Antibiotic sensitivity pattern of bacterial isolates from Acute Lower Respiratory Tract infections in tertiary care hospital, Chattogram

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Session: 2019-2020

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The thesis submitted is in the partial fulfillment of the requirements for the degree of MPH (One Health)

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March 2022

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This is to certify that we have examined the above MPH (One Health) thesis and have found that it is complete and satisfactory in all respects, and all revisions required by the thesis examination committee have been made.

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List of Abbreviations

Abbreviation	Elaboration
ABR	Antibiotic Resistance
AMR	Antimicrobial Resistance
MDR	Multi Drug Resistant
LRTI	Lower respiratory tract infection
SD	Standard Deviation
WHO	World Health Organization

Abstract

Antibiotics are frequently used for various infectious diseases e.g., acute lower respiratory tract infection (ALRTI). But, injudicious use of antibiotics often leads to antibiotic resistance which is an emerging problem. The objective of this study was taken up to analyse the antimicrobial sensitivity pattern of pathogens isolated from the sputum samples of admitted patients suffering from ALRTI in a tertiary care teaching hospital. This cross-sectional study with conducted between September 2021 to March 2022. For this study, 213 lower respiratory tract infection patients were selected by purposive sampling from Chattogram Medical College Hospital, Chattogram. Their socio-demographic information and culture-sensitivity report was recorded using a structured questionnaire. The number of male participants was higher(62%) compared to the number of female participants(32%). The majority of the participants had undergone primary education (46%) and most of the participants had an income below 20,000 BDT (67%). More than three-fourths (77%) of the participants hailed from urban areas. *Streptococcus pneumoniae* (43%) was the most common organism followed by *Klebsiella pneumoniae* (22%) and *Pseudomonasaeruginosa* (13%) isolated from the sputum sample.From 92 sputum samples with *Streptococcus pneumoniae*, 60 samples were sensitive to levofloxacin and 32 samples were resistant. From 48 sputum samples with *K. pneumoniae*, 36 samples were sensitive to levofloxacin and 11 samples were resistant. From 28 sputum samples with *Pseudomonas aeruginosa*, 26 samples were sensitive to levofloxacin and 2 samples were resistant. The commonest pathogens isolated from the sputum samples were *S. pneumoniae,* followed by *Klebsiella* and *Pseudomonas*. Imipenem, piperacillin/tazobactam combination and gentamicin was sensitive against Klebsiella and Pseudomonas.

Keywords: Antibiotic sensitivity, Klebsiella, Pseudomonas, Lower respiratory tract infection

Chapter 1

Introduction

Antimicrobials are likely one of the most effective kinds of chemotherapy in medical history. It is needless to state how many lives they have saved or how much they have contributed to the control of infectious diseases, which have been the dominant cause of human morbidity and mortality for the majority of human history (Aminov, 2010). Antibiotic resistance (ABR) has increased in recent years (ECDC, 1 B.C.E.; Okeke *et al.,* 2005)) while the rate of new antibiotic development has decreased (Luepke & Mohr, 2017; Spellberg *et al.,* 2004). ABR poses a major danger of death and economic burden over the world. The widespread misuse of antibiotics, non-human antibiotic use, poor drug quality, inadequate surveillance, and factors associated with individual and national poverty (poor healthcare standards, malnutrition, chronic and repeated infections, unaffordability of more effective and costly drugs) have a greater impact on developing ABR in different countries (Ayukekbong et al., 2017; de J. Sosa et al., 2010). Furthermore, because newer medications are scarce, resistance must be addressed before we run out of alternatives for combating it.

The first antibiotic, penicillin, was discovered by accident in London by scientist Alexander Fleming. Since then, antibiotics have been responsible for saving millions of lives (Kingston, 2000). However, less than fifty years later, the World Health Organization (WHO) released its first Global Antimicrobial Resistance Study, concluding that we are entering an action-free post-antibiotic era, in which simple diseases and injuries will once again be lethal (Venter et al., 2017). According to the

WHO's 2014 report on global antimicrobial resistance surveillance, there are major gaps in surveillance, as well as a lack of standards for methodology, data sharing, and coordination. Large gaps have been detected in Southeast Asia, Africa, and the Eastern Mediterranean (WHO, 2014). Unfortunately, because of the emergence and spread of antimicrobial resistance (AMR), a multi-faceted and complex issue affecting humans, animals, plants and the climate, some antimicrobials are rapidly losing their effectiveness (Bright-Ponte et al., 2019).

Bangladesh, a Southeast Asian emerging country with a high level of ABR, poses a regional and global concern. Numerous studies have indicated that physicians are prescribing antibiotics irrationally, that patients have a habit of self-medicating, and that antibiotics are being used indiscriminately in agriculture and farming in various sections of the country (Biswas *et al.,* 2014; Mostafa Shamsuzzaman & Kumar Biswas, 2012; Sutradhar *et al.,* 2014).

Lower respiratory tract infections are the main cause of infection-related death worldwide (WHO, 2020). People at risk of respiratory infections, such as the elderly, the immunocompromised, and children, are in greater risk (Beckett *et al.,* 2015; Troeger *et al.,* 2017; van Hecke *et al.,* 2017). Changes in immune function and anatomical characteristics of the respiratory tract, as well as comorbidities, make treating the elderly more difficult, and selecting appropriate antibiotics is critical (Kline & Bowdish, 2016). Resolving respiratory infections in all populations, especially the elderly, will remain a global health-care concern as antibiotic resistance rises.

As a result, determining the prevalence of antibiotic resistance is vital in the short- and medium-term therapy of airway infections. This study aims to investigate the prevalence and pattern of antibiotic resistance of lower respiratory tract infection patients.

Objective

General Objective

- To understand the current status of antibiogram of isolates from the lower respiratory tract infection patients of Chattogram

Specific Objective

1. To estimate the prevalence of different bacterial isolates in patients of lower respiratory tract infection in Chattogram
2. To explore the pattern of antibiotic resistance among the patients of lower respiratory tract infection in Chattogram.
3. To compare the antibiogram of isolates with different demographic variables.

Chapter 2: Review of Literature

Antibacterial agents are used to destroy or stop microbes from proliferating. Despite its widespread use, it is frequently misapplied. Antibiotics were provided without test findings in 90% of cases in Bangladesh, according to studies (Yashin *et al.,* 2018). Antibiotic misuse is a problem both in the United States and around the world. Many research have identified AMR as a global threat. Antimicrobial resistance can lead to the spread of resistant germs, which can have serious consequences such as lengthening hospital stays, increasing the risk of drug toxicity, and driving up costs. Antibiotic use that is irrational or excessive can result in resistant bacterium strains and severe responses, as well as a financial burden on the national health system (Jairoun *et al.,* 2019).

The usage of erythromycin and antibiotic resistance in *Streptococcus pyogenes* have been linked in two countries: Japan and Finland. During the period 1974–1977, Japan's yearly erythromycin consumption was estimated to be between 150,000 and 155,000 kg (165 to 170 tons), while erythromycin resistance among *S. pyogenes* isolates reached an all-time high of 61.8 percent. 4 However, after 1984, yearly erythromycin use dropped to 59,000 to 77,000 kg (65 to 85 tons), while erythromycin resistance among *S. pyogenes* isolates dropped to 1% to 3% (Fujita *et al.,* 1994).

Because of the near tripling in erythromycin use throughout the 1980s, Finland saw an increase in erythromycin resistance among *S. pyogenes* isolates collected from pharyngeal and pus samples in the late 1980s and early 1990s (Seppälä *et al.,* 1997).

Five Finnish medical authorities responded by issuing statewide guidelines to reduce the use of macrolide antibiotics for outpatient respiratory and skin diseases. Following that, macrolide antibiotic use dropped from 2.40 defined daily doses per 1000 inhabitants per day in 1991 to 1.38 in 1992, and then stayed between 1.28 and 1.74 in the following years. The decreased usage of macrolides was accompanied by a consistent decline in erythromycin resistance in *S. pyogenes* throat swabs and pus samples (from 16.5 percent in 1992 to 8.6 percent in 1996). Despite penicillin's long-standing usage as the medication of choice for *S. pyogenes*, investigators have found no evidence of penicillin resistance among *S. pyogene*s isolates.

Antibiotic usage and resistance have also been linked in other studies involving *Streptococcus pneumoniae*(Arason *et al.,* 1996; Burdge *et al.,* 1992; Duchin *et al.,* 1995; Radetsky *et al.,* 1981; Reichler *et al.,* 1992; Robins-Browne *et al.,* 1984). When comparing children who have recently used antibiotics to children who have not, it indicates that children who have recently used antibiotics have a 2–7-fold increased risk of becoming colonized with penicillin-resistant *S. pneumoniae* (Lynch & Zhanel, 2009). Most of the researchers in these studies characterized recent antibiotic use as antibiotics taken during the previous 1 to 3 months.

Antibiotic prophylaxis for otitis media in children, according to Reichler and colleagues (Reichler *et al.,* 1992), increases the likelihood of subsequent colonization with antibiotic-resistant *S. pneumoniae*. In addition to the individual's recent antibiotic use, research have linked increased *S. pneumoniae* resistance to increased antibiotic use in the overall population (Arason *et al.,* 1996). Guillemot and colleagues (Guillemot *et al.,* 1998) observed that pharyngeal carriage of penicillin-resistant S.

pneumoniae was linked to recent use of beta-lactam antibiotics administered as a low daily dose or for more than 5 days in a recently published study involving children in France. Several antibiotic families, including beta lactams, macrolides, and sulfonamides, appear to be capable of producing penicillin-resistant *S. pneumonia* (Arason *et al.,* 1996; Burdge *et al.,* 1992; Duchin *et al.,* 1995; Radetsky *et al.,* 1981; Reichler *et al.,* 1992; Robins-Browne *et al.,* 1984). In a study conducted by Arason and colleagues in Iceland,6 trimethoprim-sulfamethoxazole was found to have the strongest link to the development of penicillin-resistant *S. pneumoniae*, outperforming both macrolides and beta-lactams (Arason *et al.,* 1996). Other research, on the other hand, have not conclusively demonstrated that certain antibiotics pose a higher risk than others.

As of the beginning of 2017, the World Health Organization has published a list of priority infections for which further research and development of antibiotic medicines were required (WHO, 2017). This list includes pathogens that are frequently associated with respiratory infections, such as ampicillin-resistant *Haemophilus influenzae*; carbapenem-resistant *Pseudomonas aeruginosa*; carbapenem-resistant *Acinetobacter baumannii*; carbapenem- and third-generation cephalosporin-resistant Enterobacteriaceae, including *Klebsiella pneumoniae*; *Staphylococcus aureus* (methicillin resistant, vancomycin intermediate, and vancomycin resistant); and penicillin-nonsusceptible *Streptococcus pneumoniae* (Pfaller *et al.,* 2012; WHO, 2017). The respiratory infection *Mycobacterium tuberculosis* isn't on this list because it was previously identified as a global health priority due to multidrug resistance and the need for new medications (WHO, 2017).

