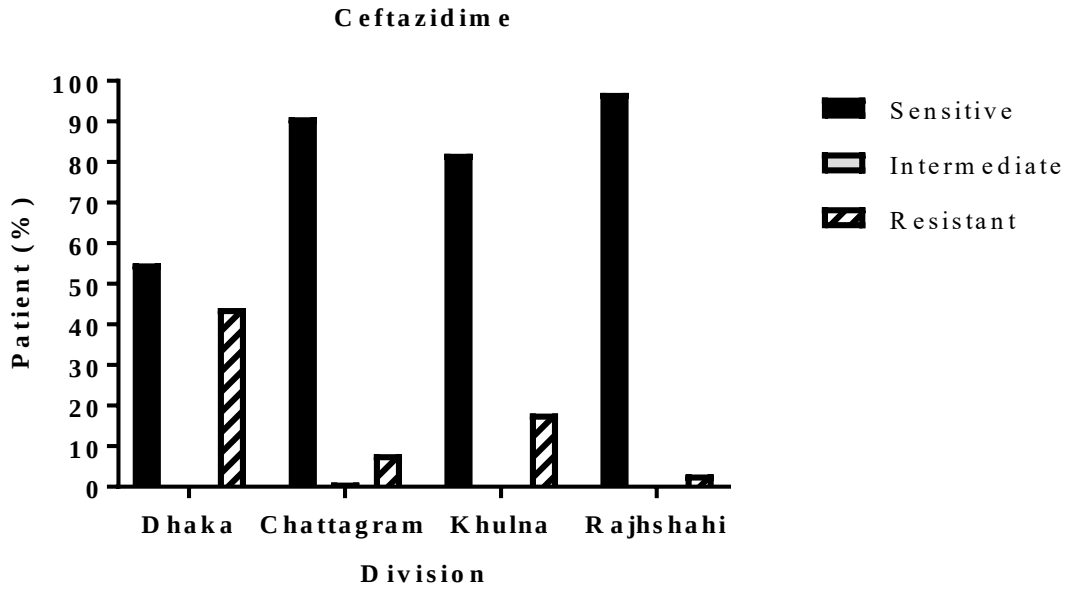


Figure 3.14: Antibiotic sensitivity of *E. coli* to ceftazidime among patients(%) in different divisions.

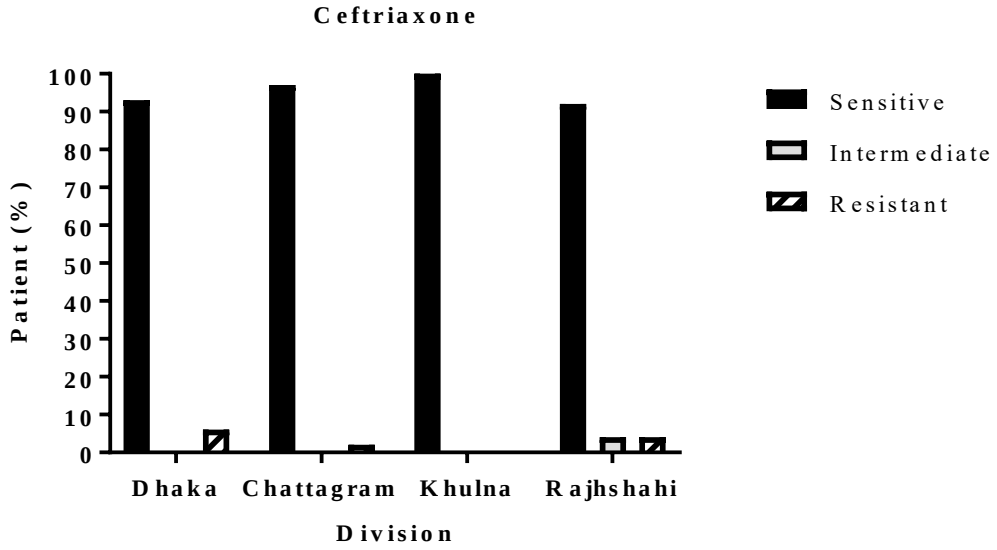


Figure 3.15: Antibiotic sensitivity of *E. coli* to ceftriaxone among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to ceftriaxone in different divisions are described here (Figure-3.15).Where, in Dhaka division, out of 135 isolates, 128(93.4%) are sensitive and 9(6.6%) are resistant. In Chattagram division, out of 76 isolates, 74(97.4%) are sensitive

and 2(2.6%) are resistant. In Khulna division out of 10 isolates, 10(100%) are sensitive.In Rajshahi division out of 27 isolates, 25(92.6%) are sensitive, 1(3.7%) is at intermediate and 1(3.7%) is at resistant.

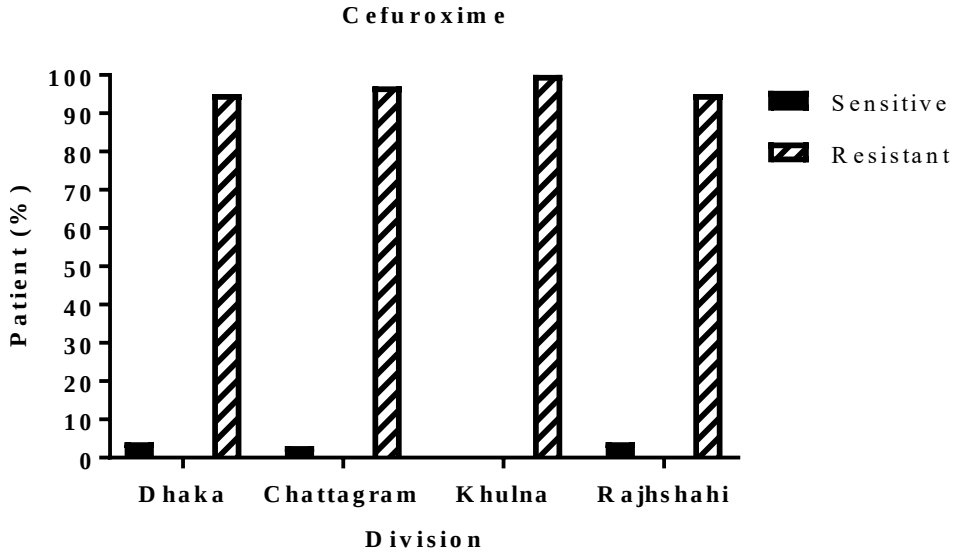


Figure 3.16: Antibiotic sensitivity of *E. coli* to cefuroxime among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to cefuroxime in different divisions are described here (Figure-3.16). Where, in Dhaka division, out of 67 isolates 3(4%) are sensitive and 63(95%) are at resistant stage. In Chattagram division, out of 265 isolates 8(3%) are sensitive and 257(97%) are at resistant stage. In Khulna division, out of 18 isolates, 0 are sensitive and 18(100%) are at resistant stage. In Rajshahi division, out of 70 isolates 3(4.3%) are sensitive and 67(95.7%) are resistant.

Antibiotic sensitivity of the isolated *E. coli* to cephradine in different divisions are described here (Figure-3.17). Where, in Dhaka division, out of 66 isolates, 3(1.6%) are sensitive and 181(98.4%) are at resistant stage. In Chattagram division, out of 266 isolates, 10(3.8%) are sensitive and 256(95.5%) are at resistant stage. In Khulna division, out of 22 isolates 1(4.5%) is sensitive and 21(95.5%) are at resistant stage.In Rajshahi divisionout of 70 isolates 2(2.9%) are sensitive and 68(97.1%) are resistant.

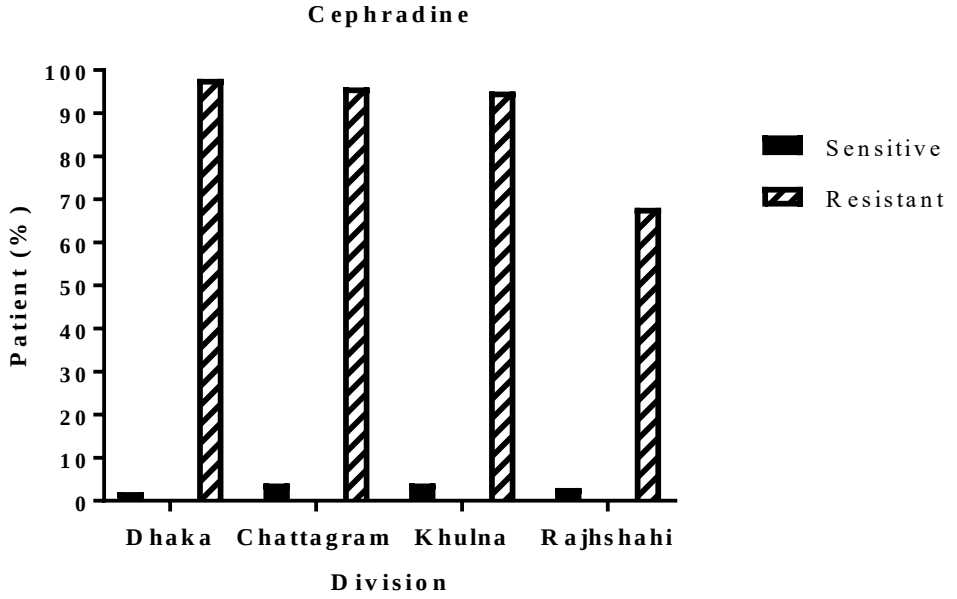


Figure 3.17: Antibiotic sensitivity of *E. coli* to cephradine among patients(%) in different divisions.

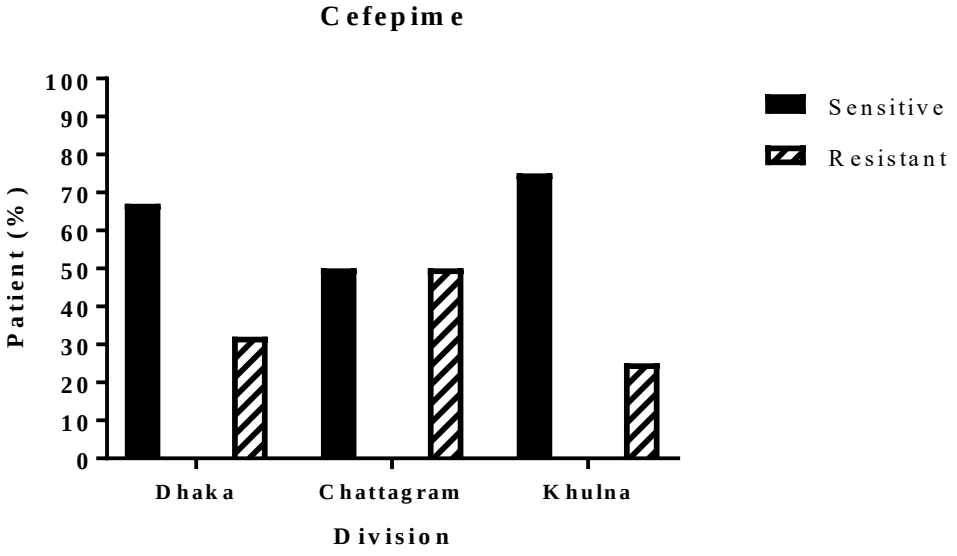


Figure 3.18: Antibiotic sensitivity of *E. coli* to cefepime among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to cefepime in different divisions are described here (Figure-3.18). Where, in Dhaka division, out of 118 isolates 80(67.8%) are sensitive and 38(32.2%) are resistant. In Chattagram division out of 2 isolates, 1(50%) is sensitive and

1(50%) is at resistant stage. In Khulna division out of 4 isolates 3(75%) are sensitive and 1(25%) is resistant.

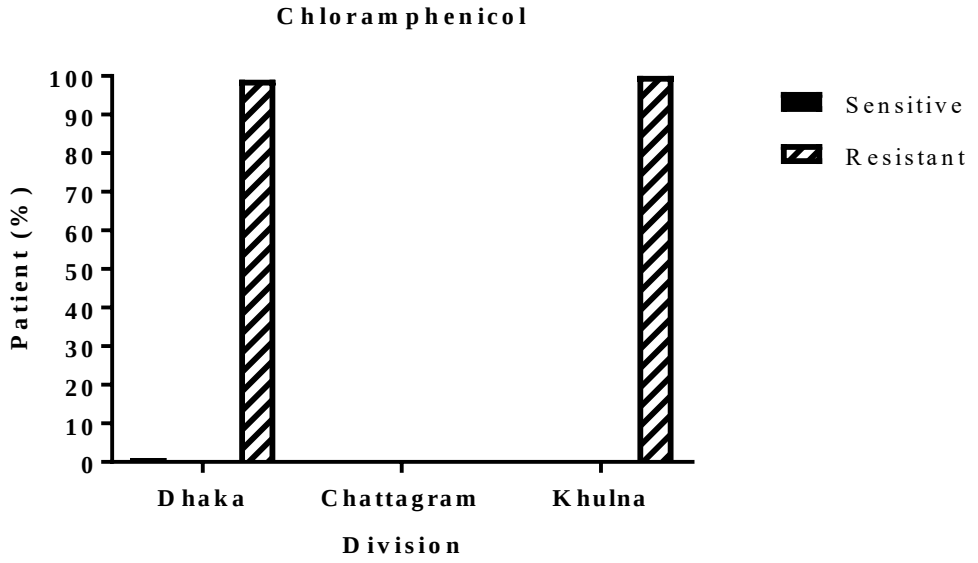


Figure 3.19: Antibiotic sensitivity of *E. coli* to chloramphenicol among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to chloramphenicol in different divisions are described here (Figure-3.19). Where, in Dhaka division, out of 117 isolates, 1(0.9%) is sensitive and 181(98.4%) are at resistant stage. In Khulna division out of 4 isolates, 4(100%) are resistant. No patient tested in Chattagram and Rajshahi division against this antibiotic.

Figure 3.20 is similar like figure 3.19 where, no patient found in Chattagram and Rajshahi tested for ciprofloxacin. Figure 3.20 antibiotic sensitivity of *E.coli*towards ciprofloxacin. Where, in Dhaka division, out of 118 isolates 106(89.8%) are sensitive and 12(10.2%) are resistant, in Khulna division out of 4 isolates, 4 (100%) are sensitive.

