A Review on Antimicrobial Agents in Pediatrics in Bangladesh: Synthetic Methods and Antimicrobial Resistance Challenges

By

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Declaration

It is hereby declared that

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

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Approval

The thesis titled "A Review on Antimicrobial Agents in Pediatrics in Bangladesh: Synthetic Methods and Antimicrobial Resistance Challenges" submitted by Al Fatima Akka (ID: 21146017) of Spring, 2021 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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Ethics Statement

This project does not involve any animal or human trials.

Abstract

Antimicrobial drugs are important in managing pediatric infections in Bangladesh. However, their misuse has contributed significantly to the rising issue of antimicrobial resistance (AMR). This review examines frequently utilized antimicrobial agents in pediatric patients in Bangladesh, focusing on their usage patterns, synthetic methodologies, and challenges related to resistance. Ciprofloxacin, azithromycin, metronidazole, ceftriaxone, and amikacin are some of the most common antibiotics. An analysis of selected articles shows that ciprofloxacin (24.1-27.9%) and metronidazole (24.5-27.8%) are the most often used antibiotics among children aged 24-59 months, followed by azithromycin (19-45%). Alarmingly, significant antibiotic usage was reported in non-bloody diarrhea. Cefixime and other cephalosporins were used in only around 1-2% of cases. Most widely utilized agents are synthetic or semi-synthetic medicines that have been chemically modified to improve efficacy and stability. Following this, the excessive and inappropriate use of broad-spectrum antibiotics in pediatric patients has significantly contributed to the emergence of antimicrobial resistance in Bangladesh.

Keywords: Pediatric, Infectious diseases, Antimicrobial drug, Synthesis, Resistance

Dedication

First and foremost, I want to express my gratitude to almighty Allah for these blessings to me. Following that, I want to express my gratitude to my supervisor, Dr. Humair Bin Md. Omer, Associate Professor, BRAC University, for his unwavering support. I also express my gratitude to the entire faculty members, lab officers and staff members of the School of Pharmacy for their support and advice. Lastly, I want to thank my parents and friends for their support and encouragement.

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List of Acronyms

ARI	Acute Respiratory Infection
BDSH	Bangladesh Demographic and Health Survey
CDD	Children Diarrheal Disease
AMR	Antimicrobial Resistance
CDC	Centers for Disease Control and Prevention
EPS	Extracellular Polymeric Substances

Chapter 1

Introduction

In Bangladesh, infectious illnesses continue to be a significant source of morbidity and mortality in children under five (Rahman & Hossain, 2022). Although child survival rates become improves but still infectious diseases are a significant factor behind morbidity and mortality of children (Rahman & Hossain, 2022). Among infectious diseases acute respiratory infections (ARIs), fever (which might indicate bacterial or viral illnesses like dengue fever, malaria, or pneumonia in some areas), and diarrheal disorders tend to be the most prevalent (Rahman & Hossain, 2022). Village surveillance conducted over an extended period of time in rural Bangladesh indicated that upper respiratory tract infections were the most prevalent diseases, followed by diarrhea (Rahman & Hossain, 2022). It was noted that children had some infectious condition on about 75% of the days that were covered by the study (Rahman & Hossain, 2022). More recent nationally representative surveys confirm that these three conditions still dominate the childhood morbidity profile (Rahman & Hossain, 2022). Analyses of Bangladesh Demographic and Health Survey (BDHS) 2017-18 data show that, in the two weeks before survey, around one-third of under-five children had fever or ARI, while a smaller but still important proportion had diarrhea (Rahman & Hossain, 2022). Community-based studies in coastal Bangladesh report even higher burdens (Akter et al., 2025). Following this report in one southwestern coastal area 64.7% of children had ARI, 42.2% had fever and 13.5% had diarrhea in the preceding period (Akter et al., 2025). Additionally, school-age children (5-12 years) also experience substantial contagious disease (Md et al., 2015). In one city sample, 8.8% had clinically identifiable contagious illnesses such as scabies, influenza, typhoid, chickenpox, measles, pneumonia, and whooping cough (Md et al., 2015). Furthermore, emerging and re-emerging infections add to this burden. For example, dengue has become a prominent pediatric problem in urban Bangladesh (Khan et al., 2025). In one tertiary pediatric hospital, 722 dengue-positive children were admitted in just four months, with most cases occurring in children aged 1-10 years and 71% showing warning signs (Khan et al., 2025). On the other hand, typhoid and paratyphoid are also common bloodstream infections in Bangladeshi children, including those under two years of age, and often require hospitalization (Saha et al., 2019). Together, these data show that Bangladeshi children confront a “cluster” of infectious risks respiratory, gastrointestinal, vector-borne, and vaccine-preventable that interact with poor nutrition, crowded living, and inequitable healthcare access to maintain a high overall infectious disease burden (Rahman & Hossain, 2022).

Several national and subnational studies give a clear data of how infectious diseases spread among Bangladeshi children. Several analyses through utilizing BDHS 2017-18 data indicates that over 33% of children under five experienced fevers, 36% exhibited cough or acute respiratory infection (ARI), and around 5% suffered from diarrhea in the prior two weeks (Rahman & Hossain, 2022). Another research based on the BDHS found that the rates of children diarrheal disease (CDD) and acute respiratory infections (ARI) were 4.9% and 3.0%, respectively (Rahman & Hossain, 2022). These differences are primarily due to how the terms are defined (for example, "cough and fast breathing" vs. more general respiratory symptoms), but most of them indicate the same factor: at any given time, respiratory and fever diseases are much more common than diarrhea (Rahman & Hossain, 2022).