Because of the high prevalence (> 80%) of β-lactamases, another respiratory infection, *Moraxella catarrhalis*, is frequently resistant to β-lactams and has showed lower susceptibility to macrolides and fluoroquinolones (Du *et al.,* 2017; Hu *et al.,* 2016; Jetter *et al.,* 2009; Saito *et al.,* 2015; Wang *et al.,* 2016; Zhang *et al.,* 2016). The respiratory pathogens *Bordetella pertussis*, *H influenzae*, and *S pneumoniae* have all been vaccinated against. *B pertussis* has been successfully reduced in incidence; however, cases are progressively being reported in select regions, with resistance to macrolides, fluoroquinolones, and tetracyclines (Yang *et al.,* 2015). Vaccination has reduced certain serotypes of *H influenzae* and *S pneumoniae*, as well as antibiotic resistance; nevertheless, other serotypes with rising resistance are increasingly dominating in infections (Dunne *et al.,* 2018; Liñares *et al.,* 2010; Sheppard *et al.,* 2016). *H influenzae* is highly resistant to ampicillin in several areas, with high levels of β-lactamase synthesis. *S pneumoniae* continues to exhibit decreasing susceptibility to β-lactam antibiotics over the world, and treatment with fluoroquinolones and macrolides has resulted in greater resistance to these drugs (Baek *et al.,* 2018; Hu *et al.,* 2016; Wang *et al.,* 2016; Zhang *et al.,* 2016). Finally, multidrug-resistant (MDR) bacteria, such as MDR *S pneumoniae* and MDR *A baumannii*, are becoming more prevalent, in addition to single-agent resistance (Zilberberg *et al.,* 2016; Zumla *et al.,* 2014).

Once an individual develops antibiotic resistance, the transmission of a resistant strain is critical in spreading the problem. Several studies have found that children in daycare centers have higher rates of antibiotic-resistant respiratory infection carriage (Duchin *et al.,* 1995; Hofmann *et al.,* 1995; Radetsky *et al.,* 1981; Reichler *et al.,* 1992). The day-care center, presumably, contributes to antibiotic resistance by encouraging frequent and close physical contact, with resistant bacteria being transmitted via respiratory droplets or shared oral secretions. Furthermore, close person-to-person contact increases the possibility of transmission of common non-resistant respiratory bacterial strains as well as viral respiratory tract infections, both of which may result in increased antibiotic use and selective pressure.

Despite the fact that Africa, the Middle East, Latin America, and Asia account for around three-quarters of the world's population, these regions account for just about 20% of global antibiotic use (Kunin, 1993). Despite this, these countries have the highest incidence of antimicrobial resistance to older antibiotics (Kunin, 1993). Antibiotic resistance might easily become a major issue in some emerging countries where poverty is great, especially when huge groups of people live in extremely cramped quarters with poor sanitation. Furthermore, a lack of antibiotic regulation, such as widespread self-prescribing and the availability of medications without a prescription through local pharmacies or open-air markets, has exacerbated the situation (Kunin, 1993).

Increased global travel in recent decades has facilitated the fast spread of antibiotic-resistant microbes across long distances. Soares and colleagues (Soares *et al.,* 1993), for example, provided solid evidence that a single multi-resistant *S. pneumoniae* clone had been transferred into Iceland from Spain, possibly as a result of Icelanders' frequent vacations to Spain. Reichler found a clone of multidrug-resistant pneumococcus involved in an epidemic in an Ohio day-care center to be identical to a Spanish isolate, implying that the strains were related (Reichler *et al.,* 1992). Munoz and colleagues (Munoz *et al.,* 1991) identified an identical antibiotic-resistant clone of *S. pneumoniae* (serotype 6B) in Spain, the United States, Mexico, Portugal, France, Croatia, South Korea, and South Africa, implying that the strain started in Spain and expanded widely around the world. As worldwide travel becomes more widespread, the transmission of antibiotic-resistant germs will almost certainly become a bigger issue.

Within their action plans to combat antimicrobial resistance, various countries and many international organizations have included a One Health solution. Improvements to the regulation and policy of antimicrobial usage, monitoring, stewardship, infection prevention, hygiene, animal husbandry and alternatives to antimicrobials are important steps (McEwen & Collignon, 2018). New recommendations on the use of medically essential antimicrobials in food-producing animals have recently been introduced by the WHO, recommending that farmers and the food industry avoid regularly using antimicrobials to encourage growth and protect healthy animals from (McEwen & Collignon, 2018). These recommendations seek to help maintain the efficacy of antimicrobials that are important for human medicine by reducing their use in animals (McEwen & Collignon, 2018).

Chapter 3: Materials and Methods

Study site

This study was undertaken from Chattogram Medical College Hospital, Chattogram, Bangladesh.

Study period

This study was conducted during the period of April 2021 to March 2022.

Study design

We carried out a cross-sectional survey among patients with lower respiratory tract infection in Chattogram between April 2021 to March 2022.We employed purposive sampling to enroll participants from the target groups based on their willingness to participate. A total of 213 lower respiratory tract infection patients from Chattogram Medical College Hospital with available sputum culture and sensitivity reports were included in the study. Before the interview, the purpose of the study was informed to all participants and oral consent was obtained from each of them. No incentives were given for participating in the survey. Participants refusing to participate in the study were excluded from the study.

Data collection tool

We drafted a structured questionnaire that inquired into sociodemographic information of the participants through face-to-face interviews and recorded the culture & sensitivity report. The survey questionnaire was designed in collaboration with experienced physicians, relevant researchers, and epidemiologists. The questionnaire was intended to extract information on demographics, type of sample collected, type of organism, and pattern of antibiotic resistance. Data collection was performed with the assistance of a group of trained medical students.

Ethical considerations

This study was carried out in accordance with the recommendations of the Chattogram Veterinary and Animal Sciences University's ethics committee. EC of CVASU Approval No: Memo No.- CVASU/Dir(R&E)EC/2019/126(16)

Data analysis

The responses were entered in Microsoft Excel 2019 (Microsoft Corporation, Redmond, Washington, USA) then coded and analyzed using STATA version 16. We summarize quantitative variables with mean and standard deviation and qualitative variables with frequency and relative frequency. We visualized the results with bar and pie charts. We also performed Pearson's chi square test to test for association between two categorical variables. A p-value of <0.05 was considered statistically significant.

Chapter 4: Results

4.1 Demography of the study population

4.1.1 Age Distribution

Mean age of the participants were 42.4 years with a standard deviation of 6.6 years. Majority of the patients were in the 41-48 years age group (Figure 1)

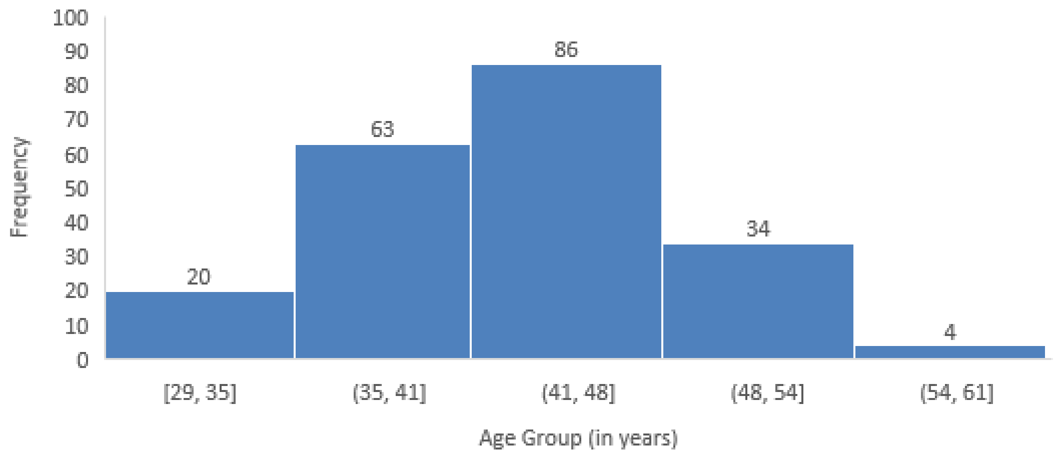

Figure 1: Age distribution of the study participants

4.1.2 Gender Distribution

The number of male participants was higher compared to the number of female participants with 68% of the participants being male and 32% of the participants being female (Figure 2).

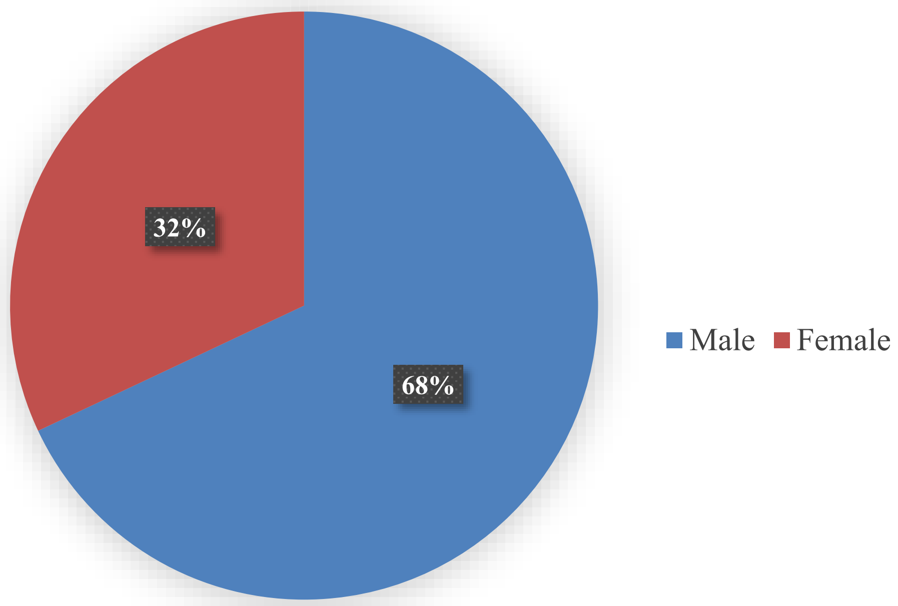

Figure 2: Gender distribution of study participants

4.1.3 Distribution of Educational Status

The majority of the participants had undergone primary education (46%), with 22% being illiterate, 15% had secondary education, 10% had higher secondary education, and 7% had bachelor and above education (Figure 3).

