

Original Article

Factors contributing to antibiotic use among children younger than five years old with fever, acute respiratory illness, and diarrhea in Bangladesh

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Abstract

Introduction: Increasing antibiotic usage is a leading health threat that develops antibiotic resistance. The current practice of antibiotic use among under-five children are unavailable in Bangladesh. We aim to identify the factors of antibiotic use among under-five children with infectious diseases.

Methodology: A cross-sectional multiple indicators cluster survey (MICS) was conducted in 2019 across Bangladesh. This survey of 23,099 children under the age of five was randomly selected by using a two-stage stratified sampling method. The first stage involved randomly selecting 32,200 enumeration clusters. In second stage, households where 15-45-years-old women lived were randomly selected from within each cluster. The Poisson regression models were performed to estimate the prevalence ratio (PR).

Results: We found 36.7% (8447/23,099) under-five children with infectious diseases. The proportion of antibiotic use was reported as 32.6%. Antibiotic use was associated with wealth (poorest vs. rich adjusted prevalence ratio (APR) = 1.07; 95% CI: 0.94-1.22) and mother's education (pre-primary vs. higher: APR = 1.14; 95% CI: 1.03-1.27). Oral and injectable antibiotics were used in cases of fever (30.5%), diarrhea (4.5%), fever with cough (47.6%). Cotrimoxazole (31.0%) and amoxicillin (29.0%) were consumed for fever with cough while cotrimoxazole (14.0%) and amoxicillin (11.0%) were consumed for fever with diarrhea. They received antibiotics from drug stores (71.9%) without prescription and private healthcare (52.1%).

Conclusions: Overall, one-third of the under-five children in Bangladesh consumed antibiotics to treat infectious diseases. Multiple factors contribute to the prevalence of antibiotic use. The results highlight the need to regulate antibiotic use and prioritize national intervention programs.

Key words: Fever; diarrhea; ARI; antibiotic; under-five; Bangladesh.

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Introduction

Antibiotic resistance in bacterial pathogens is a leading cause of global health challenges associated with the high prevalence of contagious diseases. The overuse, misuse, and improper use of broad-spectrum antibiotics in animals, agriculture, and healthcare settings, as well as poor infection control practices, are all contributing to the steady rise in antibiotic resistance [1]. Consequently, bacteria resistance can quickly spread to patients around the globe [2]. Furthermore, poor surveillance systems and available poor-quality antibiotics in resource-poor settings are implicated in the emergence of antibiotic resistance [3]. Additionally, antibiotic use plays a significant role in developing antibiotic resistance [3,4]. Since 2000, the antibiotic consumption rate has increased by 77% from 7.6 to 13.5 defined daily doses (DDDs) per 1,000 people per day in low-income countries [5]. Therefore, multi-drug

resistance in resource-poor settings, which has a strong positive correlation with antibiotic use, has led to mortality and morbidity [6–9].

The increasing prevalence of antibiotic resistance threatens child health, particularly in low-income countries. The Sustainable Development Goals for reducing child mortality are not currently achieved due to the emergence of multi-drug resistance in infectious diseases [10,11]. Mainly, the excessive use of antibiotics for treating infectious diseases is higher in low-income countries than in high-income countries [12], and antibiotic use is more in children than adults due to increased vulnerability [4]. Therefore, optimizing antibiotic use should be maintained and it is a significant challenge in resource-poor settings with a high rate of infectious diseases where broad-spectrum antimicrobials are usually used [13]. So, the World Health Organization (WHO) has recommended that

antimicrobial agents should be prioritized in the global action plan on antibiotic resistance [14]. This objective is still behind the target as there is limited data on antibiotic use among children under five years of age in low-income countries, particularly Bangladesh.