Multimorbidity children having two or more concurrent infectious conditions is common (Rashmi & Paul, 2022). Using BDHS 2017-18 data, one analysis found that 28% of under-five children had at least two infectious morbidities (fever, cough/ARI, or diarrhea) in the prior two weeks, and 47% had at least one of the main common conditions (Rashmi & Paul, 2022). Another nationwide study reported that about 27% of children experienced comorbidity, most often combinations of fever and cough, sometimes with ARI (Rashmi & Paul, 2022). Spatial analyses identify “hotspots” of childhood fever, cough, diarrhea, and ARI in the northwest, southwest, and central-southern regions, highlighting regional inequities in disease risk (K. N. Islam et al., 2024). Long-term trend analyses show progress but persistent burden. Despite the fact that the prevalence of acute respiratory infections (ARI) in children under the age of five has decreased from around 12.8% in 1996 to 3% in 2018. But children who are underdeveloped, and children whose mothers have a lower level of education continue to be at a higher risk (M. Islam et al., 2024). Despite overall declines, about 45-55% of under-five children still experience some infectious morbidity within a two-week recall period in recent surveys (Rashmi & Paul, 2022). In rural longitudinal cohorts, nearly 75% of observed child-days showed at least one infectious condition, demonstrated how "normal" illness remains in early childhood (Rashmi & Paul, 2022). These national and regional data together represent infectious diseases in Bangladeshi children as frequent, often overlapping, and strongly patterned by age, place, and social disadvantage (Rahman & Hossain, 2022).

Bangladesh survey studies consistently identify child age, nutrition, household poverty, environmental conditions, and care-seeking behavior as key determinants of infectious disease risk (Kundu et al., 2022). Following this, infants and toddlers under 24 months, have the highest prevalence of diarrhea, ARI, and fever (Kundu et al., 2022). Furthermore, a six-month break from breastfeeding significantly raises a child's chance of developing infectious diseases (Abdulla et al., 2022). It indicates that children have a 1.4 times increased risk of acute respiratory infections and a 2.1 times increased risk of diarrhea (Abdulla et al., 2022). So emphasizing the international recommendations supporting full breastfeeding as an efficient, affordable preventative strategy of preventing infectious diseases (Abdulla et al., 2022). On the other hand, socioeconomic and environmental determinants are equally critical (Rashmi & Paul, 2022). Children from poorer households, with unimproved floors, unsafe drinking water, and inadequate sanitation, face higher chance of diarrhea and ARI (Rashmi & Paul, 2022). Also maternal education plays an important role in protecting children from infectious diseases

(Rashmi & Paul, 2022). Maternal education strongly protects against morbidity (Rashmi & Paul, 2022). Children of mothers with no or primary education experience higher ARI and diarrhea prevalence, and ARI risk is especially high when mothers have no formal education about diseases management (Rashmi & Paul, 2022). And finally, rural and semi-urban children, and those living in high-risk or high-altitude communities, have significantly greater multimorbidity compared with children in city corporations (Rashmi & Paul, 2022).

Chapter 2

Methodology

This study was conducted as a narrative review focusing on keywords antimicrobial agents used in pediatric patients in Bangladesh, with particular emphasis on usage patterns, synthetic methods, and antimicrobial resistance (AMR) challenges. A systematic search was conducted in databases such as PubMed, Google Scholar, and Scopus using to complete this narrative review. Research conducted from 2010 to 2024 addressing common antibiotics used to treat pediatric patients in Bangladesh and their synthetic methods, along with resistance mechanisms, was included. Selected studies were screened for relevance, and data were extracted on commonly prescribed antibiotics, frequency of use, chemical class, synthetic origin (synthetic or semi-synthetic), and resistance concerns. Inclusion criteria covered peer-reviewed original research articles, surveillance reports and review papers addressing pediatric antimicrobial use in Bangladesh. Exclusion criteria included non-English publications, publications that not relevant to the selected topics and articles lacking methodological clarity. The findings were organized in order to provide an overview of the present scenario of antimicrobial use tendency among pediatric patients in Bangladesh and the challenges of antimicrobial resistance.

Chapter 3

Antimicrobials Commonly Used in Pediatrics in Bangladesh

The Bangladeshi pediatric population faces a significant burden of infectious diseases, driving the widespread and often empiric use of antimicrobial agents (Harun et al., 2024). This therapeutic landscape is dominated by a range of antibiotics, antivirals and antifungals, whose clinical efficacy is fundamentally rooted in their distinct chemical architectures and their targeted interference with pathogen-specific cellular processes (Harun et al., 2024). But the frequent unregulated use of these important antibiotic drugs has led to an alarming rise in antimicrobial resistance (Harun et al., 2024). This is a complex threat that works by preventing drugs from being inactivated, altering their target sites, and forcing drugs out of microbial cells (Harun et al., 2024). Additionally, this abuse of drug critically relates to the loss of therapeutic options (Harun et al., 2024a). It is important to have a clear knowledge of this dynamic in order to protect public health and make sure that these important therapies continue to work against pediatrics illnesses (Harun et al., 2024).

Recent studies and national surveillance data consistently mention that ceftriaxone, azithromycin, ceftazidime/amikacin, cefixime, metronidazole are the most commonly prescribed antimicrobials for children in Bangladesh (Harun et al., 2024). Ceftriaxone is a third-generation cephalosporin that is used in most of the cases in pediatric treatment (Harun et al., 2024). For example, especially in hospitals for serious infections like pneumonia, sepsis, and complicated diarrhea (Harun et al., 2024). According to Harun et al., 2024, 63.8% pediatrics patient received ceftriaxone antibiotics from a regular prescription. Another study demonstrated that the most common antibiotic prescribed for pediatric patients was ceftriaxone (62.39%), followed by azithromycin (18.65%) (Sarker et al., 2021). After that amikacin is also a frequently prescribed antibiotic for pediatric patients in Bangladesh. Two studies in

Bangladesh reported 8% and 4.58% pediatrics patient suggested amikacin among the total sample size (Table 1). According to table 1, data from the prescribing pattern of antibiotics among children in a tertiary-care hospital, ceftriaxone (57%) was the most prevalent antibiotic, followed by azithromycin (14%) (Chowdhury et al., 2020). Furthermore, cefixime is another frequently used antibiotic (5% among the sample size) in pediatrics patient in Bangladesh (Sarker et al., 2021). It's also a third-generation cephalosporin which is a common treatment for respiratory and urinary tract infections mainly to its oral formulation and broad-spectrum efficacy (Sarker et al., 2021). On the other hand, a recent study in Bangladesh demonstrated that out of 7,289 children presented with diarrhea, 3,823 (52.45%) children consumed antibiotics before visiting the hospital and the most prevalent single antibiotic consumed in bloody diarrhea was metronidazole (Bashar et al., 2024).