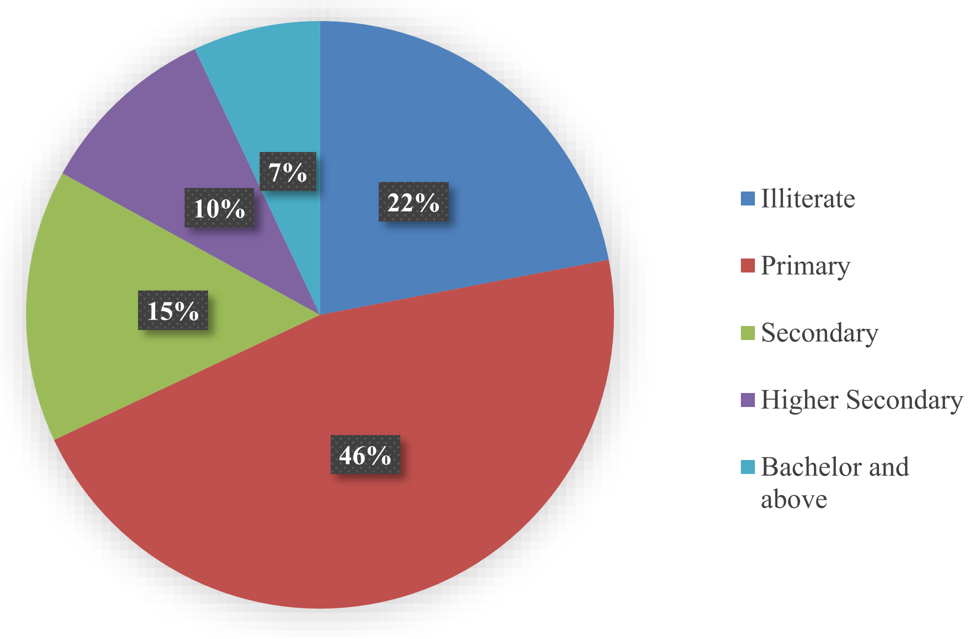

Figure 3: Distribution of educational status of study participants

4.1.4 Income Status

Most of the participants had an income below 20,000 BDT per month (67%) followed by more than or equal to 20,000 BDT per month (37%) (Figure 4).

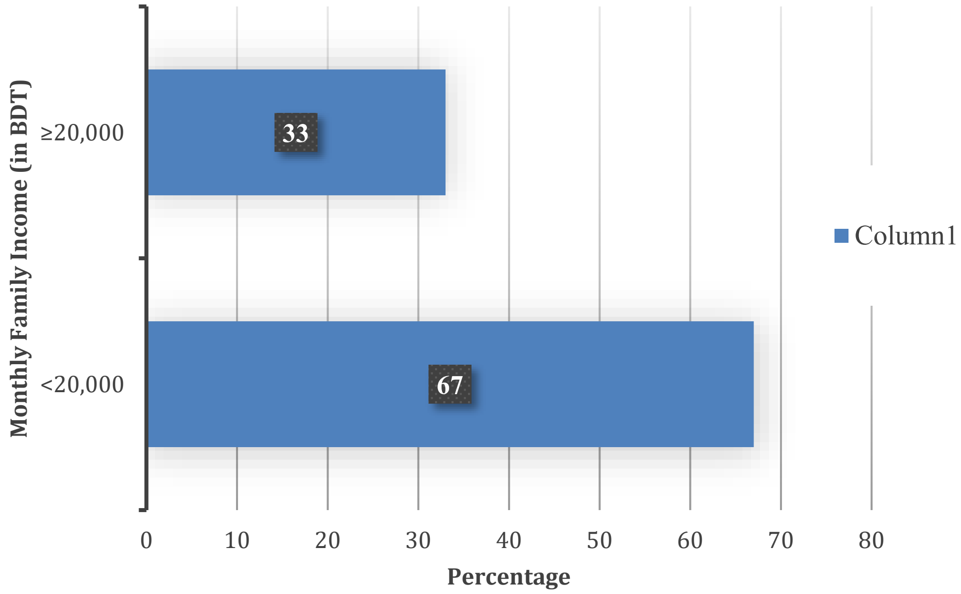

Figure 4: Distribution of monthly family income of study participants

4.1.5 Distribution of Residence

More than three-fourths (77%) of the participants hailed from urban areas. Rest of them came from rural areas (23%) (Figure 5).

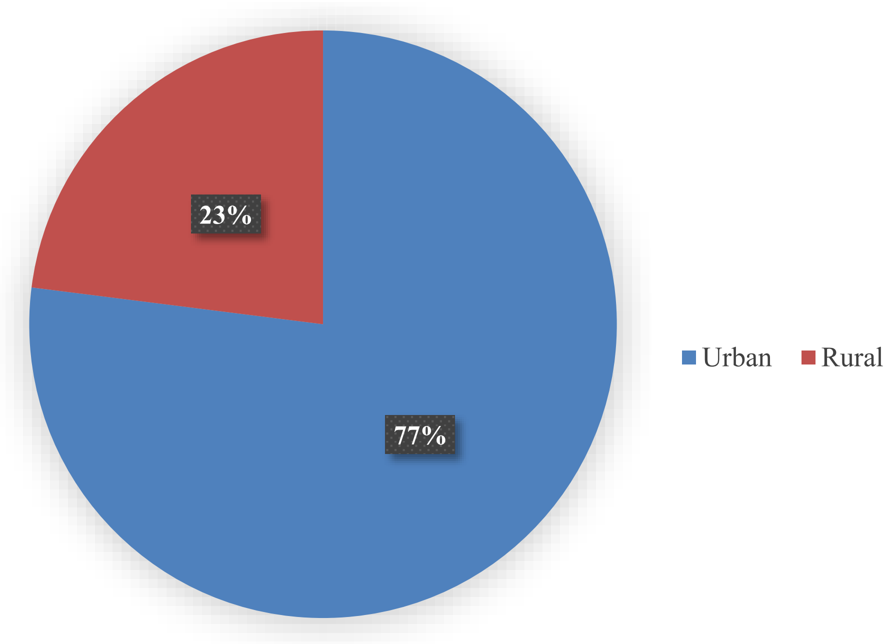

Figure 5: Distribution of residence of study participants

4.2 Prevalence of bacterial isolates found in sputum samples

During the study period, a total of 213 sputum samples were analyzed. *Streptococcus pneumoniae* (43 %) was the most frequently isolated bacteria, followed by *Klebsiella pneumoniae* (22%), *Pseudomonas aeruginosa* (13%), and *Escherichia coli* 10%. The common pathogens that were isolated from the sputum sample are shown in Figure 6.

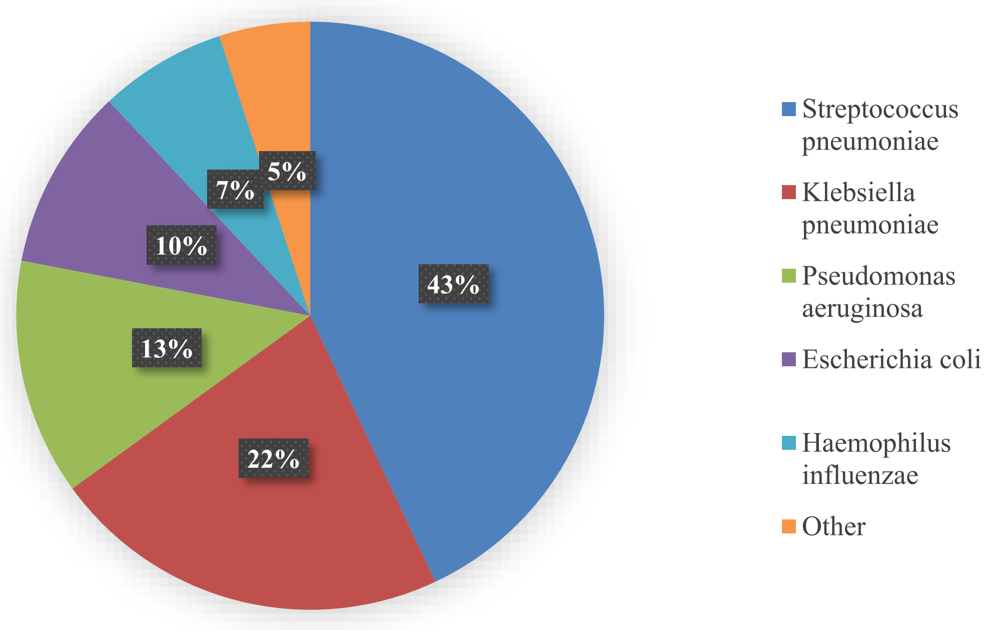

Figure 6: Common bacteria in sputum samples

4.3 Antibiotic sensitivity pattern of isolates

4.3.1 *Streptococcus pneumoniae*

Antibiotic sensitivity pattern of *Streptococcus pneumoniae* is shown in Figure 7. Out of 92 sputum samples with *Streptococcus pneumoniae*, 60 samples were sensitive to levofloxacin and 32 samples were resistant. Sensitivity to the rest of the antibiotics are: Cefotaxime (97%), Imipenem (96%), Ceftazidime (96%), Meropenem (94%), Cefepime (93%), Ceftriaxone (93%), Cefuroxime (92%), Ampicillin (91%), Amoxiclav (89%), Piperacillin/tazobactam (85%), Amikacin (76%), Azithromycin (76%), Ofloxacin (45%). Ciprofloxacin (33%), and Gentamicin (26%).

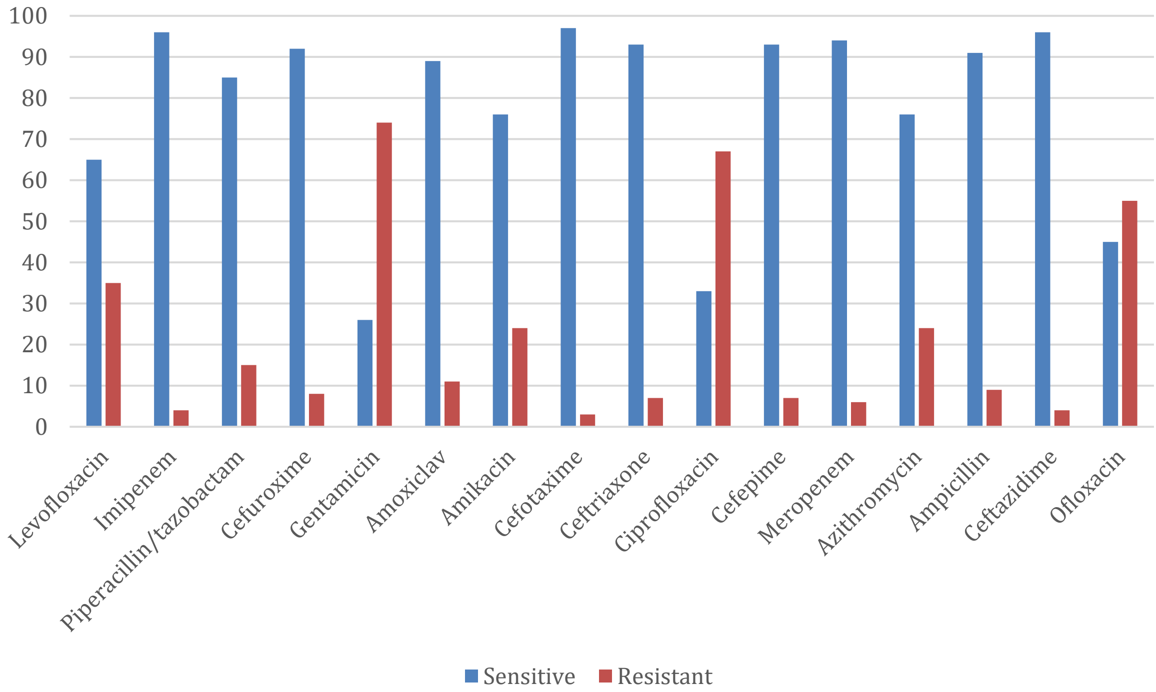

Figure 7: Antibiotic Sensitivity Pattern of Streptococcus pneumoniae

4.3.2 *Klebsiella pneumoniae*

Antibiotic sensitivity pattern of *Klebsiella pneumoniae* is shown in Figure 8. Out of 48 sputum samples with *K. pneumoniae*, 36 samples were sensitive to levofloxacin and 11 samples were resistant. Sensitivity of the rest of the antibiotics are: Ofloxacin (100%)**,** Meropenem (96.67%), Amikacin (87.61%), Imipenem (86.24%), Gentamicin (79.86%), Ciprofloxacin (76.09%), Piperacillin/tazobactam (75.84%), Cefuroxime (75.58%), Cefepime (52.78%), Cefotaxime (50.46%), Ceftriaxone (48.45%), Azithromycin (45.83%), Ceftazidime (20%), Amoxiclav (3.52%), and Ampicillin (0%).