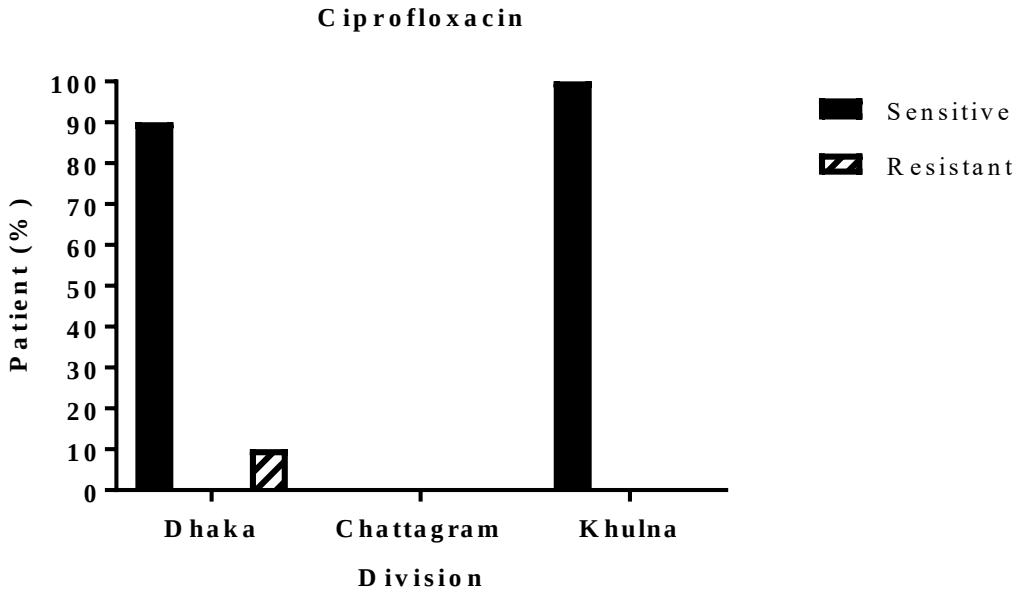


Figure 3.20: Antibiotic sensitivity of *E. coli* tociprofloxacin among patients(%) in different divisions.

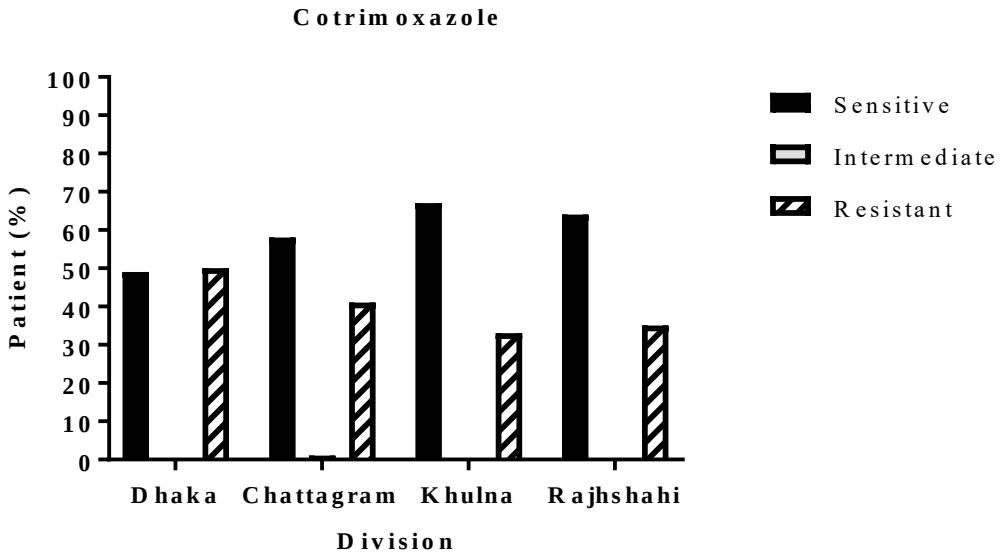


Figure 3.21: Antibiotic sensitivity of *E. coli* to cotrimoxazole among patients(%) in different divisions.

Percentage of *E. coli* sensitivity towardscotrimoxazole is shown here (Figure 3.21). Where, in Dhaka division, out of 67 isolates, 33(49.3%)are sensitive, 0 patients are intermediate and 34(50.7%) isolates are resistant. In Chattagram division out of 266 isolates, 156(58.6%) are

sensitive, 1(0.4%) is at intermediate and 109(41.0%) are at resistant stage. In Khulna division, out of 18 isolates, 12(66.7%)are sensitive 0 are intermediate and 6(33.3%) are resistant. In Rajshahi division out 70 isolates, 45(64.3%) are sensitive, 0 is intermediate and 25(35.7%) are resistant.

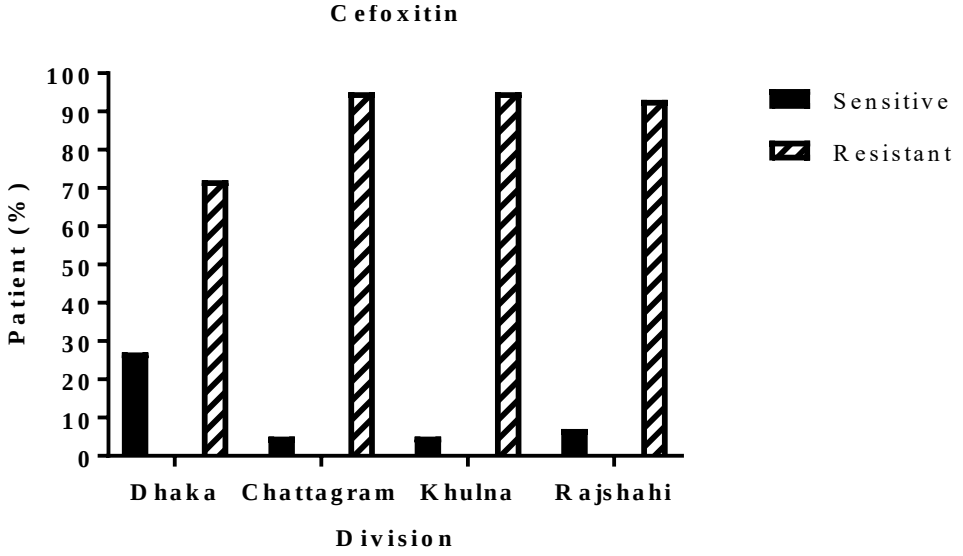


Figure 3.22: Antibiotic sensitivity of *E. coli* to cefoxitin among patients(%) in different divisions.

Percentage of *E. coli* sensitivity towardscefoxitin is shown here (Figure 3.22).Where, in Dhaka division, out of 185 isolates, 51(27.6%) are sensitive and 134(72.4%) are resistant. In Chattagram division out of 262 isolates 13(5.0%) are sensitive and 249(95%) are at resistant. In Khulna division, 1(4.5%) is sensitive and 21(95.5%) are resistant, in Rajshahi division out of 70 isolates, 5(7.1%) are sensitive and 65(92.9%) are at resistant stage.

Percentage of *E. coli* sensitivity towardscolisitin is shown here (Figure 3.23). Where, in Dhaka division, out of 185 isolates 71 (38.4%) are sensitive, 1 (0.5%) is intermediate and 113 (61.1%) are resistant. In Chattagram division out of 266 isolates, 258 (97.0%) are sensitive, 0 patient is intermediate and 8(3.0%) are at resistant stage. In Khulna division out of 22 isolates 19 (86.4%) are sensitive 0 are at intermediate and 3 (13.6%) are resistant, out of 70 isolates, 64 (92.8%) are sensitive, 0 is intermediate and 5 (7.2%) are resistant in Rajshahi division.

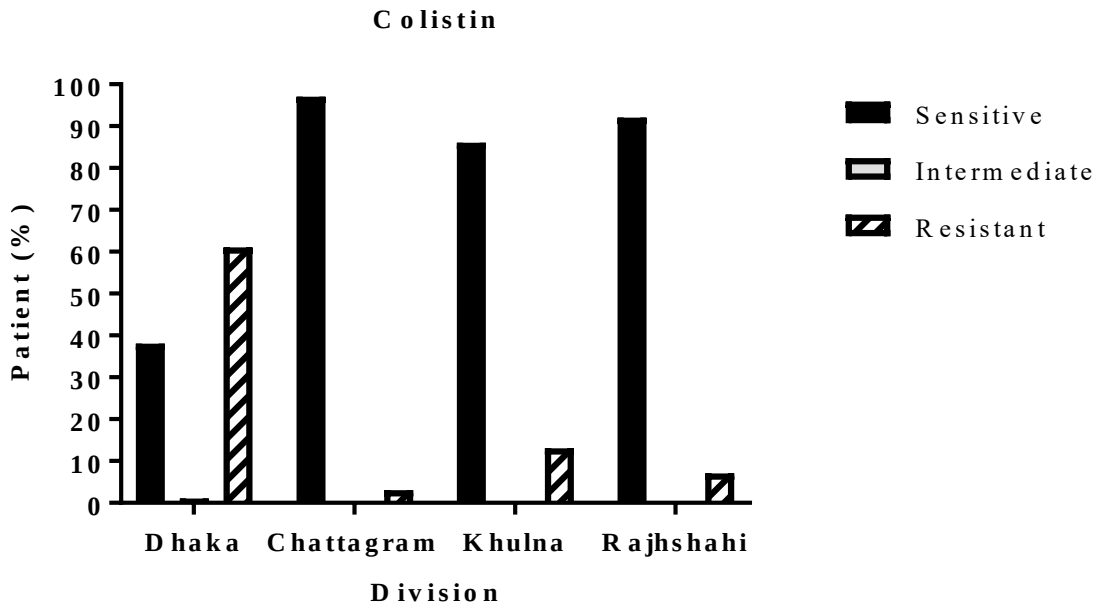


Figure 3.23: Antibiotic sensitivity of *E. coli* to colistin among patients(%) in different divisions.

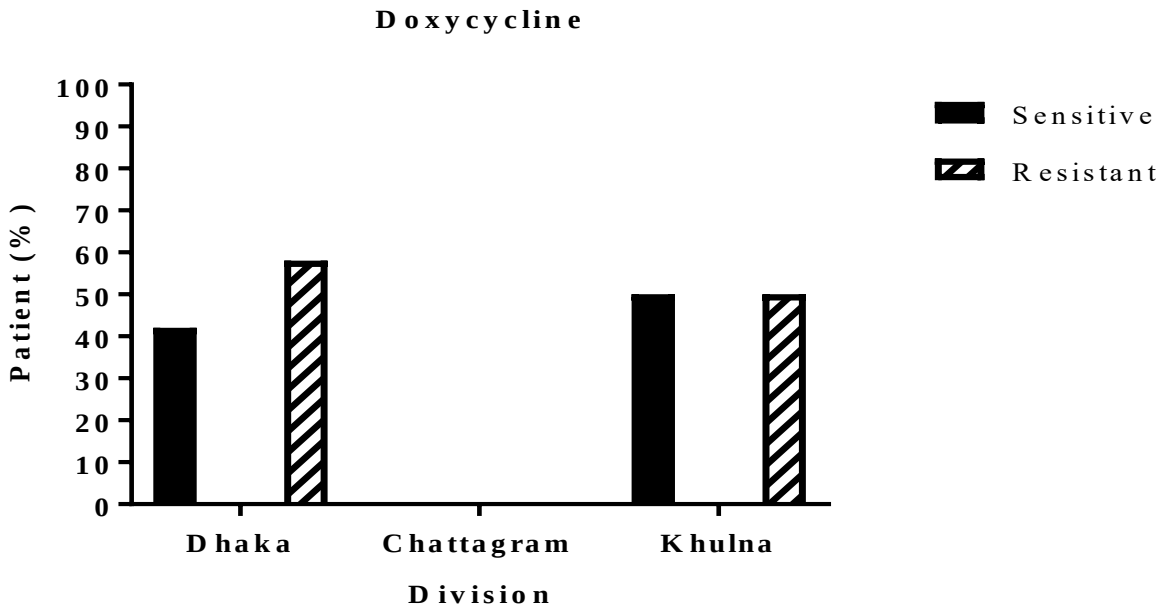


Figure 3.24: Antibiotic sensitivity of *E. coli* to doxycycline among patients(%) in different divisions.

Figure 3.24 is similar like figure 3.19 and figure 3.20. Where, patients have not been found Chattagram and Rajshahi tested for doxycyclin. Figure 3.24 showspercentage of antibiotic sensitivity of *E. coli* towardsdoxycyclin. Where in Dhaka division out of 118 isolates, 50(42.4%) are sensitive and 68(57.6%) are at resistant stage. In Khulna division out of 4 isolates, 2(50%) are sensitive and 2(50%) are at resistant.

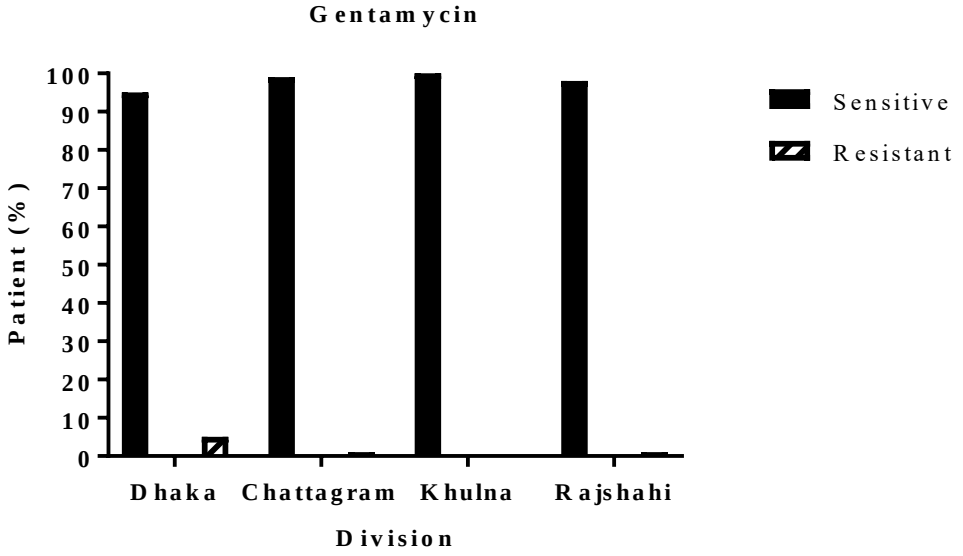


Figure 3.25: Antibiotic sensitivity of *E. coli* to gentamycin among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to gentamycin in different divisions are described here (Figure-3.25). Where, in Dhaka division, out of 185 isolates, 176 (95.1%) are sensitive and 9 (4.9%) are resistant. In Chattagram division out of 266 isolates, 263 (98.9%) are found sensitive and 3 (1.1%) are at resistant stage, in Khulna division out of 22 isolates, 22(100%) are sensitive. In Rajshahi division out of 70 isolates, 69(98.6%) are sensitive and 1(1.4%) is at resistant stage.