Table 1: Common prescribed antibiotics of pediatric patients in hospitals of Bangladesh

Sample size (N)	**Percentage of prescribed common antibiotics of pediatric patients in tertiary hospitals**			**References**
	Ceftriaxone	**Azithromycin**	**Amikacin**	
327	204 (62.38%)	61 (18.65%)	15 (4.58%)	(Chowdhury et al., 2020)
189	120 (63.8%)	-	15 (8%)	(Harun et al., 2024)
400	228 (57%)	56 (14%)	-	(Sarker et al., 2021)

Study shows that ciprofloxacin (27.89% non-bloody; 24.07% bloody), metronidazole (24.50% non-bloody; 27.78% bloody) and azithromycin (19.89% non-bloody; 19.75% bloody) were the most frequently consumed antibiotics among children aged 24-59 months with diarrhea (Figure 1). Additionally, combination therapy such as ciprofloxacin + metronidazole (10.49% bloody; 6.06% non-bloody) and metronidazole + azithromycin (4.32% vs 2.90%) also demonstrate significant percentage uses of antibiotics in diarrhea (Figure 1). On the other hand according to Figure 1, cefixime use was comparatively low among pediatric diarrhea patients (1.42% non-bloody; 1.32% bloody). And it also mentions that a significant number of bloody and non-bloody diarrhea patients cannot identify the antibiotic class which is about 5.56% and 13.99% respectively (Figure 1).

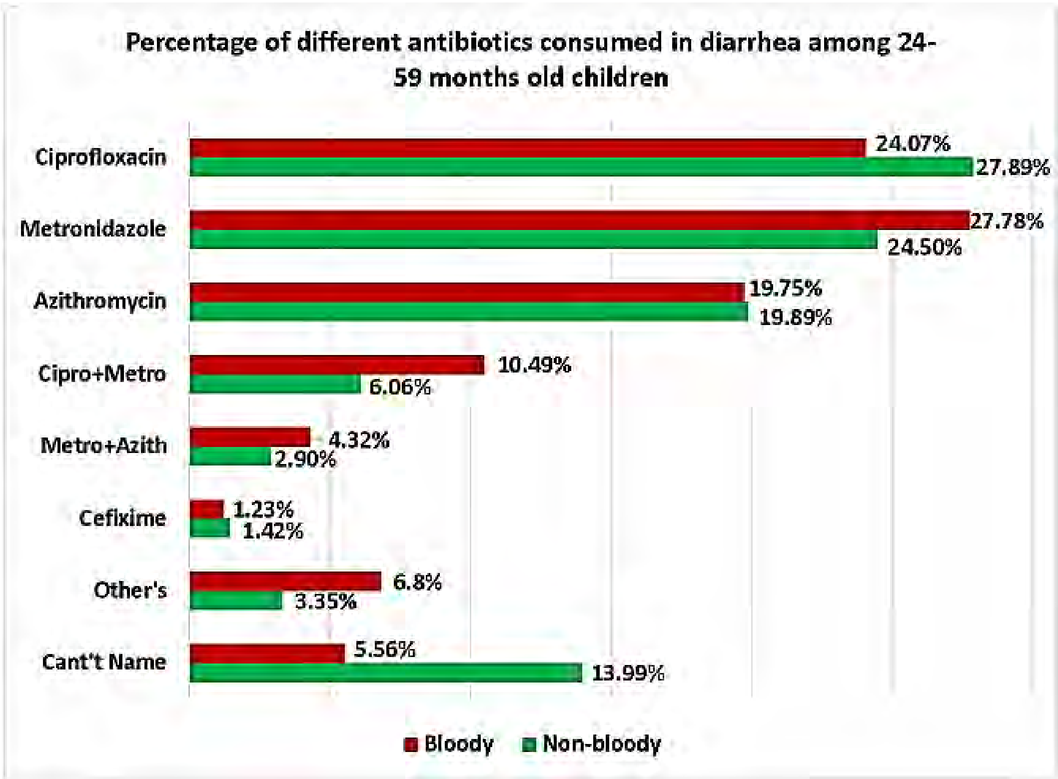

Figure 1: Percentages of different antibiotics consumed in diarrhea among 24-59 months old children at Dhaka Hospital, International Centre for Diarrheal Disease Research (icddr,b), Bangladesh(Bashar et al., 2024)

It is significantly noted that, for children with bloody diarrhea, metronidazole (alone or in combination with other antibiotics) was used by 44.44% of patients (Bashar et al., 2024). And this was significantly higher than in non-bloody diarrhea cases (Bashar et al., 2024). Ciprofloxacin and metronidazole were the most frequently used antibiotics in the first sample (N = 3,823). After that, regardless of the type of diarrhea, azithromycin use remained around 20% (Table 2). In contrast, the second sample (N = 4,562) found a much greater dependence on azithromycin, with a notable increase in non-bloody diarrhea (44.92%) (Table 2). From first and second sample groups, metronidazole usage was similarly high and it reflects frequent empirical use in diarrheal illnesses (Table 2). Finally in the third study (N = 2,745) reported substantially lower antibiotic use overall, especially for metronidazole (2.6%) (Table 2).

Table 2: Commonly used antibiotics received by children before hospital admission.

Sample size consumed antibiotic (N)	**Percentage of commonly used antibiotics received by children before hospital admission**						**References**
	Ciprofloxacin		**Azithromycin**		**Metronidazole**		
	Bloody	**Non-Bloody**	**Bloody**	**Non-Bloody**	**Bloody**	**Non-Bloody**	
3823	24.07%	27.89%	19.75%	19.89%	27.78%	24.50%	(Bashar et al., 2024)
4562	21.22%	11.86%	34.69%	44.92%	27.35%	26.78%	(Dash et al., 2025)
2745	7.7%		13.3%		2.6%		(M. R. Islam et al., 2020)

3.1 Chemical Structure of Commonly Used Antibiotics

3.1.1 Ceftriaxone

Ceftriaxone is a third-generation cephalosporin with a β-lactam ring fused to a dihydrothiazine ring (PubChem CID: 5479530). This ring is the component that makes it work against bacteria (PubChem CID: 5479530). It has a syn-oxime group creating a β-lactamase more stable and a thiotriazinedione side chain that makes its half-life longer and covers a wider range of Gram-negative bacteria (PubChem CID: 5479530).