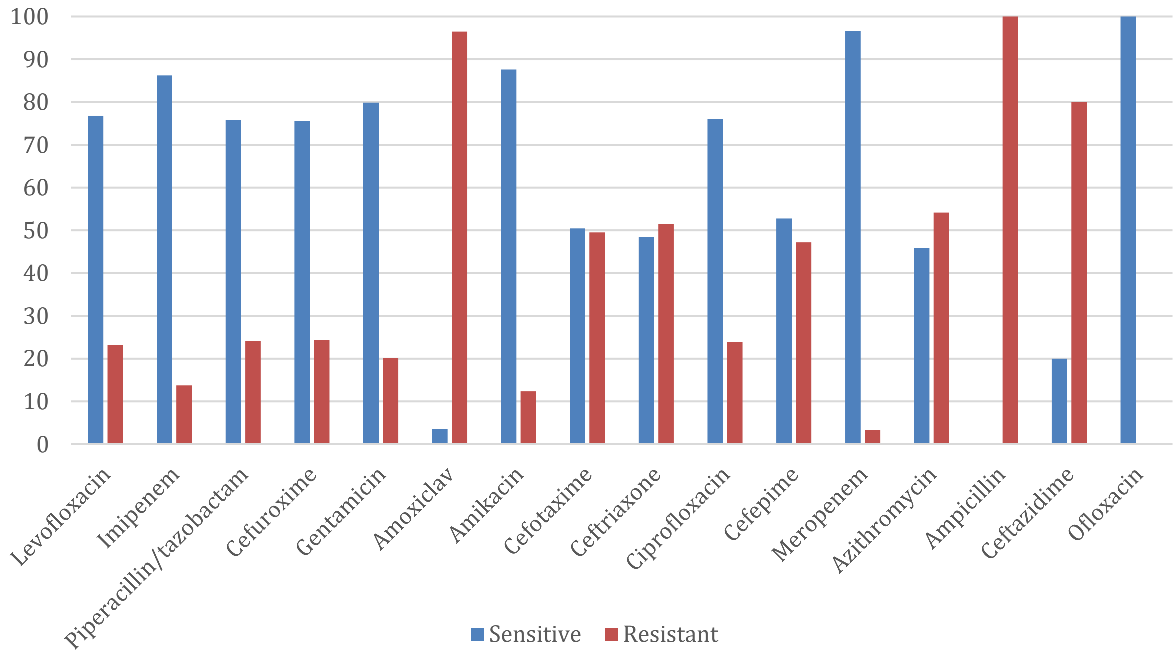

Figure 8: Antibiotic Sensitivity Pattern of Klebsiella pneumoniae

4.3.3 *Pseudomonas aeruginosa*

Antibiotic sensitivity pattern of *Pseudomonas aeruginosa* is shown in Figure 9. Out of 28 sputum samples with *Pseudomonas aeruginosa*, 26 samples were sensitive to levofloxacin and 2 samples were resistant. Sensitivity to the rest of the antibiotics are: Meropenem (100%), Ciprofloxacin (90%), Amikacin (87%), Ceftriaxone (86%), Gentamicin (84.85%), Imipenem (83.72%), Piperacillin/tazobactam (83.72%), Ceftazidime (69%), Amoxiclav (24%), Cefuroxime (14.29%), and Cefepime (3%).

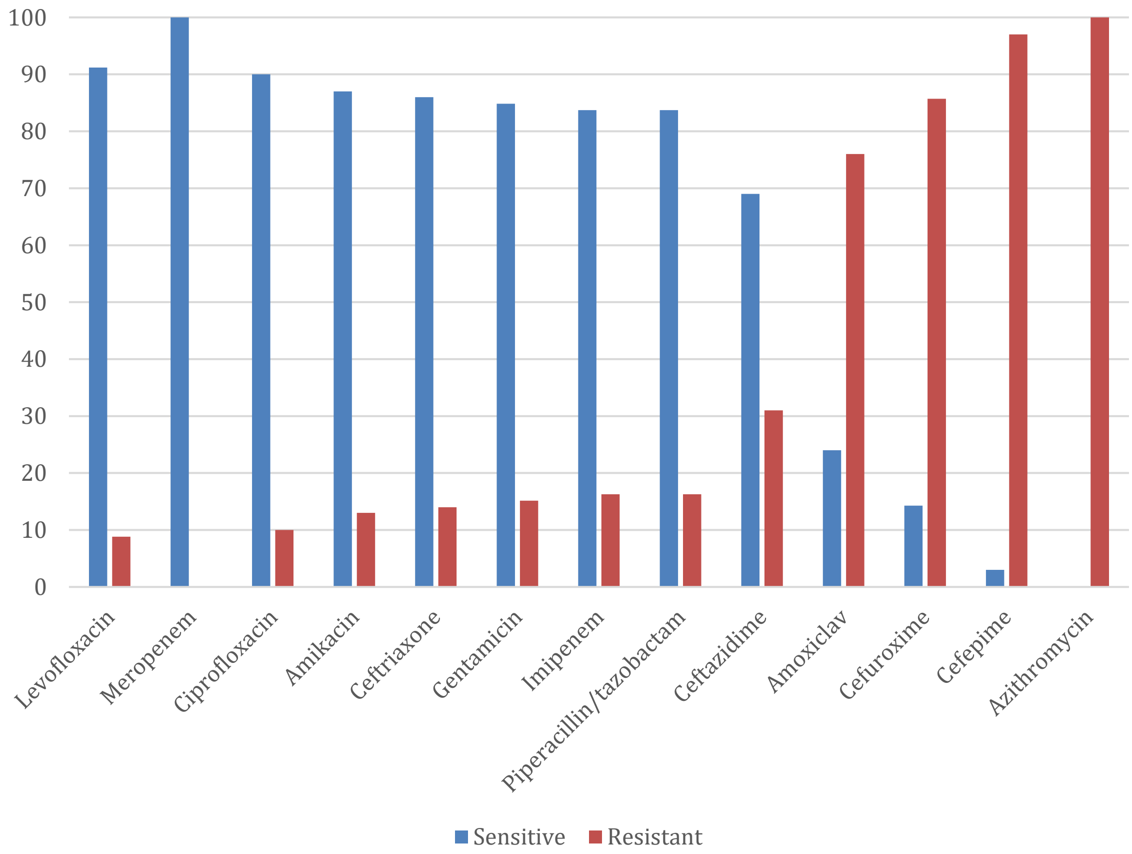

Figure 9: Antibiotic Sensitivity Pattern of Pseudomonas aeruginosa

4.4 Comparison of antibiotic sensitivity pattern of *Streptococcus pneumoniae* according to gender

Comparison of antibiotic sensitivity pattern of Streptococcus pneumoniae according to gender is shown in Figure 10. There was observed no difference between male and female in the sensitivity of antibiotics against *Streptococcus pneumoniae*from descriptive analysis. However, males have a slightly better sensitivity in case of levofloxacin, piperacillin/tazobactam, gentamicin, cefotaxime, ciprofloxacin, ampicillin, and ceftazidime. On the other hand, females have a slightly better sensitivity in case of imipenem, cefuroxime, amoxiclav, amikacin, ceftriaxone, cefepime. meropenem, azithromycin, and ofloxacin.

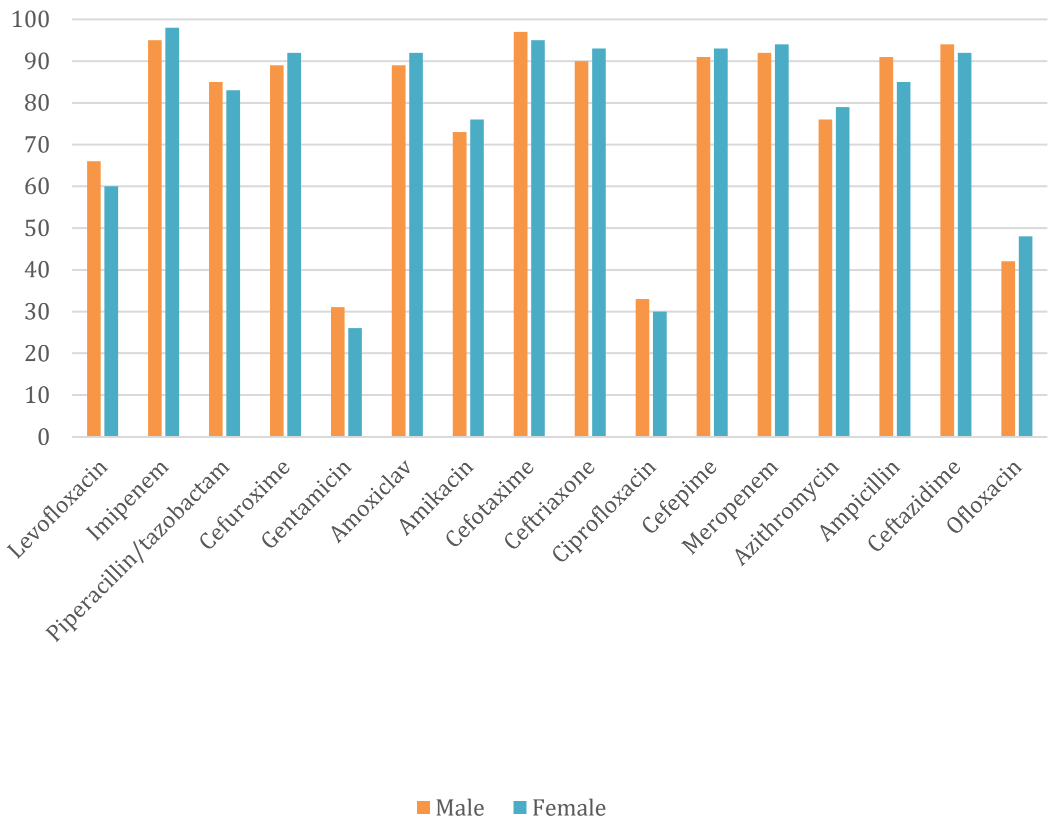

Figure 10: Comparison of antibiotic sensitivity pattern of Streptococcus pneumoniae according to gender

4.5 Comparison of antibiotic sensitivity pattern of *Streptococcus pneumoniae* according to educational status

Comparison of antibiotic sensitivity pattern of Streptococcus pneumoniae according to educational status is presented in Figure 11. Literate individuals have an overall better antibiotic sensitivity in case of all antibiotics;especially visual difference was observed in case of levofloxacin, gentamicin, amoxiclav, and azithromycin.