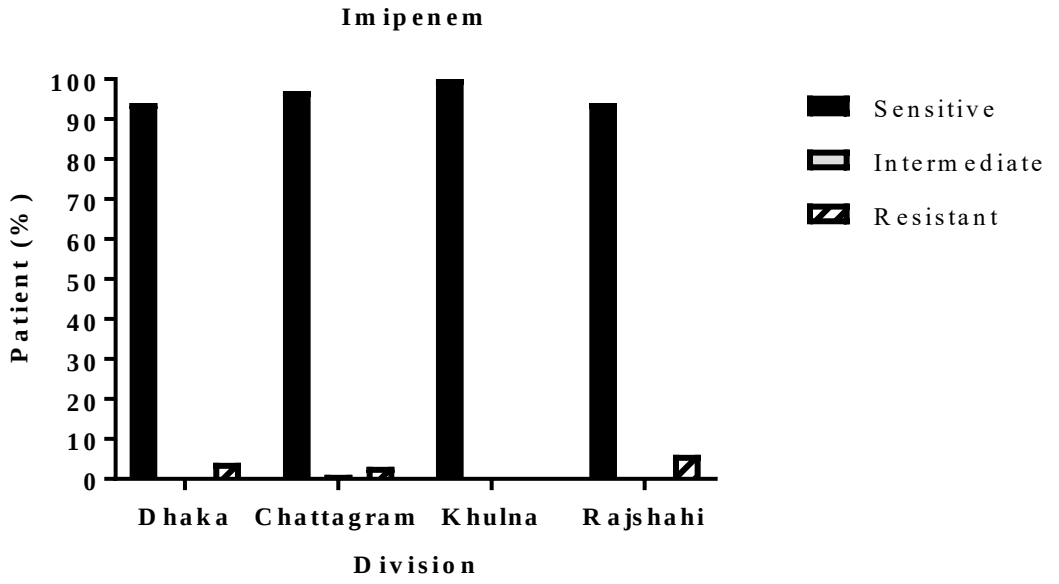


Figure 3.26: Antibiotic sensitivity of *E. coli* to imipenem among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to imipenem in different divisions are described here (Figure-3.26). Where, in Dhaka division, out of 67 isolates, 63(94.0%) are sensitive, 0 is intermediate and 4(6%) are resistant. In Chattagram division out of 266 isolates, 246(92.5%) are sensitive, 1(0.4%) is intermediate and 19(7.1%) are at resistant stage. In Khulna division out of 18 isolates, 18(100%) are sensitive. In Rajshahidivision out of 70 patients, 66(94.3%) are sensitive and 4(5.7%) are at resistant stage.

Percentage of *E. coli* sensitivity towardsmeropenem is shown here (Figure 3.27). Where in Dhaka division out of 185 isolates, 171(92.4%) are sensitive and 14 (7.6%) are resistant. In Chattagram division, out of 261 isolates, 252(97.4%) are sensitive and 9 (3.4%) are resistant. In Khulna division, out of 22 isolates, 22 (100%) are sensitive. In Rajhshahi division out of 22 isolates 22 (100%) are sensitive and no isolate is resistant in Rajshahi division.

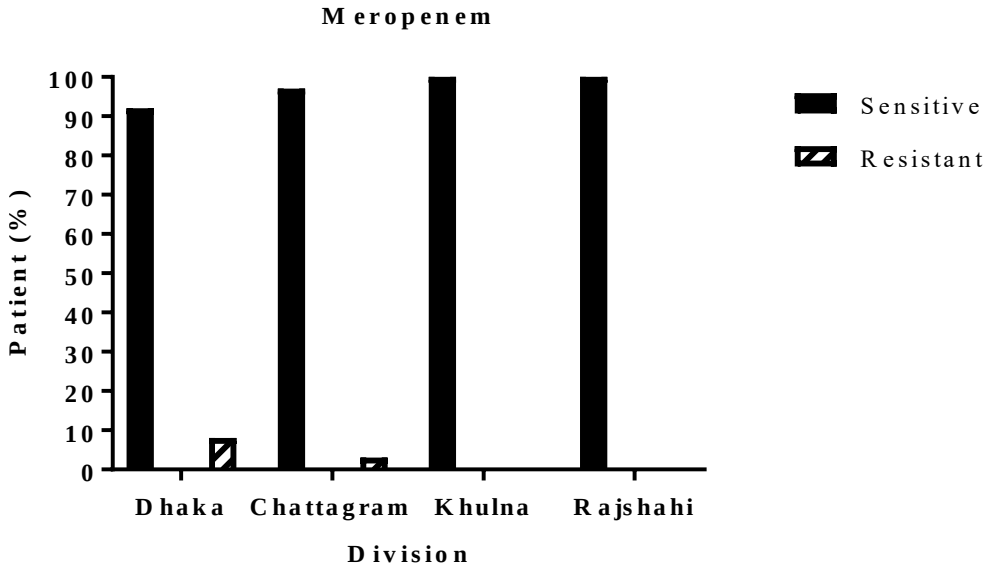


Figure 3.27: Antibiotic sensitivity of *E. coli* to meropenem among patients(%) in different divisions.

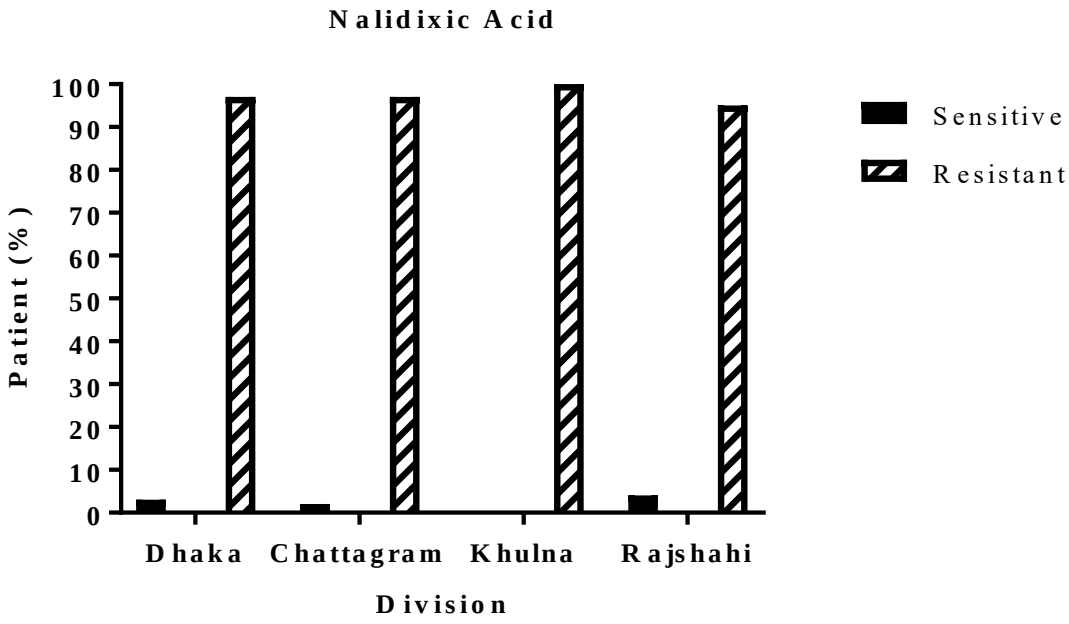


Figure 3.28: Antibiotic sensitivity of *E. coli* to nalidixic acid among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to nalidixic acid in different divisions are described here (Figure-3.28). Where, out of 67 isolates 2(3.0%) are sensitive and 65(97.0%) are resistantin Dhaka division. In Chattagram division, out of 266 isolates, 7(2.6%) are

sensitive and 259(97.4%) are resistant. In Khulna division, out of 18 isolates, 18(100%) are resistant. In Rajshahi division, out of 70 isolates, 3(4.3%) are sensitive and 67(95.7%) are resistant.

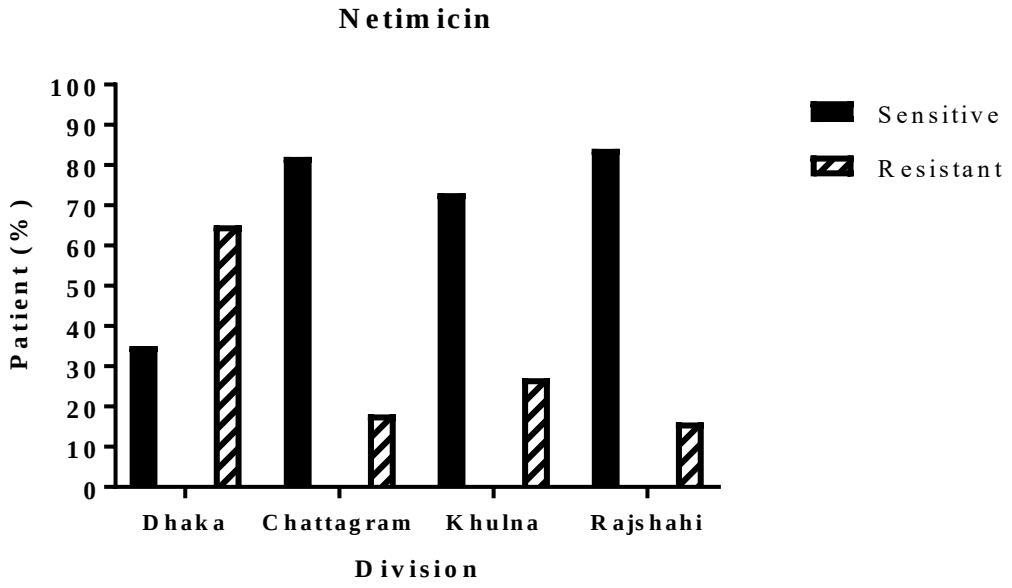


Figure 3.29: Antibiotic sensitivity of *E. coli* to netimicin among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to netimicin in different divisions are described here (Figure-3.29). In Dhaka division, out of 184 isolates, 64 (34.8%) are sensitiveand 120(65.2%) are resistant. In Chattagram division, out of 266 isolates, 218(82.0%) are sensitive and 48(18.0%) are resistant. In Khulna division, out of 22 isolates, 16(72.7%) are sensitive and 6(27.3%) are resistant. In Rajshahi division out of 70 isolates, 59 (84.3%) are sensitive and 11(15.7%) are resistant against netimicin.

Antibiotic sensitivity of the isolated *E. coli* to nitrofuration in different divisions are described here (Figure-3.30). Where, in Dhaka division, out of 67 isolates, 63 (94.0%) are sensitive and 4 (6.0%) are resistant. In Chattagram division, out of 266 isolates, 236 (88.7%) are sensitive and 30 (11.3%) are resistant. In Khulna division, out of 18 isolates, 18 (100%) are sensitive and 0 isolate is resistant. Out of 70 isolates, 65 (92.9%) are sensitive and 5(7.1%) are resistantin Rajshahi division.

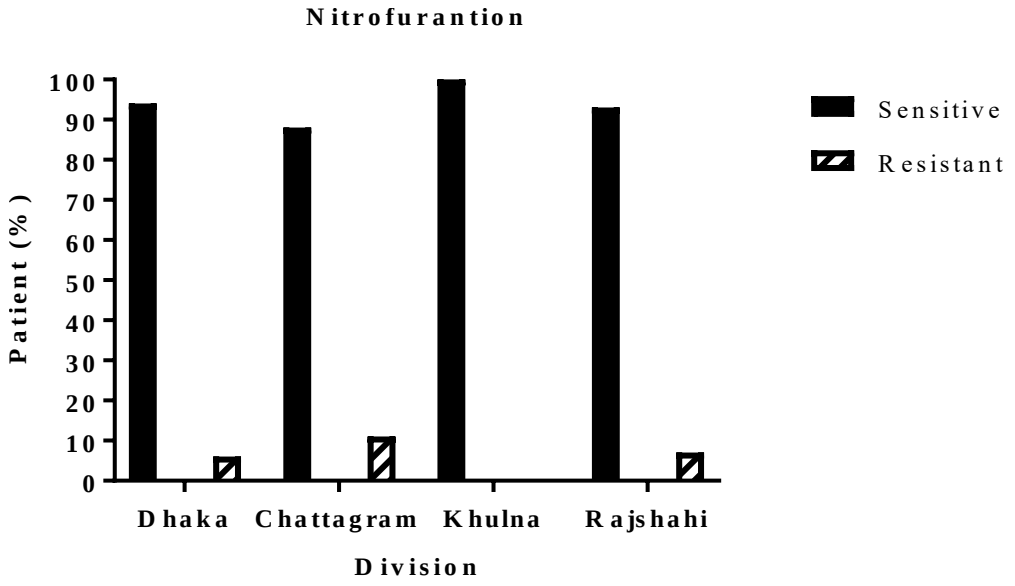


Figure 3.30: Antibiotic sensitivity of *E. coli* to nitrofuration among patients(%) in different divisions.

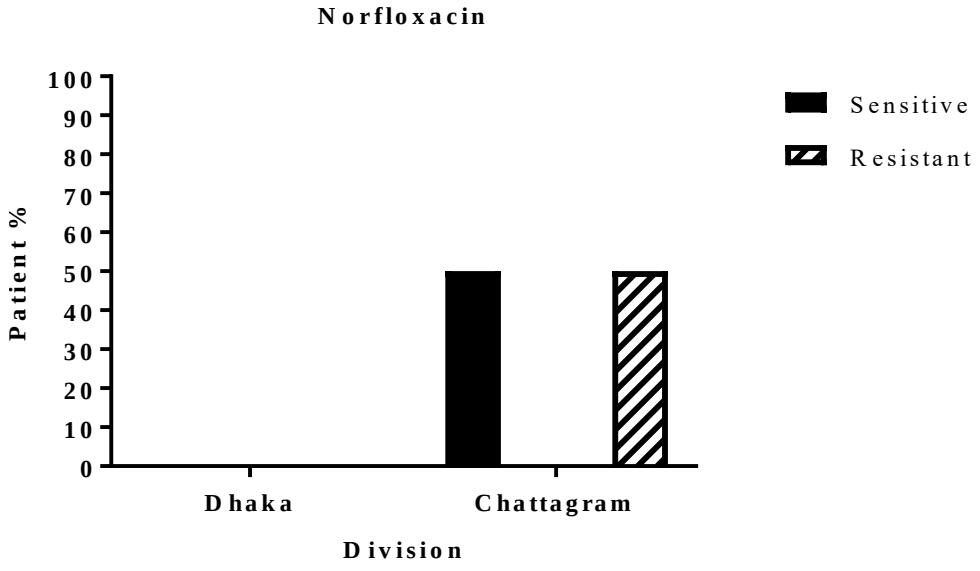


Figure 3.31: Antibiotic sensitivity of *E. coli* to norfloxacin among patients(%) in different divisions.