Figure 2: Chemical structure of Ceftriaxone (PubChem CID: 5479530)

3.1.2 Azithromycin

Azithromycin is a broad-spectrum macrolide antibiotic with a long half-life and a high degree of tissue penetration (PubChem CID: 447043). Unlike earlier macrolides such as erythromycin, azithromycin contains a 15 membered azalide ring in which a nitrogen atom is incorporated into the lactone (PubChem CID: 447043). This modification improves its chemical stability and pharmacokinetic properties. It was initially approved by the FDA in 1991 (PubChem CID: 447043).

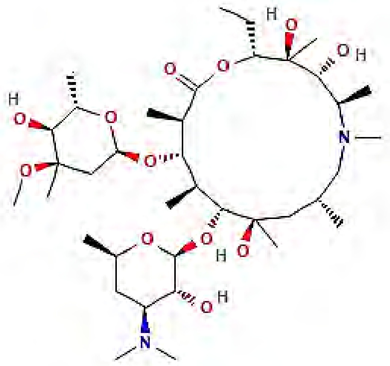

Figure 3: Chemical structure of Azithromycin (PubChem CID: 447043)

3.1.3 Amikacin

Amikacin is a semi-synthetic aminoglycoside antibiotic that is derived from kanamycin A (PubChem CID: 37768). A distinctive feature of amikacin is the L-(-)-γ-amino-α-hydroxybutyryl (AHB) side chain attached to one of the amino groups, which protects the molecule from enzymatic inactivation by many bacterial resistance mechanisms (PubChem CID: 37768).

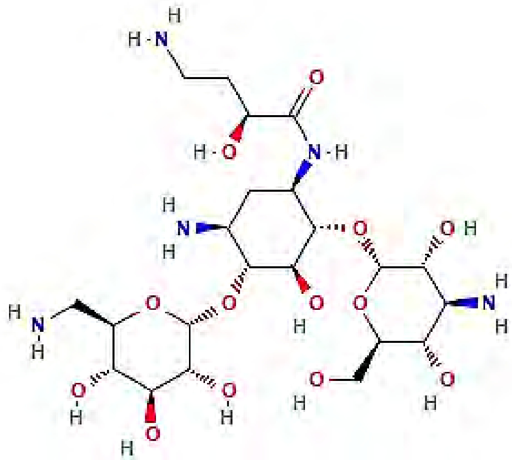

Figure 4: Chemical structure of Amikacin (PubChem CID: 37768)

3.1.4 Ciprofloxacin

Ciprofloxacin is a synthetic fluoroquinolone antibiotic and its chemical structure is highly functionalized (PubChem CID: 2764). It is a quinolin-4(1H)-one with cyclopropyl, carboxylic acid, fluoro, and piperazin-1-yl substituents in positions 1, 3, 6, and 7, respectively (PubChem CID: 2764). Moreover, Ciprofloxacin also contains a carboxylic acid group and a ketone group that are critical for binding to bacterial DNA gyrase and topoisomerase IV (PubChem CID: 2764).

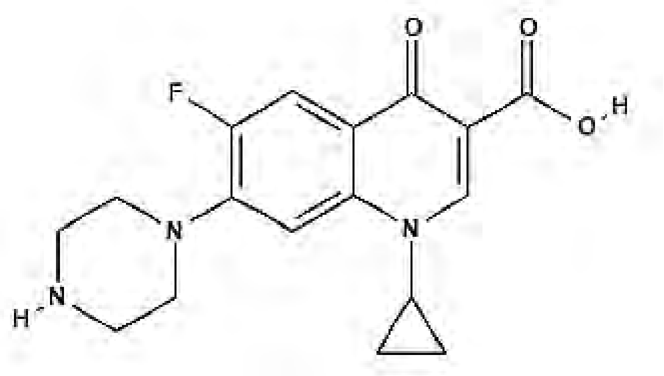

Figure 5: Chemical structure of Ciprofloxacin (PubChem CID: 2764)

3.1.5 Metronidazole

Metronidazole (2-Methyl-5-nitroimidazole-1-ethanol) is a synthetic nitroimidazole antibiotic with a relatively simple and compact chemical structure. Generally, its core consists of a five-membered imidazole ring that contains two nitrogen atoms. This imidazole ring is essential for its biological activity. Its chemical formula is $C_6H_9N_3O_3$. Metronidazole is a prodrug that is selective for anaerobic bacteria because they can decrease the nitro group of metronidazole intracellularly, resulting in nitroso-containing metabolites. These can covalently attach to DNA and alter its helical shape. As a result, it causes DNA strand breakage and limits bacterial nucleic acid synthesis.

Figure 6: Chemical structure of Metronidazole (PubChem CID: 4173)

Chapter 4

Synthetic Methods of Commonly Used Antimicrobial Drugs

4.1 Ceftriaxone

Ceftriaxone is a third-generation cephalosporin that is made by semi-synthetically breaking down cephalosporin C from Acremonium chrysogenum into 7-aminocephalosporanic acid (7-ACA) (Lin & Kück, 2022). The β-lactam-dihydrothiazine core of 7-ACA is made by adding an activated side chain at the 7-amino position and functionalizing C-3 in the right way to make the leaving group of ceftriaxone. The oxyimino group in the side chain makes β-lactamase stable (Lin & Kück, 2022). Researchers today often use ceftriaxone as a base for making new compounds instead of making the core again (Lin & Kück, 2022). For instance, the 2-aminothiazolyl moiety can be transformed into an amide using chloroacetyl chloride, and then combined with aliphatic or aromatic amines to create new ceftriaxone derivatives (Lin & Kück, 2022). These derivatives can be made in water in high yield using simple nucleophilic substitutions (Lin & Kück, 2022).