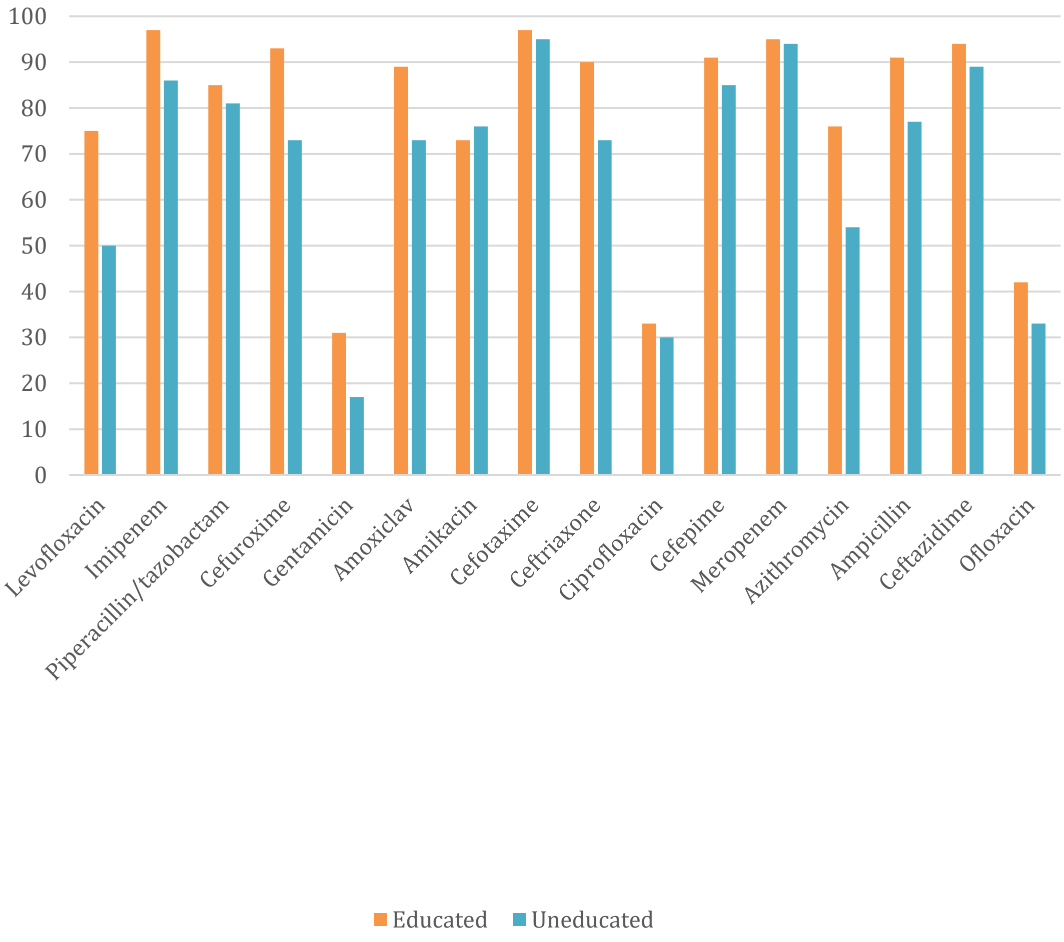

Figure 11: Comparison of antibiotic sensitivity pattern of Streptococcus pneumoniae according to educational status

4.6 Comparison of antibiotic sensitivity pattern of *Streptococcus pneumoniae* according to income status

Comparison of antibiotic sensitivity pattern of *Streptococcus pneumoniae* according to income status is presented in Figure 12. Individuals with more than or equal to 20,000 BDT monthly income had aslightly better antibiotic sensitivity than individuals with less than 20,000 BDT monthly income. Notifiable difference was observed in case of levofloxacin, imipenem, cefuroxime, gentamicin, amoxiclav and ofloxacin.

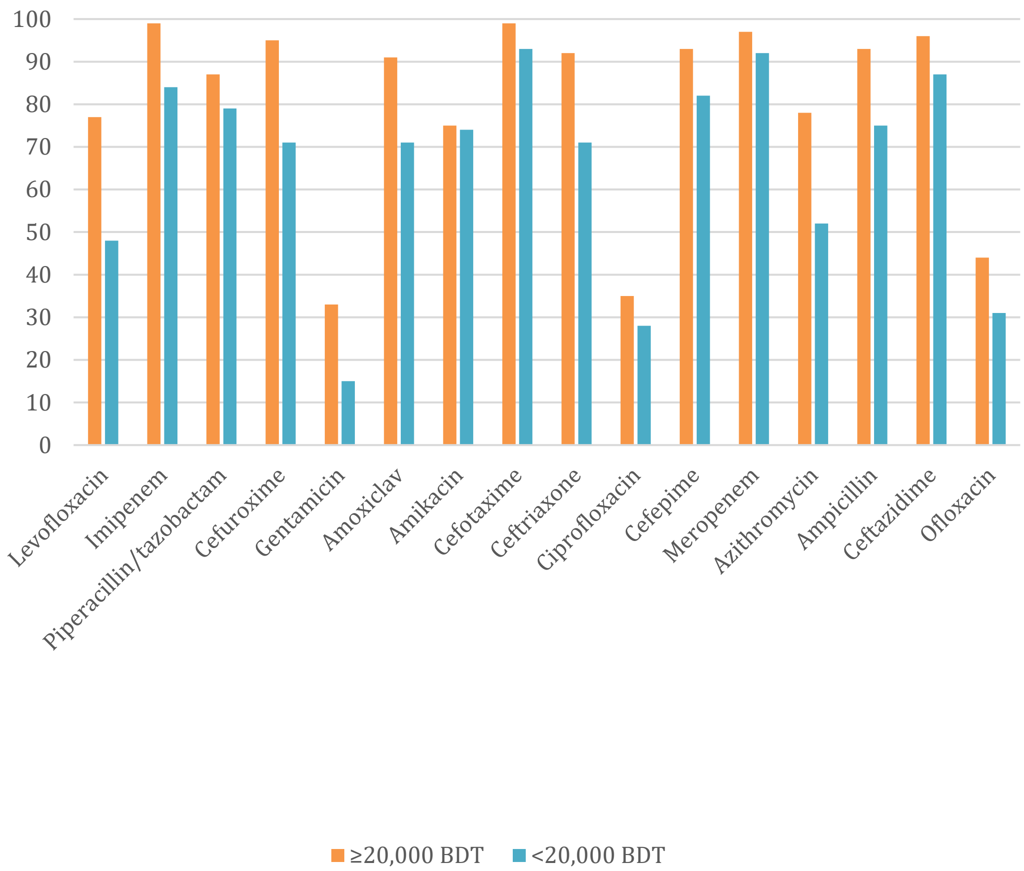

Figure 12: Comparison of antibiotic sensitivity pattern of Streptococcus pneumoniae according to income status

4.7 Comparison of antibiotic sensitivity pattern of *Streptococcus pneumoniae* according to residence

Comparison of antibiotic sensitivity pattern of *Streptococcus pneumoniae* according to residence is presented in Figure 13. Individuals from urban areas had better antibiotic sensitivity than individuals from rural areas. Notifiable difference was observed was in case of levofloxacin, gentamicin, cefuroxime, and ciprofloxacin.

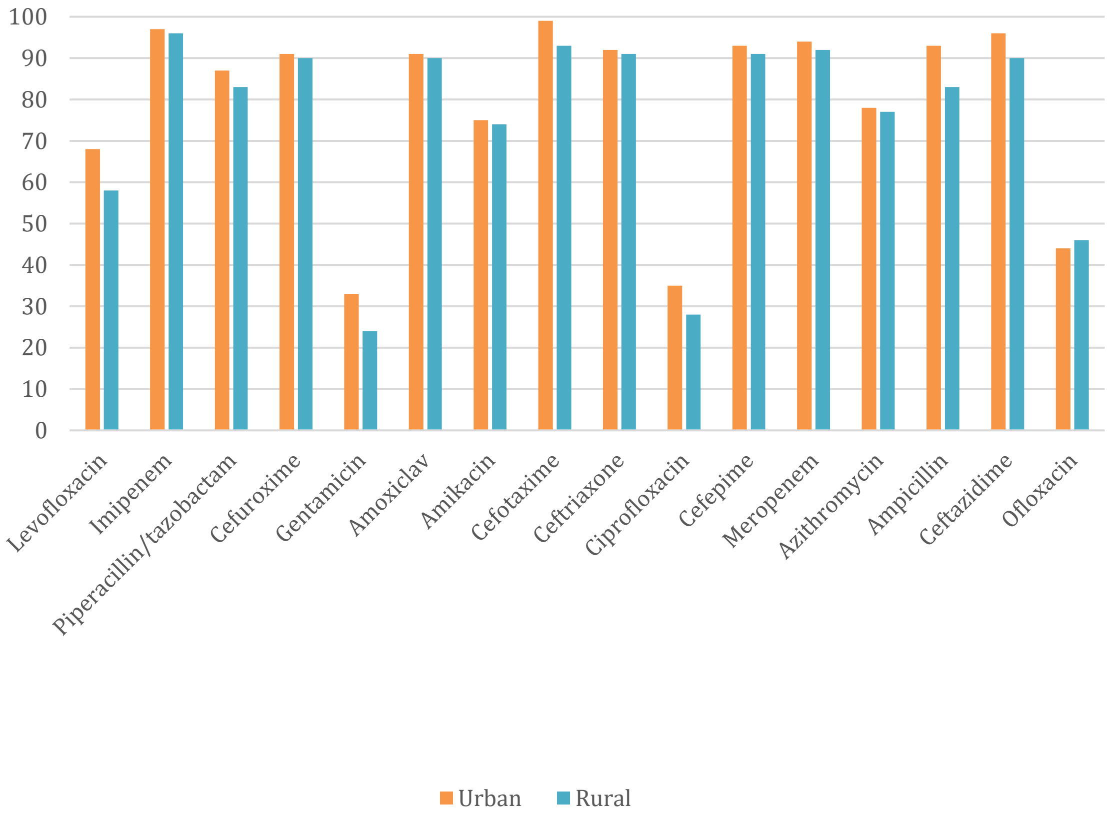

Figure 13: Comparison of antibiotic sensitivity pattern of Streptococcus pneumoniae according to residence

4.8 Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to gender

Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to gender is shown in Figure 14. There was no notifiable difference between male and female in the sensitivity of antibiotics against *Klebsiella pneumoniae*from descriptive analysis. However, males have a slightly better sensitivity in case of levofloxacin, imipenem, piperacillin/tazobactam, cefuroxime, gentamicin, amikacin, meropenem, and ceftazidime. On the other hand, females have a slightly better sensitivity in case of amoxiclav, cefotaxime, ceftriaxone, ciprofloxacin, cefepime, azithromycin, and ofloxacin,