Figure 3.31 is aboutpercentage of antibiotic sensitivity of *E. coli* to norfloxacin. Where, 4 isolates were tested only in Chattagram division where 2 (50%) are sensitive and 2 (50%) are resistant.

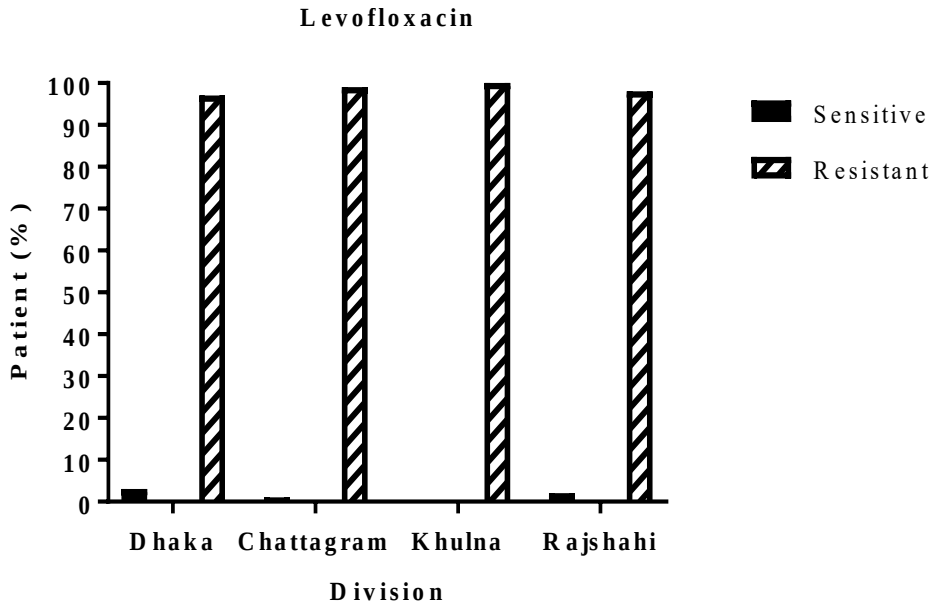


Figure 3.32: Antibiotic sensitivity of *E. coli* to levofloxacin among patients(%) in different divisions.

Percentage of antibiotic sensitivity of *E. coli* towardslevofloxacin is shown here(Figure 3.32). Where, in Dhaka division, out of 67 isolates, 2(3.0%) are sensitive and 65(97.0%) are resistant. In Chattagram division, out of 266 isolates, 1(3.0%) are sensitive and 265(99.6%) are resistant. In Khulna division, out of 18 isolates, 0 is sensitive and 18(100%) are resistant. In Rajshahi division out of 70 isolates, 1(1.4%) is sensitive and 69(98.6%) are resistant.

Antibiotic sensitivity of the isolated *E. coli* to tetracycline in different divisions are described here (Figure-3.33). Where, out of 67 isolates, 2 (3.0%) are sensitive and 65 are resistant in Dhaka division. In Chattagram division, out of 266 isolates, 8 (3.0%) are sensitive and 258 (97.0%) are resistant. In Khulna division, out of 18 isolates, 0 is sensitive and 18 (100%) are resistant. In Rajshahi division out of 70 isolates, 48 (68.6%) are sensitive and 22 (31.4%) are resistant.

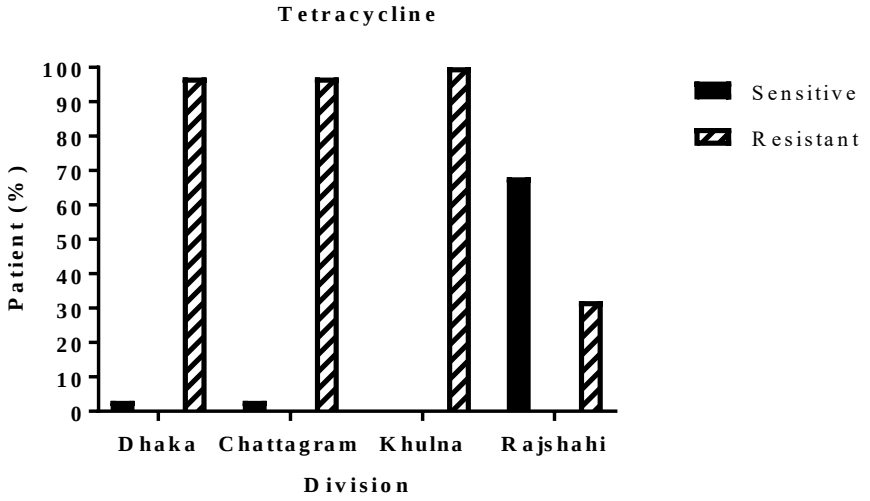


Figure 3.33: Antibiotic sensitivity of *E. coli* to tetracycline among patients(%) in different divisions.

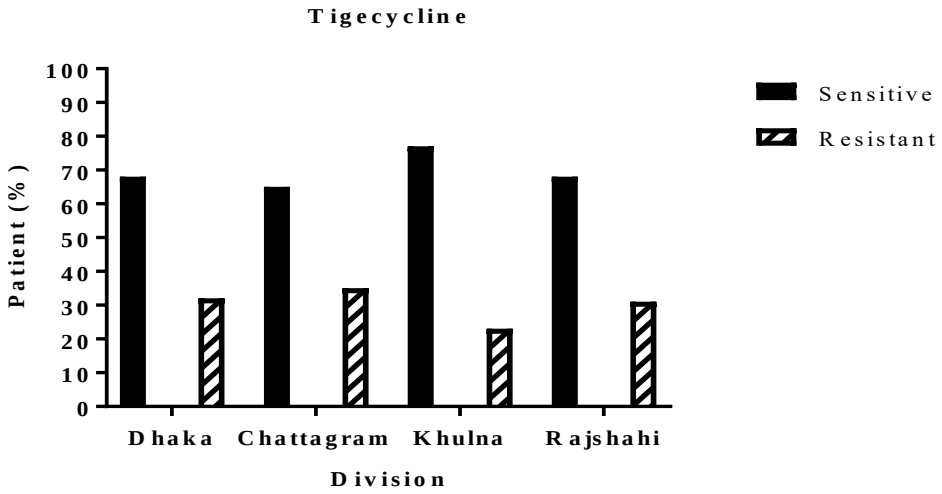


Figure 3.34: Antibiotic sensitivity of *E. coli* to tigecyclin among patients(%) in different divisions.

Antibiotic sensitivity of the isolated *E. coli* to tigecycline in different divisions are described here (Figure-3.34). Where, in Dhaka division out of 185 isolates, 126 (68.1%) are sensitive and 59 (31.9%) are resistant. In Chattagram division, out of 266 isolates, 173 (65.0%) are sensitive and 93 (35.0%) areresistant. In Khulna division, out of 22 isolates, 17 (77.3%) are sensitive and 5 (31.4%) are at resistant stage. Out of 70 isolates, 48 (68.6%) are sensitive and 22 (31.4%) are resistant in Rajshahi division.

From figure 3.35 to figure 3.52 shows percentage of antibiotic sensitivity of E. coli to different antibiotics. Here, sensitivity is shown on the basis of stratified age, patients are divided mainly in 3 groups of age. The groups are equal or less than 30 years (≤30 years), 31-45 years and more or equal to 46 years (≥46 years). Here, in figure 3.35, 3.36, 3.37, 3.42, 3.43, 3.44, 3.45, 3.48 and 3.52 statistical significances (p-value) are reported above the graph. Where, n.s. (not significant) indicates p= >0.05; * signifies p= 0.05; ** signifies p= 0.01; *** signifies p= 0.005; **** signifies p= <0.001.

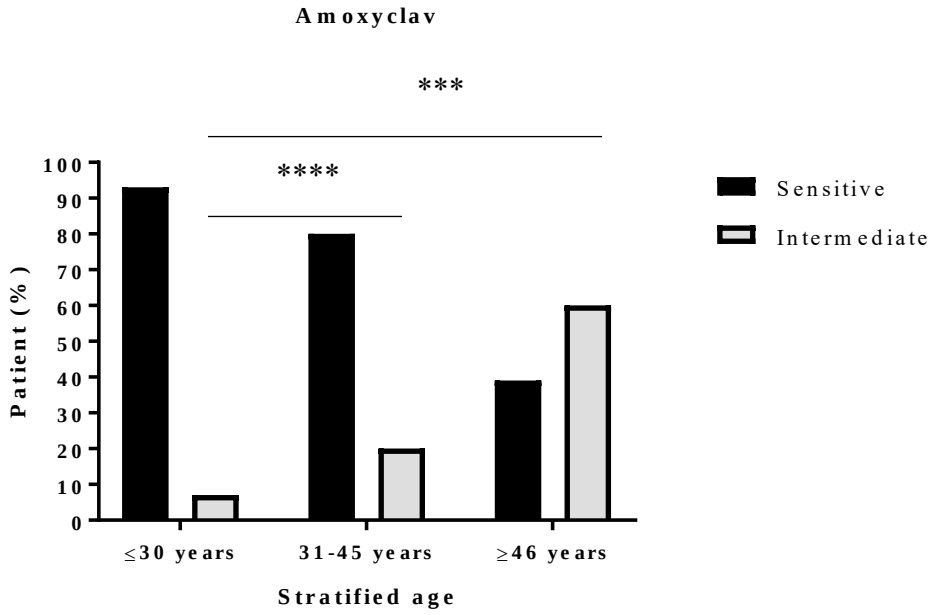


Figure 3.35: Antibiotic sensitivity of *E. coli* to amoxyclav among patients (%) based on stratified age groups. Statistical significance (p-value) is reported above the graph.[**** signifies p= <0.001]

Antibiotic sensitivity of the isolated *E. coli* is shown (Figure 3.35) toamoxyclav against different age group. Where the patients are divided in three group on the basis of different age.In ≤30 years age group out of 133 isolates,132(92.6%) are sensitive and 10(7.4%) are at intermediate stage which is considered as reference value (Figure3.34). In 31-45 age group,out of 147 isolates, 118(80.27%) are sensitive and 29(19.73%) are at intermediate stage with the odd ratio 3.42 (CI95%;1.60-7.32;p= 0.002). In ≥46 years age group, out of 132 isolates, 52(39.39%) are sensitive and 80(60.61%) are at intermediate stage where the odd ratio is 22.47 (CI95%;10.63-47.47; p= <0.001)

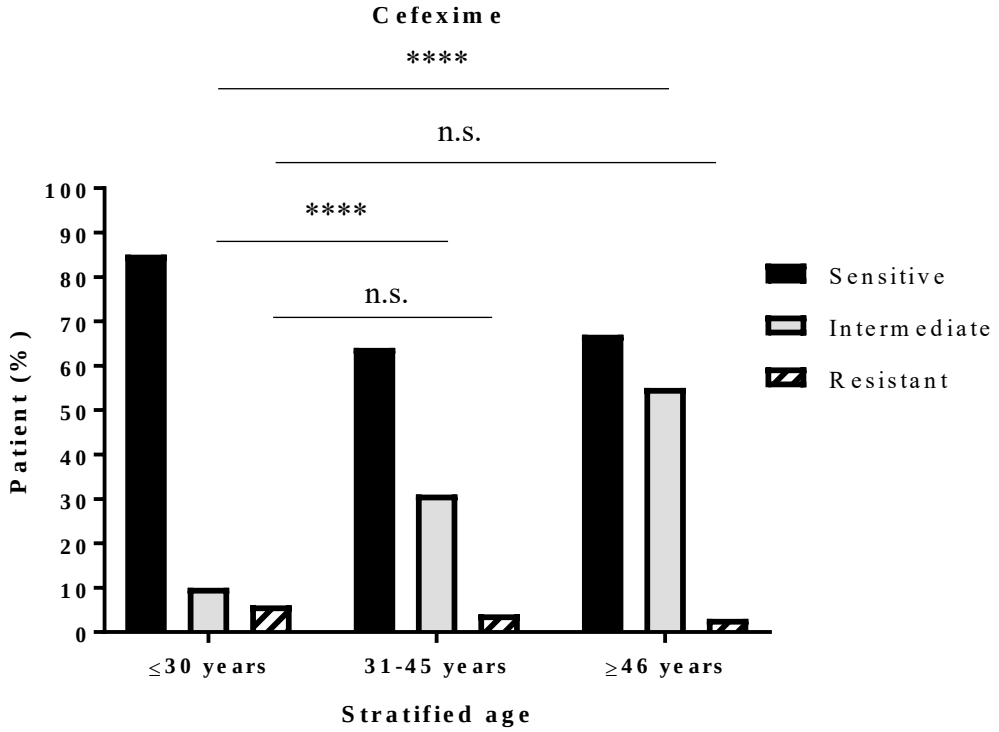


Figure 3.36: Antibiotic sensitivity of *E. coli*to cefexime among patients (%) based on stratified age groups. Statistical significance (p-value) is reported above the graph.[n.s. (not significant) indicates p= >0.05; **** signifies p= <0.001]

Percentage of antibiotic sensitivity of *E. coli* is shown (Figure-3.36) towardscefexime against different age group where the patients are divided in three group on the basis of different age. In figure 3.36, for ≤30 years age group,out of 205 isolates, 174(84.88%) are sensitive, 20(9.76%) are intermediate and 11(64.41%) are resistant.In 31-45 age group, out of 177 isolates, 114(64.41%) are sensitive, 56(31.64%) are intermediate and 7(3.95%) are at resistant with odd ratio 1.08 (CI95%;0.40-2.89; p= 0.883). In ≥46 years age group,out of 161 isolates, 67(41.61%) are sensitive, 89 (55.28%) are intermediate and 5(3.11%) are resistant with odd ratio1.4 (CI95%; 0.46-4.26; p=0.554) and this is for resistant compared to sensitive. At the same time in case of intermediate compared to sensitive for age group 31-45 years, odd ratio is 4.48 (CI 95%;2.56-7.93; p= <0.001) andfor age group ≥46 years odd ration is 12.43 (CI95%; 7.07-22.27; p= <0.001).