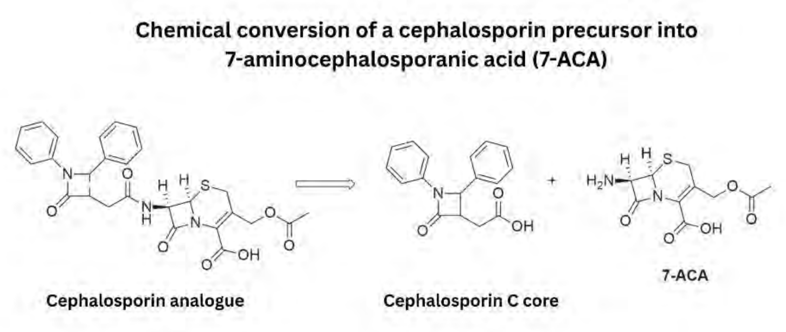

Figure 7: Chemical conversion of a cephalosporin precursor into 7-aminocephalosporanic acid (7-ACA)

4.2 Azithromycin

Azithromycin is a semi-synthetic 15-membered macrolide (an azalide) made from the natural 14-membered macrolide erythromycin A (Mutak, 2007). The primary transition is a Beckmann rearrangement of a 9-oxime derivative of erythromycin (Mutak, 2007). This happens when an oxime is formed at C-9 and then rearranged to make a 15-membered lactam/iminether arrangement with a nitrogen atom added to the macrocycle (Mutak, 2007). After the imino ether is reduced, it becomes the cyclic aminolactone (azalide scaffold). Then it is methylated with formaldehyde and formic acid to make 9-deoxo-9a-aza-9a-methyl-9a-homoerythromycin A, which is also known as azithromycin (Mutak, 2007). Process chemistry has improved the protection and deprotection of sugars and hydroxyls, the control of stereochemistry and the conditions that keep glycosidic bonds from breaking down in acid (Mutak, 2007). The scaffold has many hydroxyl and amino groups that can be used to make second-generation azalides (esters, carbamates, bridged derivatives) and new macrolide analogues with better pharmacokinetics and activity against respiratory pathogens that are resistant to treatment (Mutak, 2007).

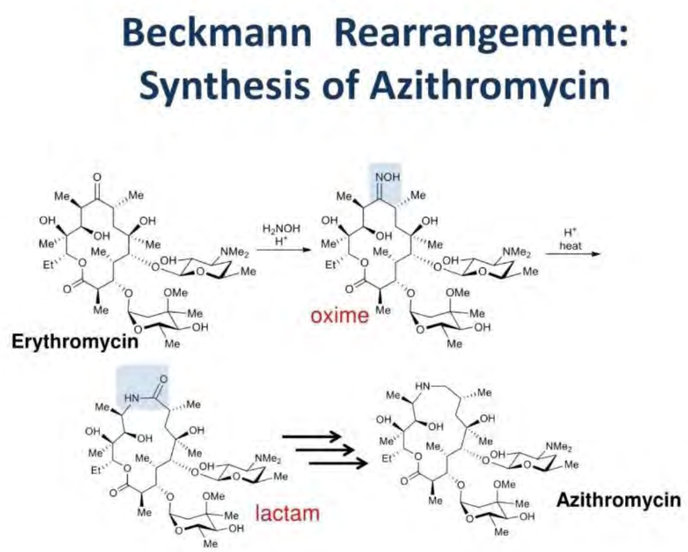

Figure 8: Synthesis of Azithromycin through Beckmann Rearrangement

4.3 Amikacin

Amikacin is a semi-synthetic aminoglycoside synthesized through the attachment of acyl groups to the side chains of the natural antibiotic kanamycin A (Ramirez & Tolmasky, 2017). Kanamycin A has a 2-deoxystreptamine core with many amino groups and it is very important to selectively functionalise the C-1 amino group (Ramirez & Tolmasky, 2017). To synthesize amikacin, we need to acylate this position with L-(-)-4-amino-2-hydroxybutyryl (AHB) (Ramirez & Tolmasky, 2017). Throughout this process makes an amide that protects important hydroxyl and amino sites from many enzymes that change aminoglycosides (Ramirez & Tolmasky, 2017). To make sure that the reaction is regioselective, this transformation uses kanamycin that is properly protected, activation of the AHB carboxyl group, and careful coupling (Ramirez & Tolmasky, 2017). Similar 1-N acylation methods made other semisynthetic aminoglycosides (netilmicin, isepamicin) by adding ethyl or hydroxyamino side chains (Ramirez & Tolmasky, 2017). The AHB side chain in amikacin keeps acetyltransferases, phosphotransferases, and nucleotidyltransferases from getting to it (Ramirez & Tolmasky, 2017). This makes it resistant to most common aminoglycoside-modifying enzymes and the reason behind it works against resistant Gram-negative pathogens in the clinic (Ramirez & Tolmasky, 2017).