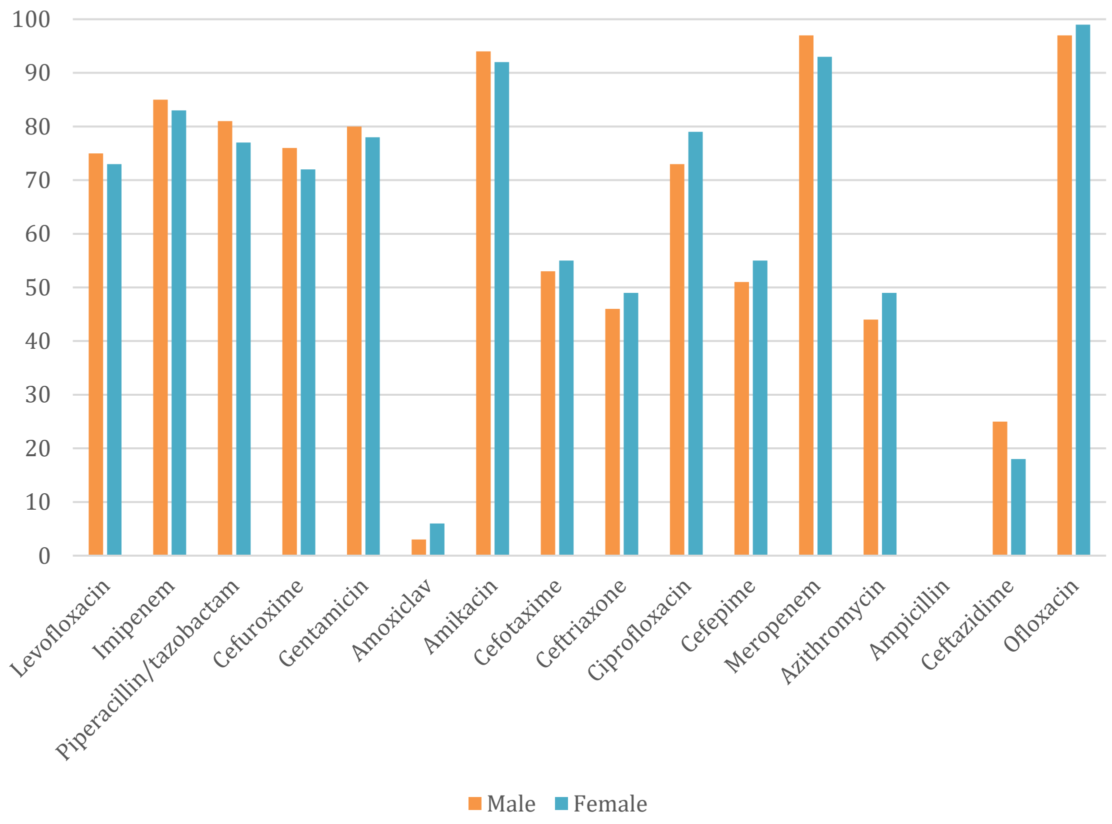

Figure 14: Comparison of antibiotic sensitivity pattern of Klebsiella pneumoniae according to gender

4.9 Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to educational status

Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to educational status is presented in Figure 15. Literate individuals have an overall slightly better antibiotic sensitivity in case of all antibiotics. And there was a notifiable difference in case of levofloxacin, gentamicin, amoxiclav, ampicillin and piperacillin/tazobactam.

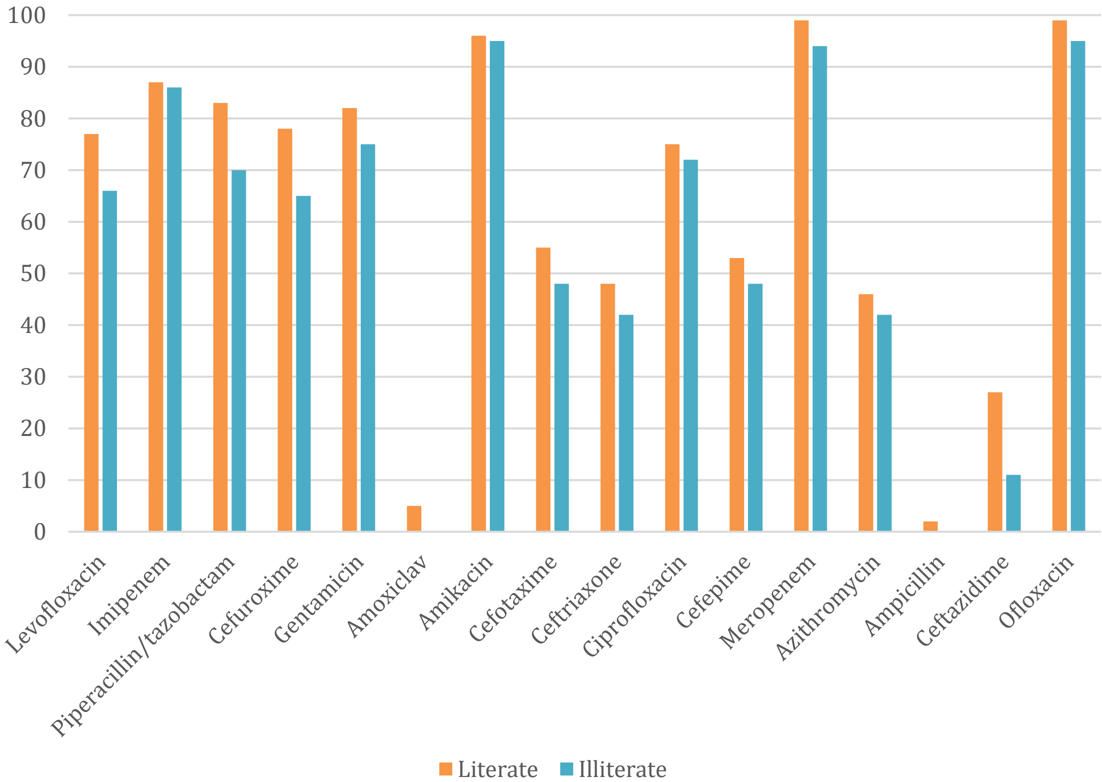

Figure 15: Comparison of antibiotic sensitivity pattern of Klebsiella pneumoniae according to educational status

4.10 Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to income status

Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to income status is presented in Figure 16. Individuals with more than or equal to 20,000 BDT monthly income had a slightly better antibiotic sensitivity than individuals with less than 20,000 BDT monthly income. Notifiable difference was observed in case of levofloxacin, ceftazidime, piperacillin/tazobactam, gentamicin, amoxiclav, and ofloxacin.

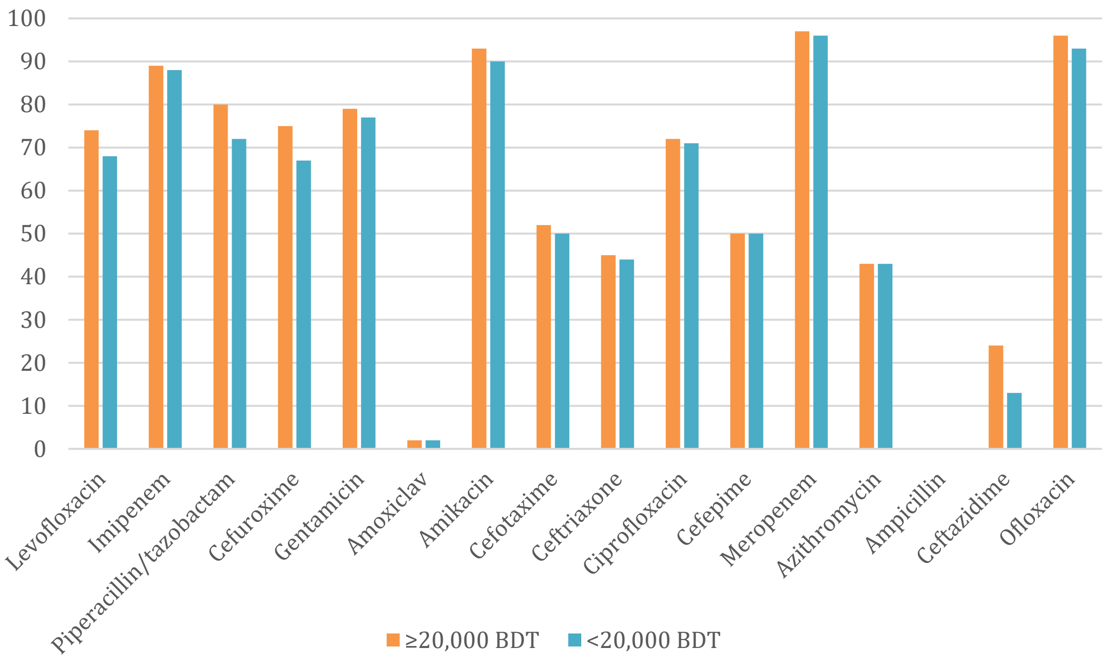

Figure 16: Comparison of antibiotic sensitivity pattern of Klebsiella pneumoniae according to income status

4.11 Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* residence

Comparison of antibiotic sensitivity pattern of *Klebsiella pneumoniae* according to residence is presented in Figure 17. Individuals from urban areas had a slightly better antibiotic sensitivity than individuals from rural areas. However, there were no Notifiable difference was observed in antibiotic sensitivity between two groups.

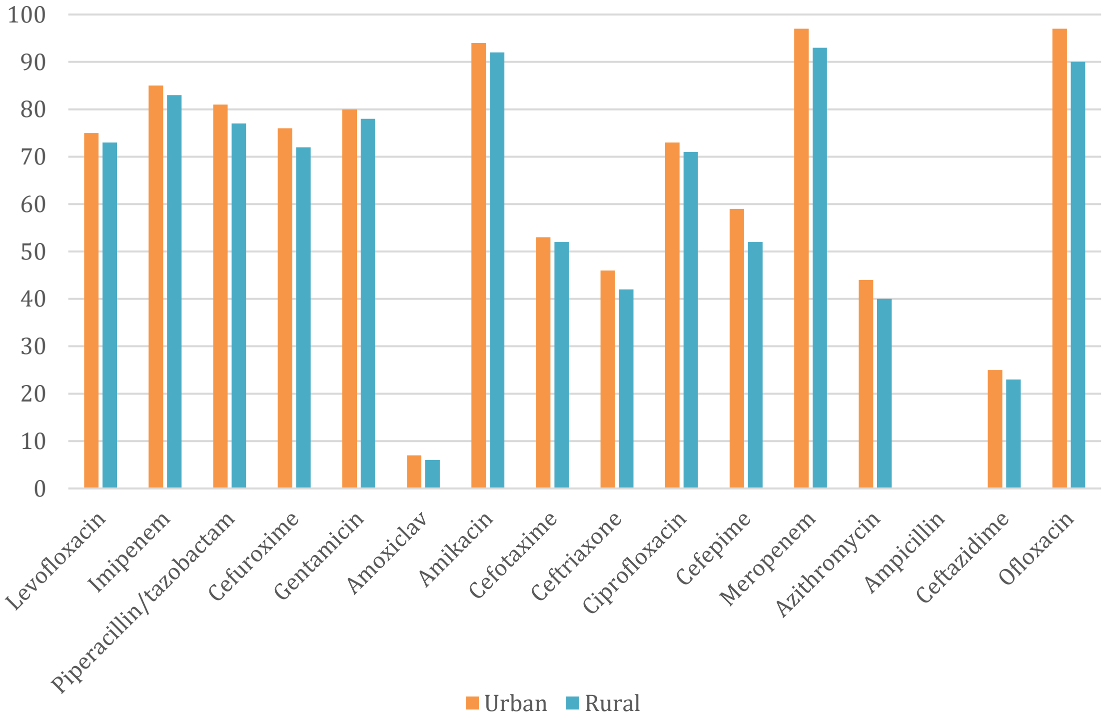

Figure 17: Comparison of antibiotic sensitivity pattern of Klebsiella pneumoniae according to residence

4.12 Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to gender

Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to gender is shown in Figure 18. There was no Notifiable difference between male and female in the sensitivity of antibiotics against *Pseudomonas aeruginosa.* However, males have a slightly better sensitivity in case of levofloxacin, meropenem, ciprofloxacin, amikacin, ceftriaxone, and gentamicin. On the other hand, females have a slightly better sensitivity in case of imipenem, piperacillin/tazobactam, ceftazidime, amoxiclav, cefuroxime, and cefepime.