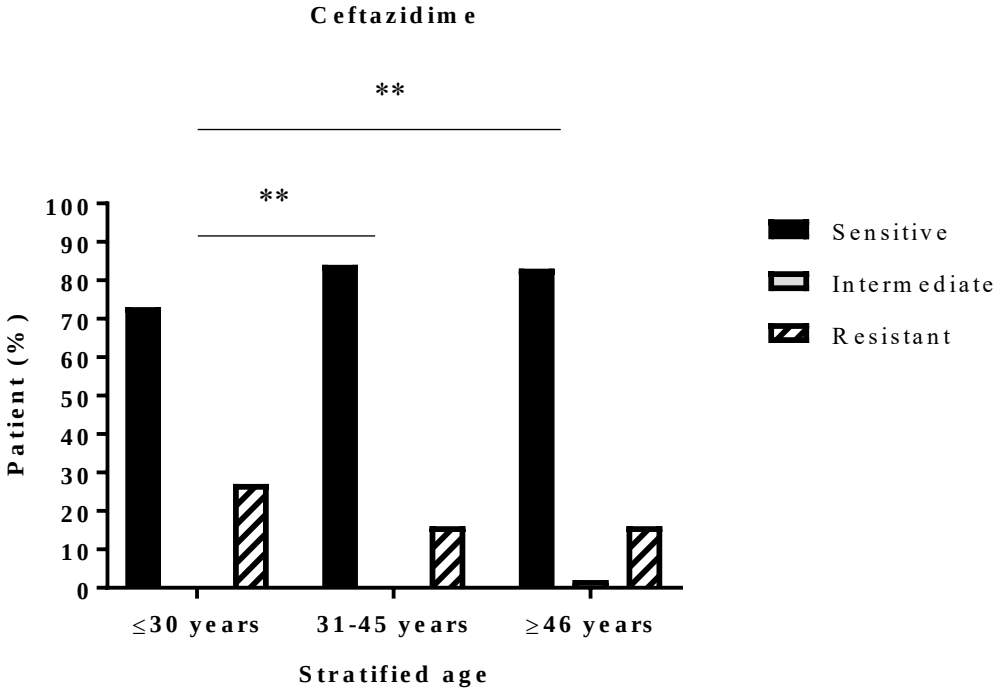


Figure 3.37: Antibiotic sensitivity of *E. coli* to ceftazidime among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph. [** signifies p= 0.01]

Antibiotic sensitivity of the isolated *E. coli*is shown (Figure 3.37) to ceftazidime against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group , out of 205 isolates, 150(73.17%) are sensitive, 0 are at intermediate and 55(26.83%) are at resistant stage and this is reference value. In 31-45 age group, out of 177 isolates, 149(84.18%) are sensitive, 0 are at intermediate and 28(15.82%) areresistant with odd ratio 0.52 (CI95%; 0.23-0.60; p=0.012). In ≥46 years age group, out of 161 isolates, 133(82.62%) are sensitive, 2(1.24%) are at intermediate and 26(16.15%) are resistant, odd ratio is 0.54 (CI95%; 0.32-0.92; p= 0.024)).

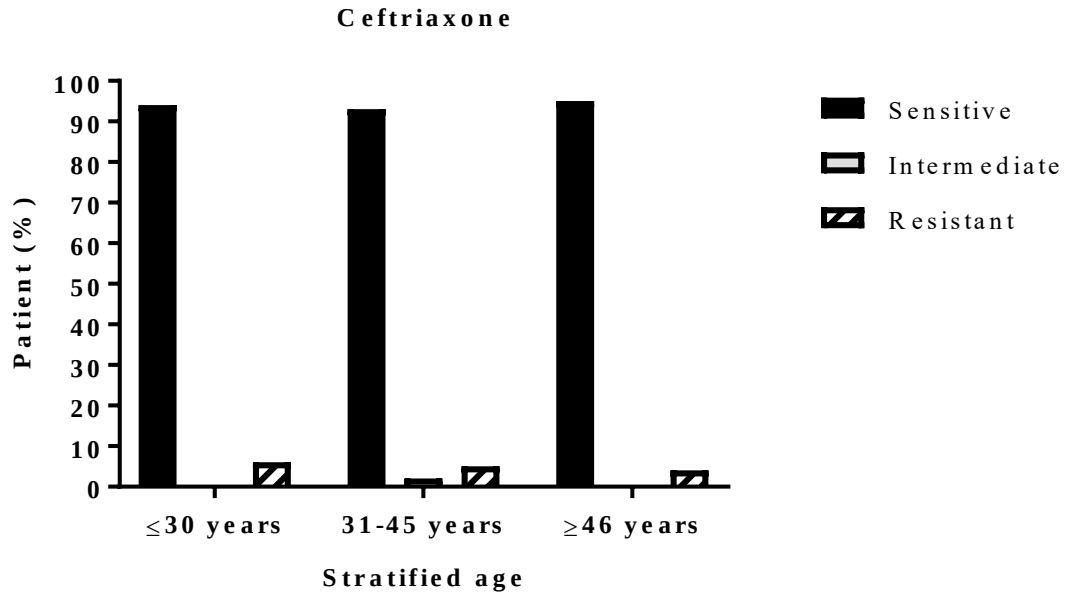


Figure 3.38: Antibiotic sensitivity of *E. coli* to ceftriaxone among patients (%) based on stratified age groups.

Antibiotic sensitivity of the isolated *E. coli*is shown (Figure 3.38) to ceftriaxone against different age group. Where the patients are divided in three group on the basis of different age. In≤30 years age group,out of 87 isolates, 82(94.25%) are sensitive, 0 are at intermediate and 5(5.75%) are resistant. In 31-45 age group out of 66 isolates, 62(93.94%) are sensitive, 1(1.52%) are at intermediate and 3(4.55%) patients are resistant. In ≥46 years age group out of 97 isolates, 93(95.88%) are sensitive, 0 patient is at intermediate and 4(4.12%) are at resistant stage.

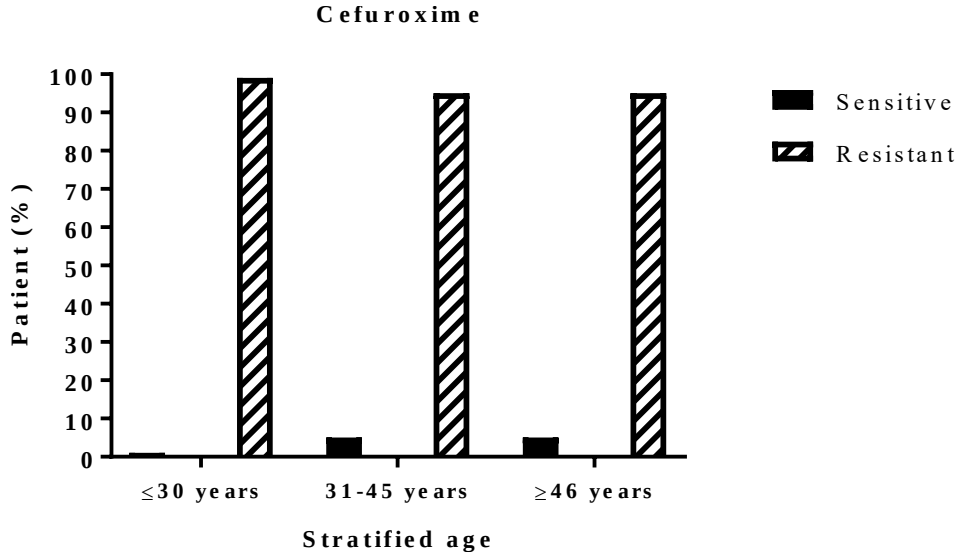


Figure 3.39: Antibiotic sensitivity of *E. coli* to cefuroxime among patients (%) based on stratified age groups.

Antibiotic sensitivity of the isolated *E. coli* is shown (Figure 3.39) to cefuroxime against different age group. Where the patients are divided in three group on the basis of different age. These are equal or less than 30 years (≤30 years), 31-45 years and more or equal to 46 years (≥46 years). In ≤30 years age group, out of 140 isolates, 1 (0.71%) is sensitive and 139 (99.29%) are at resistant stage (Figure 3.38). In 31-45 age group out of 147 isolates, 7 (4.76%) are sensitive and 140 (95.24%) are at resistant stage. In ≥46 years age group out of 132 isolates, 6 (4.55%) are sensitive and 126 (95.45%) are resistant.

Antibiotic sensitivity of the isolated *E. coli* is shown (Figure 3.40) to cephradine against different age group. Where the patients are divided in three group on the basis of different age. Out of 204 isolates, 6(2.94%) is sensitive and 198(97.06%) are resistant for ≤30 years age group. In 31-45 age group out of 178 patients, 2(1.13%) are sensitive and 175(98.87%) are resistant. In ≥46 years age group out of 161 patients, 8(4.97%) patients are sensitive and 153(95.03%) are at resistant.

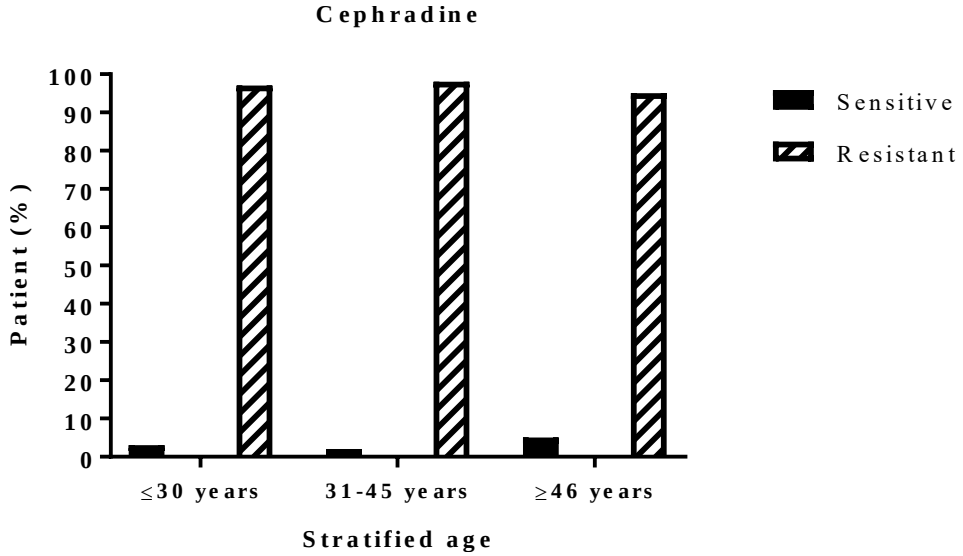


Figure 3.40: Antibiotic sensitivity of *E. coli* to cephradine among patients (%) based on stratified age groups.

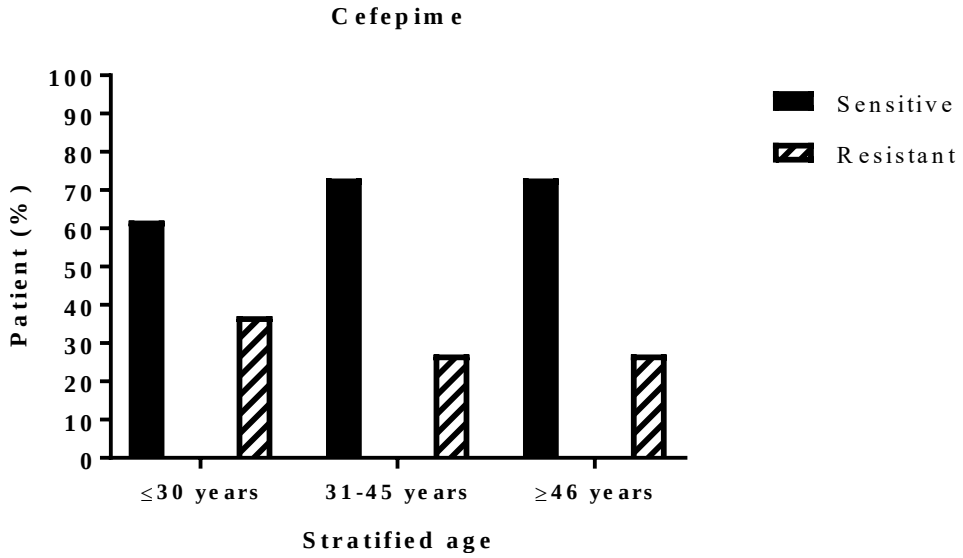


Figure 3.41: Antibiotic sensitivity of *E. coli* to cefepime among patients (%) based on stratified age groups.

Antibiotic sensitivity of the isolated *E. coli* to cefepimeis shown here (Figure 3.41), against different age group. Where the patients are divided in three group on the basis of different age. In figure 3.40, out of 64 isolates 40 (62.50%) are sensitive and 24 (37.50%) are at

resistant stage for ≤30 years age group. In 31-45 age group out of 30 isolates, 22(73.3%) patients are sensitive and 8(26.67%) patients are resistant.In ≥46 years age group out of 30 isolates, 22 (73.33%) are sensitive and 8 (26.67%) are resistant.