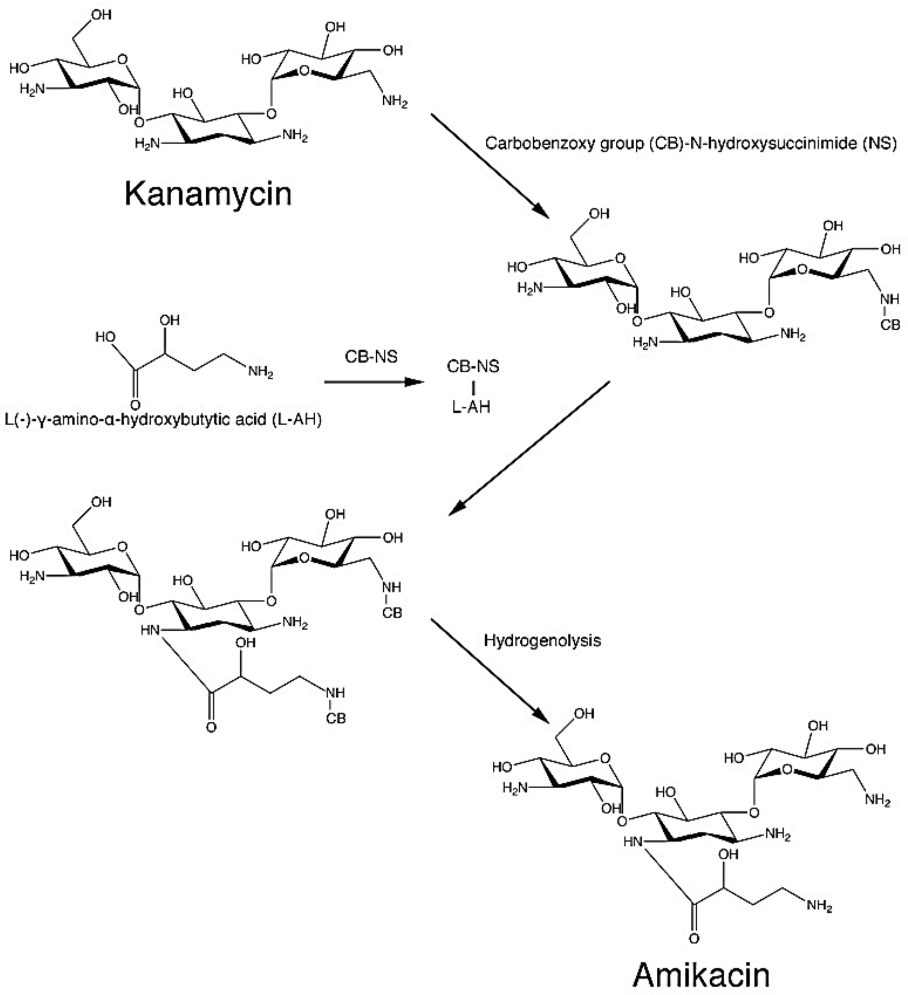

Figure 9: Chemical reactions sequence to obtain amikacin by modification of kanamycin A (Ramirez & Tolmasky, 2017).

4.4 Ciprofloxacin

Ciprofloxacin is a fully synthetic second-generation fluoroquinolone that is based on a 4-oxo-3-carboxyquinoline core (Armstrong et al., 2021). Most of the time, industrial processes formulate the fluoroquinolone scaffold first, and then they add the C-6 fluorine and C-7 piperazinyl groups that give ciprofloxacin its spectrum and strength (Armstrong et al., 2021). Modern process development emphasizes telescoped, continuous syntheses to reduce isolation steps and enhance purity (Armstrong et al., 2021). A new plug-and-play continuous process uses four reactors and five chemical transformations (Armstrong et al., 2021). It also has a continuous liquid-liquid extraction unit (Armstrong et al., 2021). It keeps each intermediate above 95% purity and gets about 700 g of crude ciprofloxacin in 24 hours at 94 ± 2% purity by HPLC (Armstrong et al., 2021).

4.5 Metronidazole

Metronidazole is a nitroimidazole, and its traditional synthesis begins with a properly substituted imidazole, followed by the addition of the 2-methyl and 5-nitro groups, and finally the installation of the 2-(hydroxyethyl) side chain (Ansari et al., 2020). Medicinal chemistry often uses the primary alcohol to make derivatives. One method makes 4-[2-(2-methyl-5-nitro-1H-imidazol-1-yl)ethoxy]benzaldehyde and then combines it with thiazolidinone derivatives through Knoevenagel condensation to make metronidazole-based thiazolidinones that are better at killing amoebas and less toxic to cells (Ansari et al., 2020).

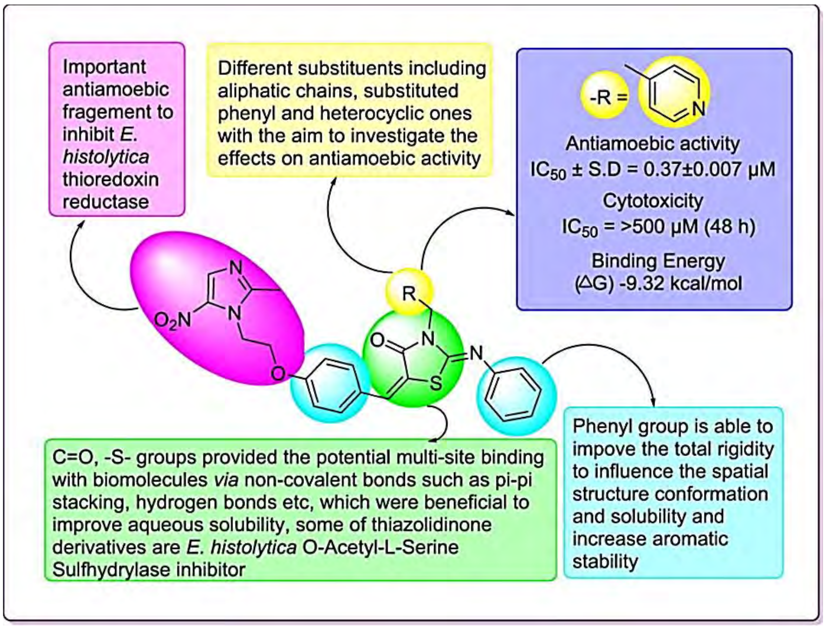

Figure 10: Rational designing of the metronidazole-based thiazolidinone analogs (Ansari et al., 2020)

Chapter 5

Challenge Associated Due to Antimicrobial Resistance

Antimicrobial resistance (AMR) is a serious and growing threat to the health of children in Bangladesh, where infectious diseases are still the main cause of death and illness (Sharif et al., 2023). There are a number of problems that are connected that make it especially hard to control AMR in Bangladeshi children. Resistance is now common in common pediatric pathogens in the clinic (Sharif et al., 2023). Resistance to the WHO recommended first-line drug ciprofloxacin has increased to over 70% among children under five with shigellosis (Sharif et al., 2023). There have also been significant rises in resistance to azithromycin and ceftriaxone, as well as in multidrug resistance, in both urban Dhaka and rural areas over the past 20 years (Nuzhat et al., 2022). In bloodstream infections in infants and pediatrics the most common germs are coagulase-negative staphylococci, Escherichia coli, Staphylococcus aureus, and Klebsiella spp (Hoque et al., 2020). From the study, 29.4% of blood cultures from newborns with sepsis were positive for these germs, and 72% of isolates in one ICU study were multidrug-resistant (Hoque et al., 2020). This means that these microbes are very resistant to ampicillin, gentamicin, and commonly used staphylococci (Hoque et al., 2020). High recent irrational antibiotic consumption and easy access to antibiotics without a prescription are two major factors that make the challenge against antimicrobial resistance (Harun et al., 2023). For example, 62.9% of parents said they had given antibiotics to their children under the age of five in the past year, and 52.7% said they had bought antibiotics from drug stores without a prescription (Figure 11). Additionally, 46.5% of parents said they had stopped taking antibiotics early and 62.6% said they had reused leftover antibiotics (Figure 11). These behaviors are linked to education, income, and convenience factors like cost and travel time to see a doctor (Harun et al., 2023). There is also not enough capacity for monitoring and management. In a large number of infections, national and local studies show that people are becoming more resistant to commonly used antibiotics and "superbugs" that are resistant to many drugs (Yesmin et al., 2025). However, Bangladesh still doesn't have fully functional nationwide surveillance or strong pediatrics antimicrobial surveillance programs (Yesmin et al., 2025). Overall, in Bangladesh, antimicrobial resistance in children is primarily influenced by a high burden of infectious diseases, inappropriate antibiotic usage in homes and healthcare settings, inadequate control of pharmaceutical sales, and limited diagnostic and monitoring frameworks (Yesmin et al., 2025).