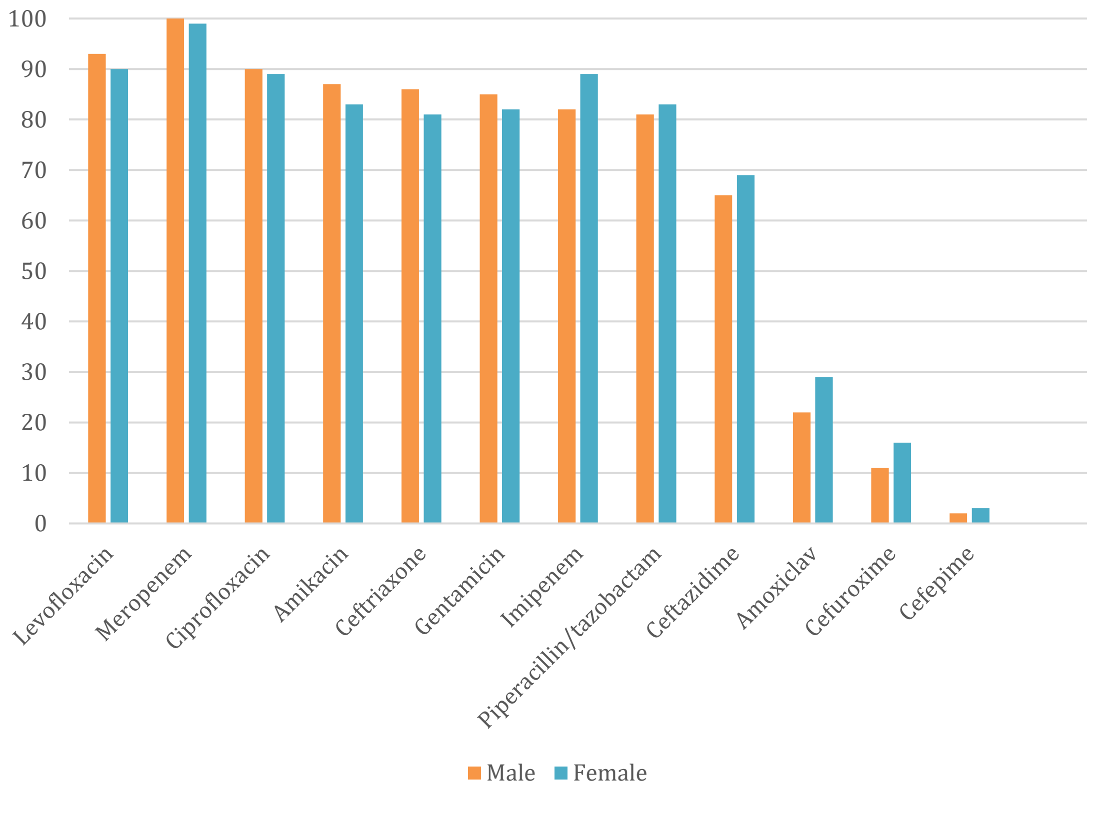

Figure 18: Comparison of antibiotic sensitivity pattern of Pseudomonas aeruginosa according to gender

4.13 Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to educational status

Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to educational status is presented in Figure 19. Literate individuals have an overall slightly better antibiotic sensitivity in case of all antibiotics. And a notifiable difference was observed in case of, amikacin, gentamicin, amoxiclav, ceftriaxone and imipenam.

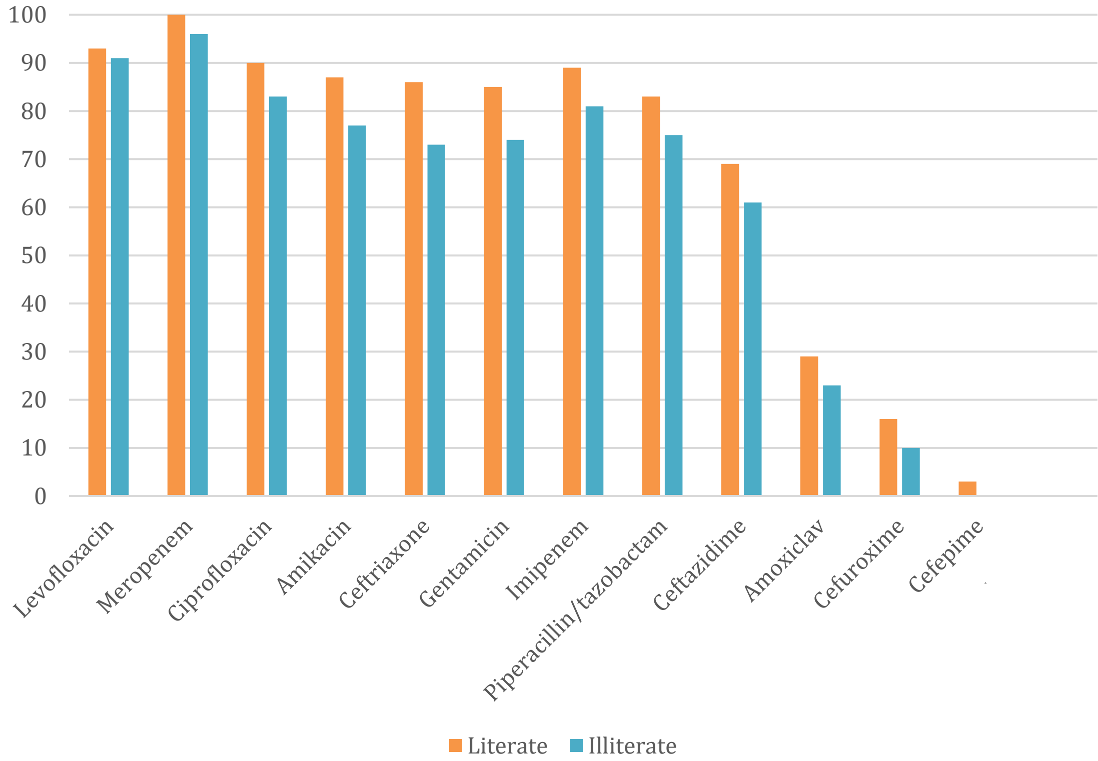

Figure 19: Comparison of antibiotic sensitivity pattern of Pseudomonas aeruginosa according to educational status

4.14 Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to income status

Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to income status is presented in Figure 20. Individuals with more than or equal to 20,000 BDT monthly income had a slightly better antibiotic sensitivity than individuals with less than 20,000 BDT monthly income. Notifiable difference was observed was in case of amikacin, ceftriaxone, piperacillin/tazobactam, gentamicin, cefepime, and ceftazidime.

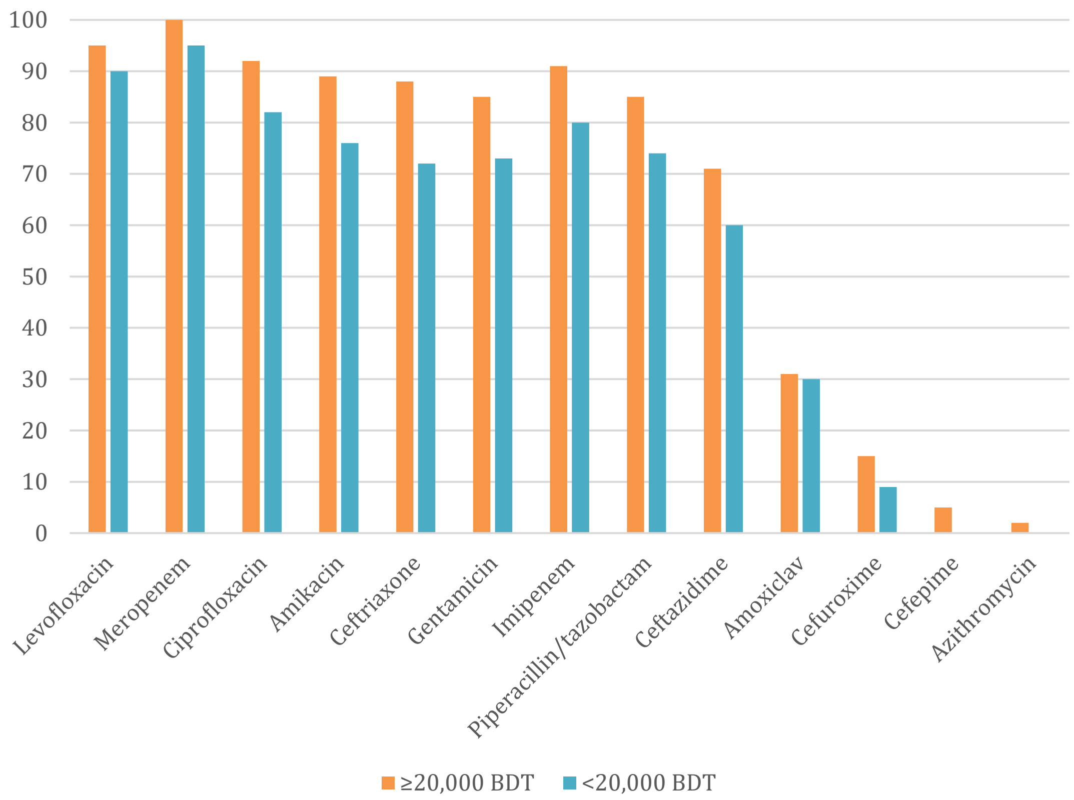

Figure 20: Comparison of antibiotic sensitivity pattern of Pseudomonas aeruginosa according to income status

4.15 Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to residence

Comparison of antibiotic sensitivity pattern of *Pseudomonas aeruginosa* according to residence is presented in Figure 21. There was no notifiable difference was observed in antibiotic sensitivity between two groups.