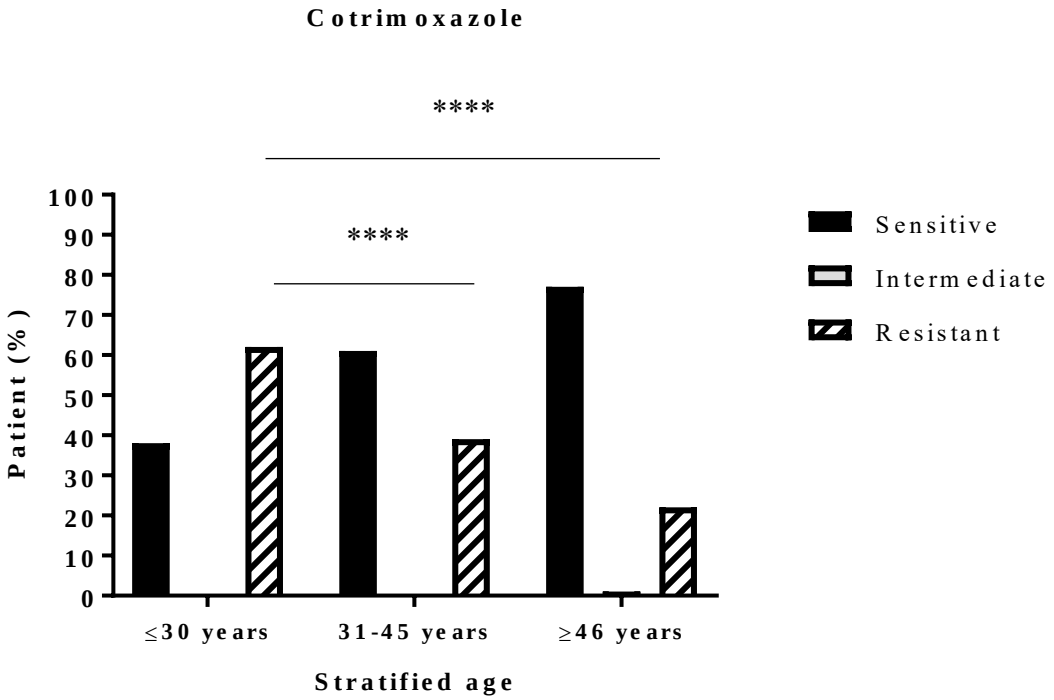


Figure 3.42: Antibiotic sensitivity of *E. coli* to cotrimoxazole among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph.[**** signifies p= <0.001]

Antibiotic sensitivity of the isolated *E. coli* to cotrimoxazoleis shown here (Figure 3.42), against different age group.Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 142 isolates, 54 (38.03%) are sensitive, 0 are intermediate, 88 (61.97%) are at resistant and this is considered as reference group. In 31-45 age group out of 147 isolates, 90(61.22%) are sensitive, 0 are at intermediate and 57(38.78%) are resistant with 0.38 odd ratio (CI95%; 0.40-1.34; p= <0.001). In ≥46 years age group out of 132 isolates, 102(77.27%) are sensitive, 1(0.76%) is at intermediate and 29(21.9%) are at resistant stage with odd ratio 0.16 (CI95%; 0.10-0.29; p= <0.001) this is for resistance compared to sensitive of cotrimoxazole.

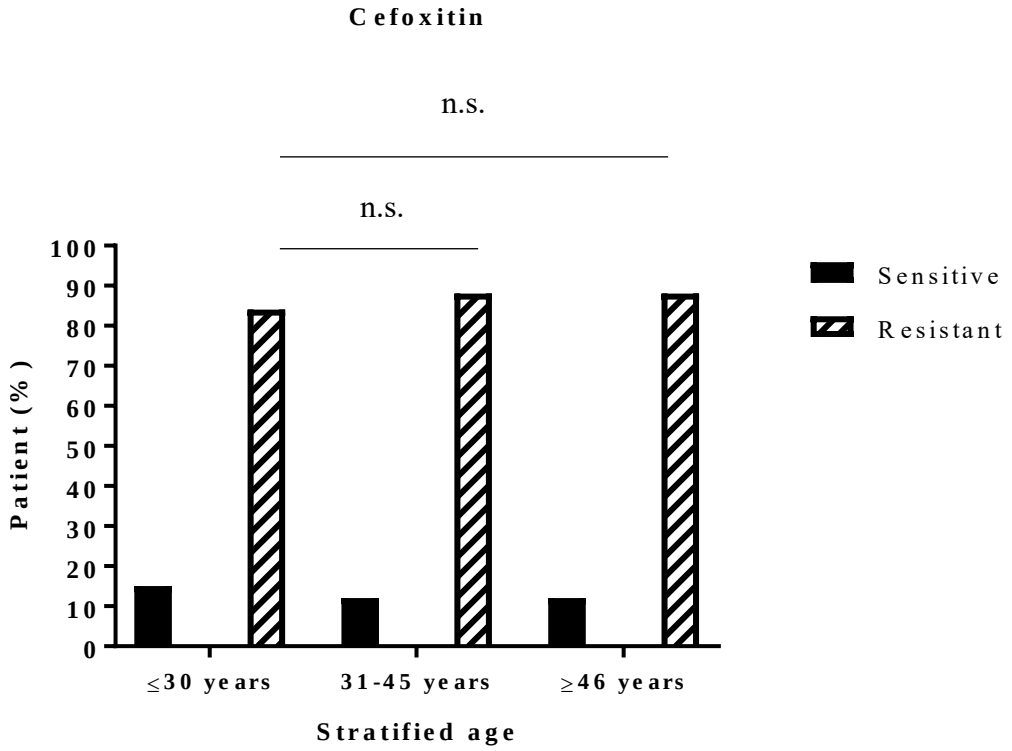


Figure 3.43: Antibiotic sensitivity of *E. coli* to cefoxitin among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph.[n.s. (not significant) indicates p= >0.05]

Antibiotic sensitivity of the isolated *E. coli* to cefoxitinis shown here (Figure 3.43), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 203 isolates, 31 (15.27%) is sensitive and 172 (84.73%) are at resistant and this is considered as reference group. In 31-45 age group out of 176 isolates, 20 (11.36%) are sensitive and 156 (88.64%) are at resistant stage where odd ratio is 0.73 (CI95%; 0.40-1.34; p= 0.309). In ≥46 years age group out of 160 isolates, 19 (11.88%) are sensitive and 141 (88.13%) are at resistant stage where odd ratio is 0.78 (CI95%; 0.42-1.5; p= 0.431).

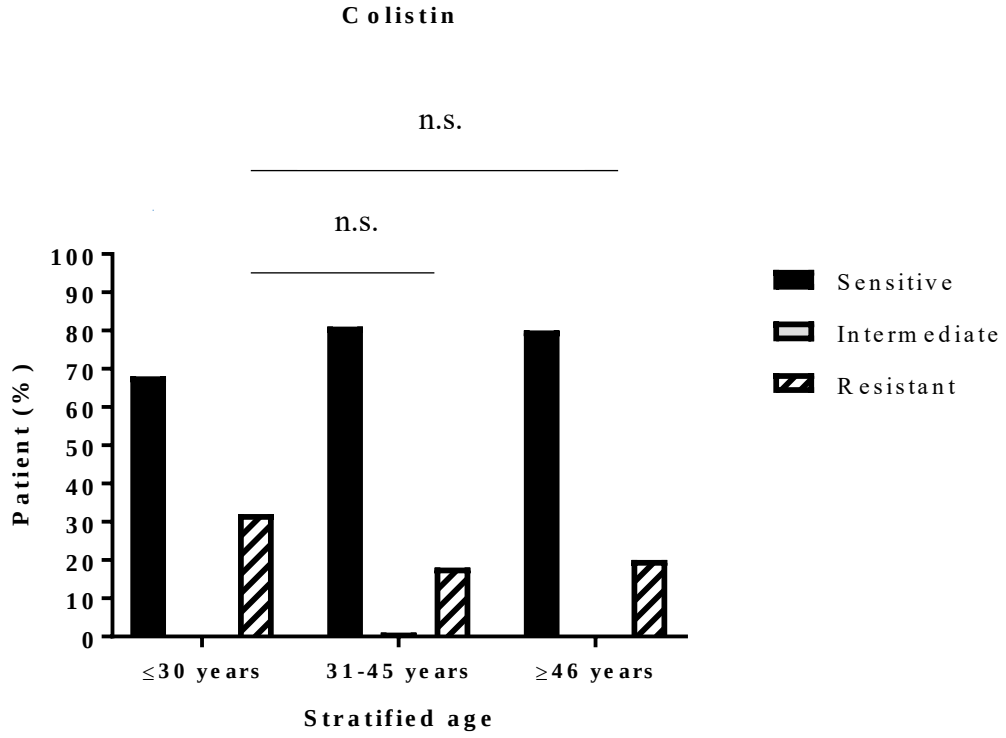


Figure 3.44: Antibiotic sensitivity of *E. coli* to colistin among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph.[n.s. (not significant) indicates p= >0.05]

Antibiotic sensitivity of the isolated *E. coli* to colistinis shown here (Figure 3.44), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 205 isolates, 140(68.29%) are sensitive, 0 are intermediate and 65(31.71%) are at resistant stage and this considered as reference group. In 31-45 age group out of 177 isolates 144(81.36%) are sensitive, 1(0.56%) is at intermediate and 32(18.08%) are at resistant stagewith odd ratio 0.51 (CI95%; 0.31-0.84; p= 0.007). In ≥46 years age group out of 160 isolates, 128(80%) are sensitive, 0 patient is intermediate and 32(20%) are at resistant with odd ratio 0.60 (CI95%;0.57-3.53; p= 0.046).

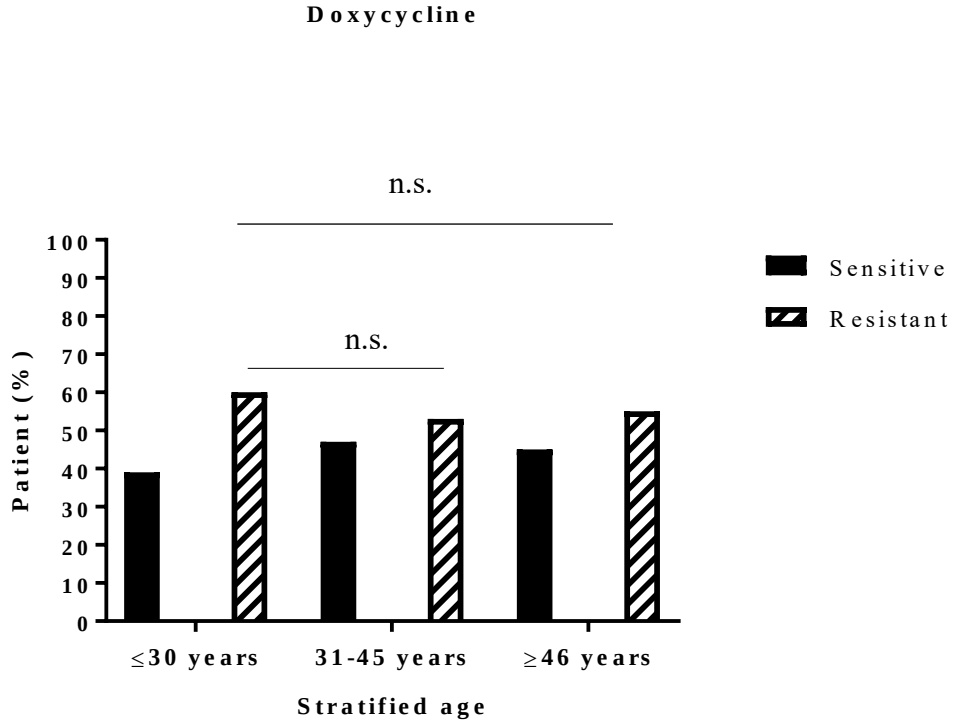


Figure 3.45: Antibiotic sensitivity of *E. coli* to doxycycline among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph.[n.s. (not significant) indicates p= >0.05]

Antibiotic sensitivity of the isolated *E. coli* to doxycyclineis shown here (Figure 3.45), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 63 isolates, 25(39.68%) is sensitive and 38(60.32%) are at resistant and this is considered as reference group. In 31-45 age group out of 30 isolates 14(46.67%) are sensitive and 16(53.33%) are resistant with 1.43 odd ratio (CI95%; 0.59-3.53; p= 0.424). In ≥46 years age group out of 29 isolates 13(44.83%) are sensitive and 16 (53.33%) are resistant with odd ration 1.41 (CI95%; 0.57-3.53; p= 0.463). This is for resistance compared to sensitive of doxycycline.

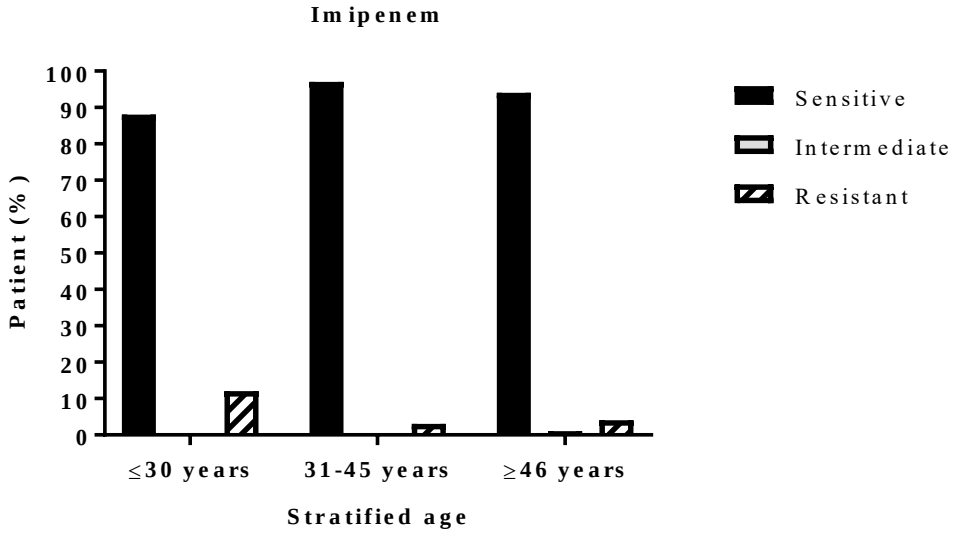


Figure 3.46: Antibiotic sensitivity of *E. coli* to imipenem among patients (%) based on stratified age groups.

Antibiotic sensitivity of the isolated *E. coli* to imipenemis shown here (Figure 3.46), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 142 isolates, 125(88.03%) are sensitive, 17(11.97%) are at intermediate and 0 patient is at resistant stage. In 31-45 age group out of 147 isolates, 143(97.28%) are sensitive, 0 patient is at intermediate and 4(2.72%) are at resistant stage. In ≥46 years age group out of 132 isolates, 125(94.70%) are sensitive, 1(0.76%) is at intermediate and 6(4.55%) are at resistant.

Antibiotic sensitivity of the isolated *E. coli* to nalidixic acidis shown here (Figure 3.46), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group, out of 142 isolates, 4(2.82%) are sensitive and 138(97.18%) are resistant. In 31-45 age group out of 147 isolates, 6(4.08%) are sensitive and 141(95.92%) are at resistant stage. In ≥46 years age group out of 132 isolates, 2(1.52%) are sensitive and 130(98.48%) are resistant.