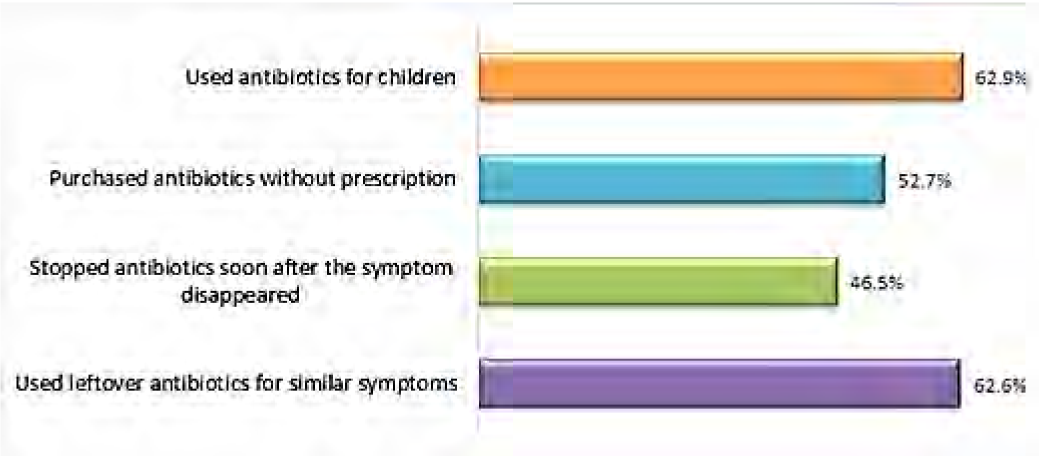

Figure 11: Pattern of Antibiotic Consumption among ≤5-Year Children in Low-Income Urban Bangladesh (Harun et al., 2023)

Chapter 6

Major Mechanisms of Antimicrobial Resistance

Antimicrobial resistance (AMR) occurs when microorganisms survive exposure to drugs that generally eradicate them or inhibit their proliferation (C Reygaert, 2018). Most bacterial resistance can be put into a few main groups at the molecular level. These groups of bacteria work alone or together to limit drug entry, pump drugs out, change or protect the target, inactivate the drug, and form biofilms (C Reygaert, 2018). All of these processes are driven and spread by powerful genetic processes (C Reygaert, 2018).

6.1 Limited Uptake

A first important mechanism is that Gram-negative bacteria absorb in less or have a limited permeability (C Reygaert, 2018). The lipopolysaccharide-rich outer membrane acts as a barrier, and antibiotics mostly get in through porin channels (C Reygaert, 2018). Resistance can develop when these porins lose their function, are down-regulated, or are changed in structure (C Reygaert, 2018). This alteration makes it harder for antibiotics to get inside the cell so that the intracellular concentration never reaches inhibitory levels (C Reygaert, 2018). This mechanism is particularly important for β-lactams, fluoroquinolones and some carbapenems in Gram-negative pathogens (C Reygaert, 2018).

6.2 Efflux pumps

One other significant method is known as active efflux. According to this mechanism, membrane transporters continually pump antimicrobials out of the cell (Gauba & Rahman, 2023). Multidrug efflux pumps, for example RND, MFS, ABC, MATE, and SMR families have the ability to reduce intracellular drug levels below the minimal inhibitory concentration (Figure 8). These pumps have the ability to be effective against various classes of drugs, including tetracyclines, fluoroquinolones, macrolides, and β-lactams. In general, mutations or regulatory alterations can cause activation of these pumps (Gauba & Rahman, 2023). These lead to multidrug resistance in Gram-negative "priority pathogens" such as Pseudomonas aeruginosa and Enterobacteriaceae (Gauba & Rahman, 2023).

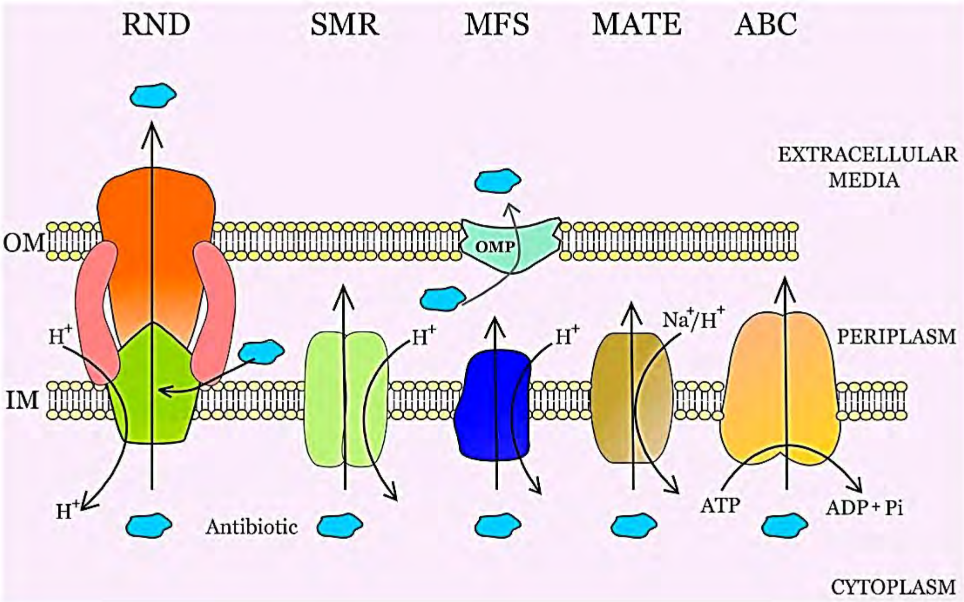

Figure 12: General structure of main efflux pump families (Blanco et al., 2016)

6.3 Target alteration

A third important mechanism is changing the drug target so that the antibiotic fails to function as well. This can happen when chromosomal genes have point mutations (like mutations in quinolone-resistance-determining regions of DNA gyrase and topoisomerase IV) or when bacteria get new target proteins (like altered penicillin-binding proteins in β-lactam-resistant bacteria or modified ribosomal RNA in macrolide resistance) (C Reygaert, 2018). Moreover, some bacteria develop enzymes that chemically protect rather than modify their targets, such as proteins that protect ribosomes from tetracyclines (C Reygaert, 2018). Resistance in metabolic pathways can occur by the production of drug-insensitive enzyme variants or the expression of bypass enzymes that skip the inhibited step. This type of phenomenon is observed with sulfonamides and trimethoprim (C Reygaert, 2018).