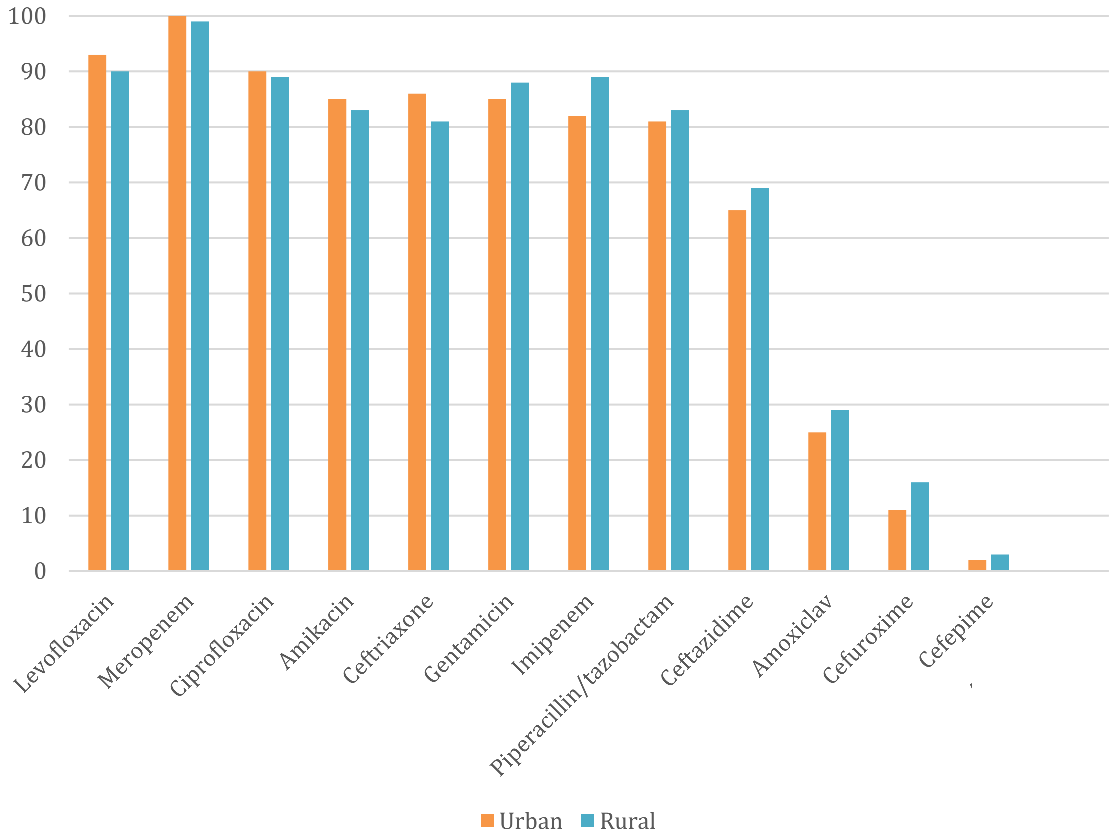

Figure 21: Comparison of antibiotic sensitivity pattern of Pseudomonas aeruginosa according to residence

Chapter 5: Discussion

Antimicrobial resistance presents an increasing apprehension globally for human and animal health (Zhuo *et al.,* 2018). Due to misuse and overuse of antibiotics, the world witnessed an enormous demonstration in the increase of microbial resistance to affect the health, economic load, elevated mortality rates, lengthened hospital stay, and the increased rate of different infections. In this study, we evaluated the Antibiotic sensitivity pattern of bacterial isolates from Acute Lower Respiratory Tract infections in a tertiary care hospital, Chattogram.

In our study, the resistance of *Streptococcus pneumoniae* to Azithromycin was found to be 24%. Despite rising incidence of *S. pneumoniae* macrolide resistance, the current guidelines for outpatient Community Acquired Pneumonia treatment include a macrolide as the first empiric medication (Dylewski and Davidson, 2006). There have been few previously documented examples of macrolide therapy failure in CAP, and opinions differ on whether macrolide resistance in *S. pneumoniae* is clinically important (Dylewski and Davidson, 2006). In a review of 33 cases describing macrolide treatment failure in the treatment of pneumococcal infections, the increased reports of clinical treatment failure with macrolides and their implications with macrolide-resistant *S. pneumoniae* were shown (Rzeszutek *et al.,* 2004).

Ampicillin was 9% resistant on *S. pneumoniae* in our study. A study found that penicillin and macrolide resistance are on the rise in Italy, whereas fluoroquinolones are still effective (Dylewski and Davidson, 2006). Another study confirmed the trend of increasing macrolide resistance among respiratory microorganisms in Italy since 1992 – despite large doses, many antibiotics, including amoxicillin and clavulanic acid, third-generation injectable cephalosporins, and fluoroquinolones, now have a reduced effect on pathogens (Rzeszutek *et al.,* 2004). The antibiotics amoxicillin and clavulanic acid, but not fluoroquinolones, are effective, according to a recent study. In this investigation, levofloxacin exhibited a notifiable resistance rate.

Klebsiella was found to be sensitive to amikacin, imipenem, gentamycin, levofloxacin, levofloxacin, ciprofloxacin, piperacillin/tazobactam, and cefuroxime in this investigation. In additional research, amikacin and gentamycin were found to be sensitive to *Klebsiella* (Promite et al., 2017).

Pseudomonas was very sensitive to imipenem (83.72%), piperacillin/tazobactam (83.72%), and sensitive to gentamycin (84.85%), ceftazidime/clavulanic acid (79.41%), ceftazidime/clavulanic acid (79.41%). According to research by Nepal *et al.,* gentamycin and amikacin are sensitive to *Pseudomonas*, whereas Dhakre et al., 2017 found ampicillin and piperacillin/tazobactam to be highly effective against Pseudomonas (Dhakre *et al.,* 2017; Sherchan & Humagain, 2021).

The widespread availability of antimicrobials without prescription in Bangladesh, a rising trend in its irrational use in humans and food animals and fisheries, and consequent spread of resistant strains through environmental contamination all contribute to the decreasing sensitivity to antibiotics (Ahmed, Rabbi and Sultana, 2019). The policies and strategies to contain ABR are at an early stage of development in the country and implementation remains a major challenge. This is due to poor awareness about AMR among the policy makers and practitioners, inadequate resources to implement measures to contain AMR, and absence of a comprehensive national surveillance system to monitor the emergence of AMR (Hoque *et al.*, 2020).

All categories of the allopathic practitioners whether qualified or not, are prone to use 'excess' antimicrobials due to poor awareness regarding its rational use. Other factors contributing to the emergence of AMR include lack of diagnostic facilities, burgeoning private practice and unreasonable demand for antibiotics from patients and 'caregivers', especially for children. Besides, there are aggressive marketing strategies of the pharmaceutical companies specifically aimed at generating prescriptions at the cost of patients. Rising trend of antimicrobials use resulting from poor consumer awareness on dangers of inappropriate use, use as a stop-gap measure, non-compliance with dosage, and self-medication are also important factors behind decreasing sensitivity to antibiotics (Nair *et al.*, 2019).

There is no dearth of policies and strategies especially since 2014, but operationalization of these remains a challenge which is true for implementing any public policy in general in Bangladesh (Rahman, 2010), including the SDGs (Sabbih, 2018). Bangladesh is one of the 100 countries with National Action Plan for containment of AMR developed (as of March 2018), however, a recent review of the Action Plans identified some challenges for its implementation in LMICs like Bangladesh (WHO, 2018). These include lack of functional mechanism for implementation or coordination, lack of adequate financial and institutional resources for relevant capacity and means for infection prevention and control (e.g., through

WASH activities), and building awareness and political commitment. To address these challenges, measures such as mainstreaming of the AMR containment process across sectors, adequate resourcing through national budgets and annual development plans, and inter-sectoral coordination for infection prevention and control are suggested (WHO, 2018).

The problem of AMR is multi-sectoral, multi-disciplinary, and multi-institutional and thus need a coordinated response of the three sectors, adopting a comprehensive approach such as that of One Health. The outbreak of avian influenza in Bangladesh in 2007 exposed the vulnerability of the country to transmission of infection from animals and environment. In 2008, stakeholders in the human, animal and environmental sectors came together to promote the concept of 'One Health' in Bangladesh (Flora, 2017). As a consequence of this movement, the GoB came up with the 'National One Health Strategy' in 2012 (IEDCR, 2012). In 2016, a One Health Secretariat was established at the IEDCR with staff from three ministries (human health, animal health and environment) and support from the development partners (Dahal, Upadhyay and Ewald, 2017). However, improving awareness among professionals and practitioners across the sectors for consensus actions, and coordination among different sectors and ministries remain a major challenge to move forward. Given the poor state of Bangladesh to 'prevent-detect-respond' to health emergencies (i.e., outbreaks of epidemics and pandemics including AMR) as revealed by Global Health Security Index (Bangladesh occupying 113/195 position, scoring 35/100), there is little time to waste (GHS Index, 2019).

Chapter 6: Conclusion

The goal of the study was to determine the antibiotic sensitivity pattern of microorganisms isolated from sputum samples at a tertiary hospital of Bangladesh. *S.pneumoniae* was the most prevalent pathogen identified from sputum samples, followed by *Klebsiella* and Pseudomonas. Imipenam, Ceftazidim, Cefotaxiame and Meropenem were the most sensitive towards *S.pneumoniae*. Imipenem, piperacillin/tazobactam combination, and gentamicin were all found to be sensitive to *Klebsiella* and *Pseudomonas*.

Chapter 7: Recommendation

1. Rational use of antibiotics.
2. Prescribing narrow-spectrum drugs.
3. Prescribing antibiotics only when it's needed.
4. Strong rules and regulations to monitor the market of antibiotics.
5. More comprehensive study at earliest basis to uncover the total scenario of this highly concerning issue.

Chapter 8: Limitations

This study has some limitations. Due to our study's cross-sectional nature, we cannot infer causality. We also acknowledge that the findings of our study may not be generalizable due to our sample size. Nevertheless, survey analysis is a cost-efficient and effective way of obtaining population data.

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Annexure A: Questionnaire

Antibiotic sensitivity pattern of bacterial isolates from Acute Lower Respiratory Tract infections in a tertiary care hospital, Chattogram

Part A: Sociodemographic Information

1. Name:

2. Age:

3. Gender: ☐Male ☐Female ☐Other

4. Educational Status: ☐Illiterate ☐ Primary ☐ Secondary ☐ Higher Secondary ☐ Bachelor and above

5. Monthly Family Income: ☐ <15,000 BDT ☐15,000-30,000 BDT ☐ ≥31,000 BDT

6. Residence: ☐ Urban ☐ Rural

Part B: Sputum culture report

7. Any growth or not: ☐ Growth ☐ No growth

8. Name of Organism: …………………………………..

9. Antibiotic Sensitivity:

Name of Antibiotic	Sensitivity (Sensitive/Intermediate Sensitive/Resistant)
Levofloxacin	
Imipenem	
Piperacillin/tazobactam	
Cefuroxime	
Gentamicin	

Amoxiclav	
Amikacin	
Cefotaxime	
Ceftriaxone	
Ciprofloxacin	
Cefepime	
Meropenem	
Azithromycin	
Ampicillin	
Ceftazidime	
Ofloxacin	

Date & signature of the data collector

………………………………………………

Annexure B: Brief biodata of the student

Dr. Sujan Chandra Nath is a Candidate for the degree of MPH in One Health under the One Health Institutes, Chattogram Veterinary and Animal Sciences University. He conceded the Secondary School Certificate Examination (SSC) in 2003 from Jornarddan Pur High School, Mirsarai, Chattogram and then Higher Secondary Certificate Examination (HSC) in 2003 from Govt. City College, Chattogram. He obtained his MBBS form BGC Trust Medical Collage in 2016.