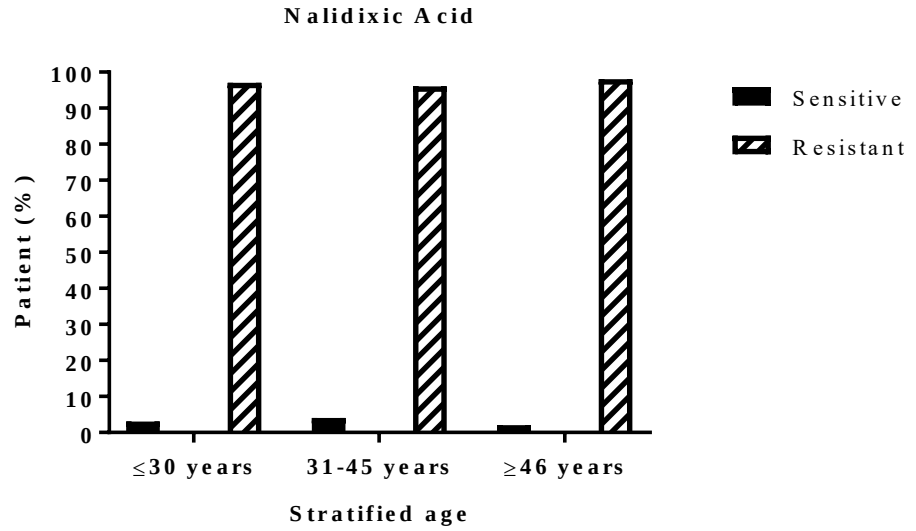


Figure 3.47: Antibiotic sensitivity of *E. coli* to nalidixic acid among patients (%) based on stratified age groups.

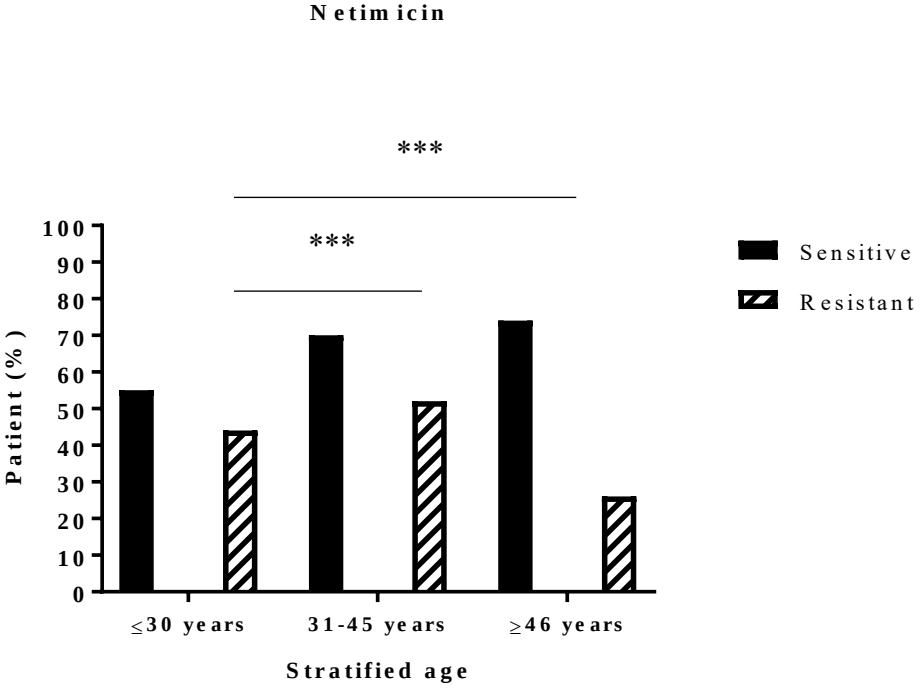


Figure 3.48: Antibiotic sensitivity of *E. coli* to netimicin among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph.[*** signifies p= 0.005]

Antibiotic sensitivity of the isolated *E. coli* to netemicinis shown here (Figure 3.48), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 205 isolates, 113(55.12%) are sensitive and 92(44.88%) are at resistant stage and this is considered as reference group. In 31-45 age group out of 177 isolates, 125 (70.62%) are sensitive and 52(29.38%) are resistant with odd ratio 0.54 (CI95%; 0.35-0.83; p= 0.005). In ≥46 years age group out of 160 isolates, 119(74.38%) are sensitive and 41(25.62%) are at resistant stage with odd ratio 0.46 (CI95%;0.29-0.73; p= 0.001). This is for resistance compared to sensitive of netimicin.

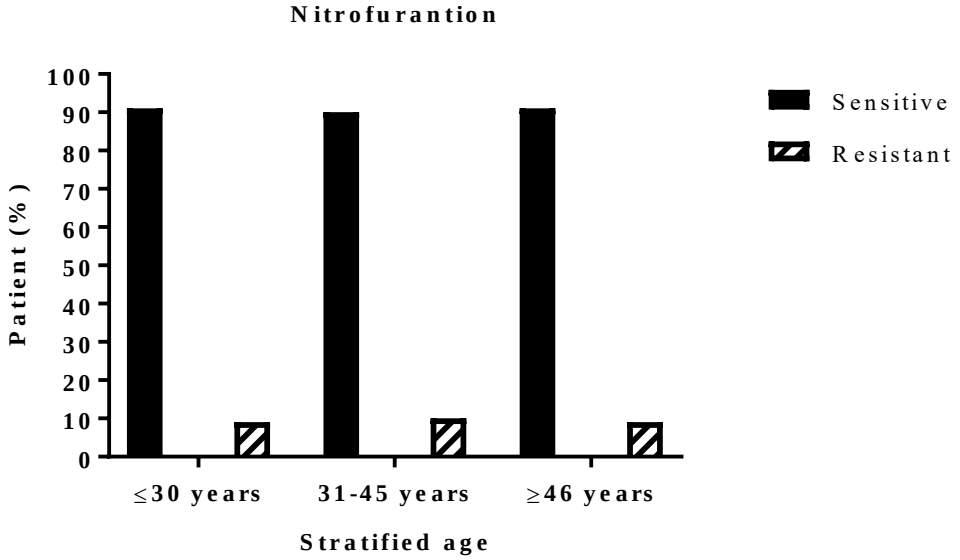


Figure 3.49: Antibiotic sensitivity of *E. coli* to nitrofuration among patients (%) based on stratified age groups.

Antibiotic sensitivity of the isolated *E. coli* to nitrofurationis shown here (Figure 3.49), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 142 isolates, 130(91.55%) are sensitive and 12(8.45%) are at resistant. In 31-45 age group out of 147 isolates, 132(89.80%) are sensitive and 15(10.20%) are resistant. In ≥46 years age groupout of 142 isolates, 120(90.91%) are sensitive and 12(9.09%) are resistant.

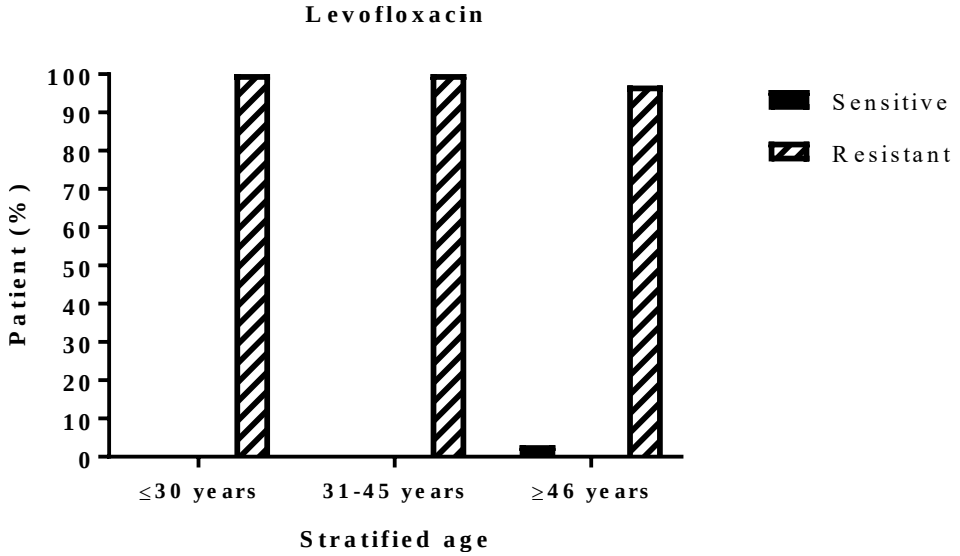


Figure 3.50: Antibiotic sensitivity of *E. coli* to levofloaxacin among patients (%) based on stratified age groups.

Antibiotic sensitivity of the isolated *E. coli* to levofloxacinis shown here (Figure 3.50), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 142 isolates, 142(100%) are resistant. In 31-45 age group out of 147 isolates, 147(100%) are at resistant stage and in ≥46 years age group, out of 131 isolates, 3(3.03%) are sensitive and 128(96.97%) are at resistant stage.

Antibiotic sensitivity of the isolated *E. coli* to tetracyclineis shown here (Figure 3.51), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 142 isolates, 8 (5.63%) are sensitive and 134 (94.37%) are resistant. In 31-45 age group out of 147 isolates, 1(0.68%) is sensitive and 146 (99.32%) are resistant.In ≥46 years age group out of 132 isolates, 2 (1.52%) are sensitive and 130(98.48%) are resistant.

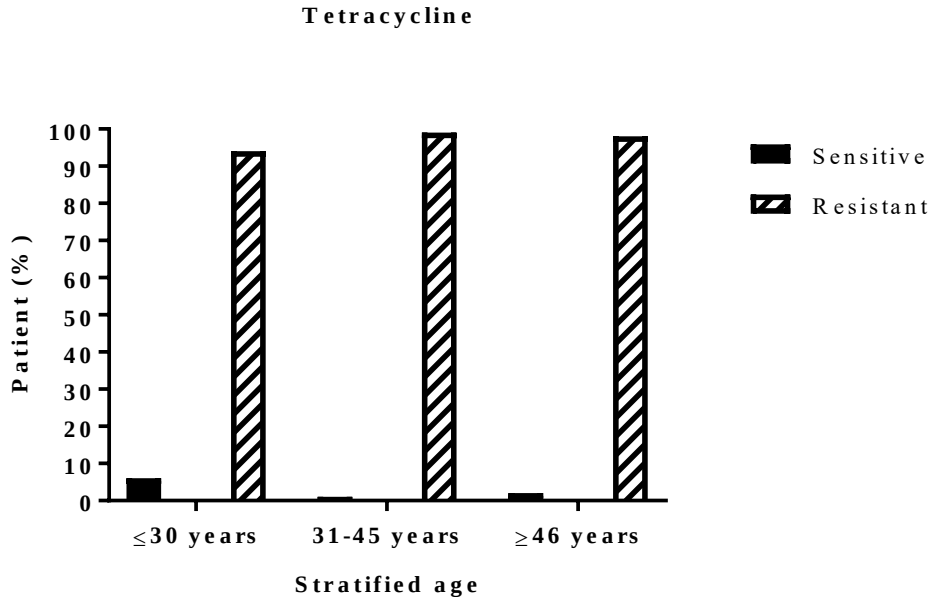


Figure 3.51: Antibiotic sensitivity of *E. coli* to tetracycline among patients (%) based on stratified age groups.

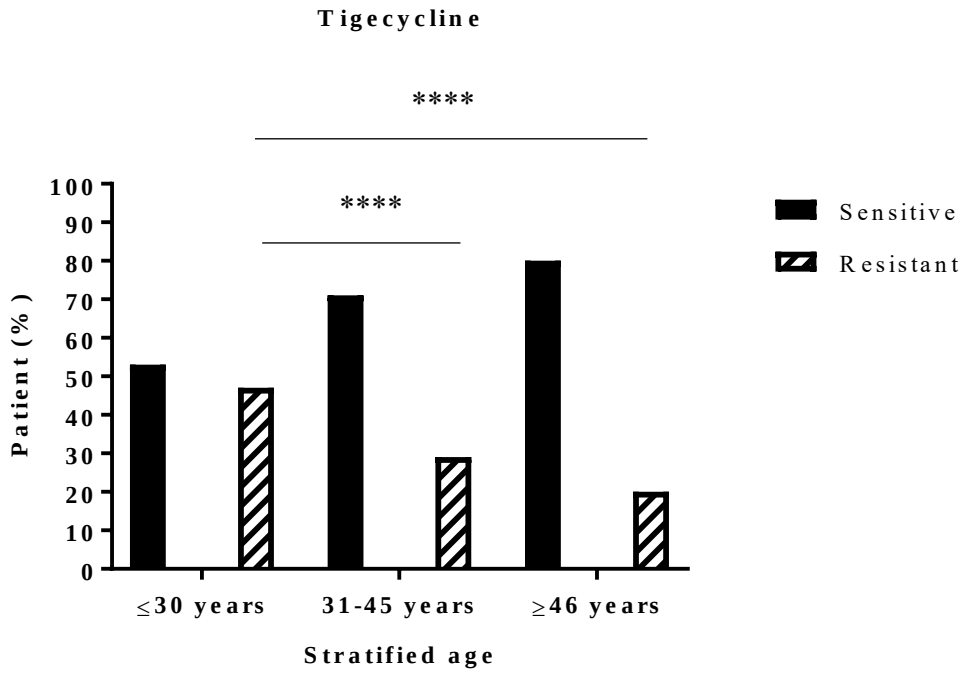


Figure 3.52: Antibiotic sensitivity of *E. coli* to tigecycline among patients (%) based on stratified age groups.Statistical significance (p-value) is reported above the graph.[**** signifies p= <0.001]

Antibiotic sensitivity of the isolated *E. coli* to tigecycline is shown here (Figure 3.52), against different age group. Where the patients are divided in three group on the basis of different age. In ≤30 years age group out of 205 isolates, 109(53.17%) are sensitive and 96(46.83%) are resistant and this is considered as reference.In 31-45 age group out of 177 isolates, 126(71.19%) are sensitive and 51(28.81%) patients are at resistant stage where odd ratio is 0.45 (CI95%; 0.29-0.68; p= <0.001).In ≥46 years age group out of 161 isolates, 129(80.12%) are sensitive and 32(19.88%) areresistant where odd ratio is 0.27 (CI95%; 0.29-0.68; p= <0.001). This is for resistance compared to sensitive of tigecycline.