6.4 Enzymes Hydrolyze or Modify Drugs

A fourth mechanism that has been explored frequently is the inactivation or modification of the antimicrobial agent by enzymes (Belay et al., 2024). Bacteria can make enzymes that break down drugs (like β-lactamases that open the β-lactam ring) or that add chemical groups (like acetyl, adenyl, or phosphoryl) to aminoglycosides and other drugs (Belay et al., 2024). These enzymatic inactivation or alteration reduce the effectiveness of antimicrobials (Belay et al., 2024).

6.5 Biofilms & Persisters

In addition to the traditional mechanisms, biofilm formation is a significant contributor to persistent infections. Biofilms are made up of bacteria that are stuck in a matrix of extracellular polymeric substances (EPSs) (Belay et al., 2024). This EPSs layer is also called a "matrixome" (Pai et al., 2023). This layer acts as a physical barrier (Pai et al., 2023). This matrix primarily consists of polysaccharides, proteins, water-insoluble compounds, and lipids (Pai et al., 2023). The EPS makes it harder for antimicrobial agents to enter cells and thereby reduces their effectiveness (Pai et al., 2023). This slows down the diffusion of some drugs that creates nutrient and oxygen gradients (Belay et al., 2024). These mechanisms lead to cells that grow slowly or stay dormant and influence the expression of certain resistance genes, including efflux pumps (Belay et al., 2024). Biofilms also contain persistent cells, which are phenotypic variants that can live in high concentrations of antibiotics without being genetically resistant. They then regenerate when treatment stops (Belay et al., 2024). Moreover, once these colonies of bacteria pass the initial attachment and adhesion phase, the attachment to surfaces can become irreversible (Figure 9). And the final stage involves the detachment and dispersion of bacteria from the mature biofilm. This process allows them to colonize new niches and start a new cycle of biofilm (Figure 9).

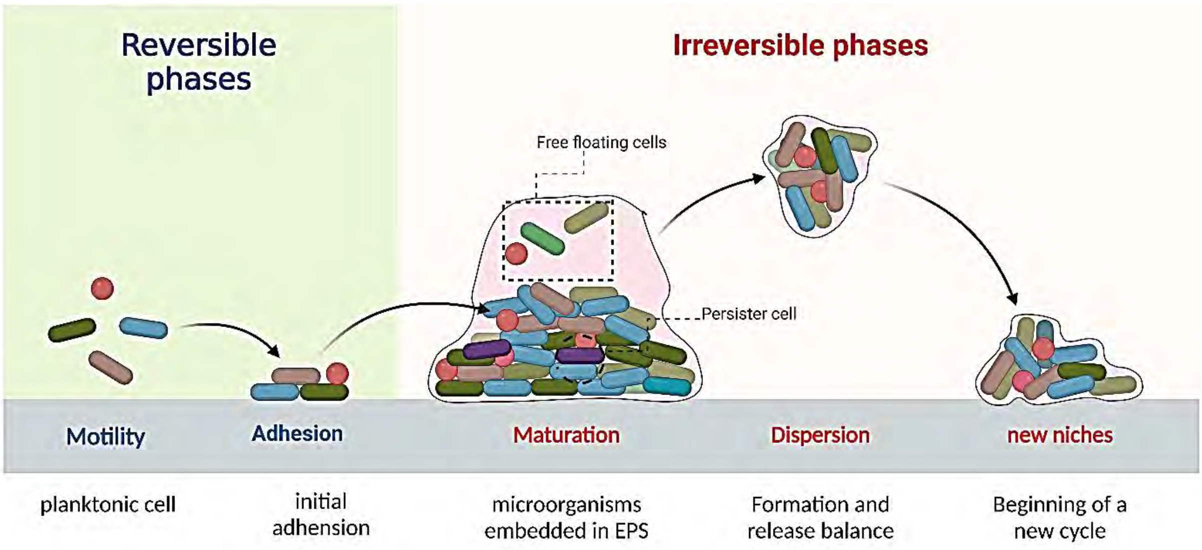

Figure 13: Life cycle of biofilm (Pai et al., 2023)

Chapter 7

Conclusion

This review project shows that the antimicrobial drugs used in children in Bangladesh are mostly synthetic or semi-synthetic drugs that work against a wide range of bacteria. These antibiotics are important for treating serious infections. On the other hand, their frequent and inappropriate use has worsened antimicrobial resistance. The data indicates that this issue mostly arises from society and doctors who fail to adhere to treatment protocols, give antibiotics randomly and neglect accepted standards. To better understand the development of resistance, it is helpful to know the sources of these medications and how they function in the body. And this practice also helps develop safe antibiotic use, especially in pediatric patients. To make sure that pediatric antimicrobial therapy is safe and effective, it is important to strengthen antibiotic stewardship and evidence-based prescribing. In order to make sure the safety and efficacy of pediatric antimicrobial therapy, it is essential to enhance the management of antibiotics and evidence-based prescribing.

Future studies should concentrate on comprehensive pediatric antimicrobial surveillance across the nation to produce accurate usage and resistance data. Future research into the development of novel antimicrobials could benefit from a synthesis of knowledge about the mechanisms by which bacteria acquire resistance to various synthetic medicines. It is very important to put into place antibiotic stewardship programs in hospitals and communities, especially for managing diarrhea in children. Furthermore, training initiatives for healthcare professionals and support teams should be enhanced to reduce the unnecessary usage of antibiotics. Policymakers should make it more difficult to sell antibiotics over the counter. These steps will work together to reduce antimicrobial resistance and improve healthcare for children in Bangladesh.

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