Chapter 4: Discussion

4. Discussion

In this research, antibiogram or report of c.s. test were collected for *Escherichia coli.* Where the population contain male and female patient, among 543 sample 164 (31.8%) are male and 379 (68.2%) are female patient. These data are also divided into three age groups and the groups are equal or less than 30 years (≤30 years), 31-45 years and more or equal to 46 years (≥46 years). Among 543 data all of the specimens were collected from urine sample of the patients. In this research, noticeable thing is percentage of female patients is higher than the percentage of male patients.

In this study, the mostly sensitive antibiotics found which are active (more than 90%) against *E. coli* are amikacin, ampicillin, amoxyclav, cefotaxim, cefexime, ceftriaxone, ciprofloxacin, colisitin, gentamycin, imipenem, meropenem, nitrofuration and tigecycline. This is similar for all four division that are included in the research. In case of comparison with other research, Kaur, Grover and Sing mentioned in their research that, amikacin, ampicillin, amoxicillin, gentamycin, piperacillin, linezolid, cefotaxim are highly susceptible (50-80%) for *E.coli*(Kaur, Singh, Upveja, & Paul, 2016). This article is for the sub-continent which similar to our research. On the other hand they also mentioned about some combination therapy which is more effective on the micro-organisms. But in our research we have studied only for single antibiotic therapy to the patients. Again, all of the mentioned antibiotics in our research have not found that are included in others. In another research in Bangladesh, Noor, Shams and Hasan have found that amikacin, imipenem, meropenem, nitrofuration and cotrimoxazole are highly susceptible (40% to 90%) for *E.coli* bacteria, which is collected from urinary tract infection (UTI) sample (Noor et al,. 2013). This relevant research was done 5 years back where they have found ampicillin is more resistant for *E. coli,* but in our research we have found ampicillin is highly susceptible or sensitive in Dhaka, Chattagram, Khulna and Rajshahi. Resistance of these mentioned antibiotics for *E.coli* is very low in all the divisions. In case of the comparison with any research of another region other than this sub-continent, in a research in Iran Momtaz, karmian and others have found that quinolones, amikacins, chloramphenicol, tetracyclines, tigecyclines and some β-lactam rings are very effective for *E.coli* bacteria (Rashki, 2014). The groups of antibiotic is similar to this study, which indicates sensitivity of these kind of drug are more or less is still similar allover the world.

In our research, we have found azithromycin, aztreonam, cefuroxime, ceftriaxone, cephradine, nalidixic acid, levofloxacin, cefoxitin and tetracycline highly (60-90%) resistant in the perspective of Dhaka, Chattagram, Khulna and Rajshahi division. Here, levofloxacin, nalidixic acid, aztreonam may considered as first generation common antibiotics.In case of resistant growth of different antibiotic in a study near northeast India, sing and other researcher have found different kind of resistance for different kind of groups like peer, community , village and others. Their main focus of the study was antibiotic resistance of *E.coli* among the children of that area. Researcher have found high resistance of ampicillin (92%), tetracycline (32%) and mentioned some general antibiotics as "first generation common antibiotics" which are almost 95% resistant for *E.coli* in that area (Singh et al., 2018). This study was done in this year. In a research in Bangladesh Afroz, Sultana and others have studied on antibiotic resistance of *E.coli*. They performed the research collecting the bacteria from milk powder not from any kind of living sample, they collected microbes and performed sensitivity test on the microbes and found resistance on E.coli. They have found resistance nalidixic acid, cefuroxime, ceftriaxone, cefexime, and erythromycin from 60%-75%. Which is similar to our study regarding the resistance of *E.coli*, as we have found resistance of azithromycin, aztreonam, cefuroxime, ceftriaxone, cephradine, nalidixic acid, levofloxacin, cefoxitin and tetracycline up to similar percentage. But the difference is we have collected our sample specimens from human sample and in case some antibiotics like tetracycline, levofloxacin, chloramphenicol, cefuroxime and aztreonam have resistance more than 90%.

From this study, some antibiotics could be highly focused for growing of resistance, such as aztreonam is 98.5% resistant in Dhaka division, in Chattgram and Khulna it is 100% resistant and in Rajshahi it is 98.6% resistant. Nalidixic acid is more than 95% resistant on an average in every division, levofloxacin another antibiotic which is more than 97% resistant on an average in 4 mentioned division. These medicines are almost resistant, which means practitioners have to find out alternative antibiotics for the patients. Day by day upgraded antibiotics may also be get resistant and that's the matter of thinking. If this is the condition, people of these community should be more concerned about ingesting antibiotics for bacterial attack. In such way people will not be able to fight against microbes to survive as a result, people may die for such simple microbes. That's why practitioners need to

perform the culture and sensitivity test to be ensure which antibiotic may be given to the patient.

There are some antibiotics which are to be resistant in near future, in our study we have noticed that some of the antibiotics are in intermediate stage which means *E. coli* producing resistance to these antibiotics day by day. These antibiotics are cefexime, cotrimoxazole, colisitin, ceftazidime, cefepime and netimicin. First of all cefexime have 11.9%, 35.7% 36.4% 57.1% intermediate stage percentage respectively in Dhaka, Chattagram, Khulna and Rajshahi division. This means cefexime is at the stage very soon it will not be effective against *E.coli* in these area. Cotrimoxazole, colistin and ceftazidime is less in percentage but they are being resistant by *E.coli*. In case of cefepime and netimicine they are at the stage where half of the *E. coli* population already became resistant and if it is not controlled this rate will increase rapidly.

In case of some positive results of our study, there are some antibiotics which are highly sensitive against *E. coli* bacterium. If we think separately about each antibiotic amikacin, ampicillin and amoxyclav is higly sensitive other than amoxyclav in Khulna and Rajshahi. In these two divisions amoxyclav is less sensitive even though it is more than 50%. Azithromycin is 99% sensitive in Dhaka and Khulna. The cephalosporin group which include cefexime, ceftazidime, ceftriaxone, cefuroxime, cephradine, ciprofloxacin are highly sensitive. Among cephalosporin second generation antibiotics are more effective than first generation. In another study in iran, researcher have found other thant amikacin and azithromycin most of the second generation antiobiotics are more effective(Azad, Mousavi, Gorzi, & Ghasemnian, 2016). Again, chloramphenicol, doxycycline, norfloxacin and tigecyclines are still effective against *E.coli*.

In Bangladesh Begum, Islam and others have studied about resistance of pathogens or microbes in this research they collected samples from animal specimens. This research is different but relevant with our study in the perspective of *E.coli* resistance, *E.coli* which are present in human body may get resistance or human may affected by the *E.coli* from other animals by any means. Researcher have found *E. coli* in this case also become resistant in contact of those. They have found *E.coli* from goats is 100 % sensitive to ciprofloxacin and norfloxacin(Begum et al., 2016). In our research ciprofloxacin is almost 90% sensitive

whereas norfloxacin is about 50/50. They are partially resistant to tetracycline and gentamycine but in our study gentamycin is highly sensitive and tetracycline is highly resistant. Mainly *E.coli* from all kind of specimen (living, non-Living, Animals) is highly sensitive to ciprofloxacin.

In a research of Michigan they collected data of past 6 years of different patients and brought out a information that *E.coli*(a gram negative bacteria) is sensitive to erythromycin, gentamycin, ceftriaxone, piperacillin, imipenem, cephalothin, ciprofloxacin and cefazolin (Boehme, Somsel, & Downes, 2010). In our study all of the antibiotics are not included but imipenem, gentamycin, ceftriaxone, ciprofloxacin and ceftriaxone shows the similar result. Those are sensitive to *E.coli*. Boehme, Somsel and Downes studied on the hospital admitted patients, where as we have studied on non-hospital living patient. These patients were susceptible to bacterial disease and thus tested for sensitivity of pathogens(Boehme et al., 2010). In a study of Stellings, Travers and others they mentioned that ciprofloxacin is given in second line therapy in hospitalized patient (Stelling et al., 2005). But here ciprofloxacin is used as primary medication and this is a higly effective antibiotic for *E.coli*.

Antibiotic resistance may also vary on different age and sex group. Before we have discussed about study conducted on children only and some common studies. As mentioned before in our research we have divided our population into 3 groups (≤30 years, 31-45 years and, ≥46 years). In china some researcher said that in case of UTI female are more susceptible than male patient which are mainly *E.coli* bacteria and fluroquinolones, cefotaxime and cefixitin are more effective (Lee et al., 2016). In our study we did not classified this group but on an overview we can see that in our sample population 68.2% is female patient. So, we can say that females are more susceptible and the mentioned antibiotics are still effective for them.

In case of age groups in Bangladesh, Sanzee, Karim and others grouped on the segment of 0-20, 21-40 and above 40 years old and they found below 20 and and above 40 patients are more susceptible which is significant and in their study amikacin, gentamycin and nitrofuration are more sensitive for *E. coli*(Sanjee et al., 2017). On the other hand nalidixic acid , amoxiclav and imipenem is more resistant to *E.coli* and ciprofloxacin and ceftriaxone are at medium stage (Sanjee et al., 2017). In our study we have three age groups (≤30 years,

31-45 years and, ≥46 years) where less than 30 years old patients are more susceptible and for this age group highly sensitive antibiotics are imipenem, nitrofuration, ceftriaxone, cefexime and amoxyclav where as more resistant antibiotics are cefuroxime, cephradine, nalidixic acid, levofloxacin and tetracycline. For age group 31-45 years they comparatively less susceptible and the antibiotics that are effective is imipenem, nitrofuration, ceftriaxone, cefexime and amoxyclav and others such as cefuroxime, cephradine, nalidixic acid, levofloxacin and tetracycline. For agegroup more than 46 years nalidixic acid, cephradine, cefuroxime, levofloxacin and tetracycline is almost resistant whereas tigecycline, nitrofuration, colistin, cotrimoxazole, ceftriaxone is highly sensitive.

In another study Noor, Shams and others grouped the population in 0-15, 16-45, 46+ years groups. Where they claimed 16-45 years group mostly suffer from UTI and the reason is pathogens(Begum et al., 2016). And they claimed amikacin, imipenem is more sensitive and ceftriaxone, cotrimoxazole, nalidixic acid, cefotaxime is highly resistant. In our study in this range of age group we have found the similar analysis.

In case of 0-6 month and up to 6 years age group Stelling, travers and others mentioned in their journal that these population are highest susceptible. But they have found different type of sensitivity in different country such as ceftazidime (11.4%) and gentamicin (15.7%) in Italy; tobramycin (21.9%) in Turkey ; and piperacillin/tazobactam in Spain (10.8%), Sweden (10.9%), Turkey (11.9%), and the United Kingdom (20.9%)(Stelling et al., 2005). In our study we have not analyzed for neonatal population and the research is done only in four division in Bangladesh.

Pounou and others conducted a research in Mexico, Brazil, China, Thailand, France and Serbia, that reported high mortality due to antibiotic-resistant bacteria in ICUs. But this is for overall kind of pathogens and they mentioned increased mortality (OR 2.8341, 95%CIs; 2.2180±3.6213; p= 0.000) which is an overall analysis (R. C. Founou, Founou, & Essack, 2017). In our study, we didn't find any kind of mortality but we have analyzed some of antibiotics for susceptibility significance on the basis of age group such as for amoxyclav 31-45 years (OR 3.42, 95%CI;1.60±7.32;p= 0.002) and for more than 46 years (OR 22.47, 95%CI; 1063±47.47; p= <0.001) on the basis of p value for ≥46 age group this is highly significant. For significance analysis of cefexime for 31-45 years it appears less significant

(OR 1.08, 5%CI;0.40±2.89; p= 0.883) and for more than 46 years (OR1.41,95%CI;0.40±2.89;p= .554). For analysis of ceftazidime (OR0.52, CI95%;0.31±0.87;p= 0.12) andfor more than 46 years (OR 0.54;CI 95%; 0.32±0.92: p= 0.24) which indicates no significant enough for this population, for cotrimoxazole 31-45 years patients OR is 0.38 and for more than 46 years OR is 0.16 in both case CI IS 95%. For cefoxitin OR is 0.73 and OR 0.78; for colisitin OR is 0.51 in case of 31-45 years age and for more than 46 years age group the OR is 0.60. In case of doxycycline 31-45 year age group (OR1.43, 95%CI; 0.59±3.53) and for more than 46 years age group (OR1.41, 95%CI;0.57±3.53; p=4.63) this population also includes in to the 95% confidence interval. In case of netimicin 31-45 years group (OR0.54, 95%CI;0.35±0.83;p= 0.005) and for more than 46 year age group (OR 0.46, 95%CI;0.29±0.73;p= 0.001). Lastly for tigecycline 31-45 years age group (OR 0.45, 95%CI; 0.29±0.68; p= <0.001) and for more than 46 years age group (OR0.27; 95%CI; 0.17±0.44; p= <0.001). Here the age group who have OR more than 1 is at higher risk and OR that are less than 1 is at less risk.

Chapter 5: Conclusion

5. Conclusion

Undoubtedly, antibiotic resistance is a major concern for the world nowadays. Especially, in third world countries, where population density is higher, it is more serious concern. In our study, we have found the susceptibility rate and resistance pattern and how it is increasing which is similar in the selected four divisions. So, the awareness should be risen, or steps should be taken, will be similar in all division. Here, less than 30 years age group is more susceptible to the antibiotic attack where the chances of growing resistance are higher. This age group people should be more careful about their health condition, and they should be more aware of taking antibiotics. Some of the antibiotics, which were used primarily for the purpose of treatment are almost resistant nowadays. Such as, azithromycin, aztreonam, cefuroxime, ceftriaxone, cephradine, nalidixic acid, levofloxacin, cefoxitin, and tetracycline. But there are some other antibiotics too which have very good effect on *E. coli*, they are amikacin, ampicillin, amoxyclav, cefotaxim, cefexime, ceftriaxone, ciprofloxacin, colisitin, gentamycin, imipenem, meropenem, nitrofuration, and tigecycline. Therefore, these antibiotics should kept under surveillance to ensure that they may not become resistant to bacteria very easily. Patients should be more careful about intake of antibiotics with a consultation of a physician and by going through a culture and sensitivity test.

Chapter 6: Future work

6. Future work

In our study, we have studied the resistance of *Escherichia coli*and the study involved regarding data collection of the population of Dhaka, Chattagram, Khulna and Rajshahi. But in future, further studies can be conducted with very common bacterial species like *Clostridium botulinum, Enterococcus, Streptococcus pneumoniae, Acinetobacter* and so on. At the same time, studies can also be conducted in all of the divisions of Bangladesh.

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