To understand the antibiotic use, we need data to access the antibiotic use of a country. However, data regarding antibiotic use is limited in resource-poor countries like Bangladesh [5]. The primary evaluation of antibiotic use depends on hospital-based surveys, which are helpful in individual-level exposure to antibiotic use in the institution but do not directly measure the factors of population-level antibiotic use. While the hospital-based antibiotic data are well documented to address antibiotic use in Bangladesh, it may be biased because it does not include non-prescribed antibiotics use which comprises a large portion of total antibiotic usage [15]. These data gaps affect the national representativeness of the existing antibiotics use and reliable population characteristics. Additionally, young children in the community are more likely to consume antibiotics because the morbidity and mortality associated with infectious diseases are higher among children than adults [16,17]. A primary population-based survey in Bangladesh was conducted to collect data on child health and antibiotic use among under-five children for treating infectious diseases. The objectives of this survey were to assess and monitor the current status of health indicators [18], but it didn't discover a set of significant distinct factors causing antibiotic use. Therefore, a secondary analysis of this data which aims to identify the factors contributing to antibiotic use among under-five children for treating infectious diseases in Bangladesh is needed.

Methodology

We used a Multiple Indicator Cluster Survey (MICS), Bangladesh in 2019 data. United Nations Children's Fund (UNICEF) and the Government of the People's Republic of Bangladesh conducted this cross-sectional survey. The MICS 2019 provides community survey data on socio-economic characteristics, 15-49-year-old women, mothers or caregivers, reported disease episodes, and health conditions of under-five children. This survey was conducted from January 2019 to June 2019 with 3,220 Primary Sampling Units (PSU), enumeration areas (EAs) of Bangladesh Census of Population and Housing 2011 in rural and urban areas of Bangladesh. The 64,400 households were enrolled by using a 2-stage stratified cluster probability

proportional to size (PPS) sampling method, detailed in the MICS preliminary report [16].

Statistical analysis

We performed descriptive statistics to calculate the proportion for categorical variables, the prevalence of sick children under five with fever, diarrhea, and ARI cases, and the proportion of antibiotic use among sick children with illness. We defined a sick child who experienced fever, diarrhea, cough, short/ rapid or fast breathing, and problems in the chest during breathing in the preceding two weeks. According to the World Health Organization (WHO), a diarrheal episode was defined as loose or watery stools occurring at least three times a day, and ARI was defined as rapid or difficult breathing and a problem in the chest with or without cough [17]. An antibiotic user who had consumed any antibiotics for treating their infectious diseases encounters [12]. Children were categorized into six groups; 0 to 5 months, 6-11 months, 12-23 months, 24-35 months, 36-47 months, and 48-59 months. The Principal Component Analysis (PCA) was performed in the list of household assets for indexing wealth. Households were classified into poorest, poor, middle, upper-middle, and rich by quintiles [18]. The composite index of anthropometric failure (CIAF), undernutrition, is defined as a child who experienced either stunting, wasting, or being underweight [19–21]. Their nutritional status; A long-term nutrition insufficiency was considered by stunting ($HAZ < -2$ SD); a short-term nutrition insufficiency was evaluated by wasting ($WHZ < -2$ SD) and underweight ($WAZ < -2$ SD) children referred to change in nutrition over time [19]. The level of education for mothers/ caregivers was classified into four groups: pre-primary, primary, secondary, and higher. The improved toilet sanitation facility was defined as the households having flush/pour flush, septic tank, pit latrine, ventilated improved pit, and a pit with slabs toilet [16]. We defined improved drinking water sources as households collecting drinking water from piped water, public taps, standpipes, tube wells, boreholes, protected dug wells and springs, bottled water, sachet water, tanker trucks and cart with small drums or tanks. Based on the care-seeking health facilities, we categorized the facility providers into five sectors: public, private, and community health providers, recommendations from relatives or friends, drug shops, and traditional healers. The public sector included medical college hospitals, specialized government hospitals, district hospitals, mother and child welfare centers, Upazilla health

complex, union health, and family welfare centers. The private sector included private medical college hospitals, private hospitals, private clinics, and qualified doctor’s chambers. Community health providers included community health workers and mobile/outreach clinics [22]. In these analyses, we used the sampling weights to adjust for sampling variation between regions [22]. We used a waffle chart to present the percentage of various symptom complaints, and a forest plot to show the proportions of antibiotic use among different symptom complaints. Bivariate analysis was conducted using the Poisson regression model to identify the significant variables associated with reported antibiotic use at level $\alpha = 0.05$.

Multivariate analysis included the selected variables that are significant. Poisson regression was performed to estimate the adjusted prevalence ratio (APR) associated with a 95% confidence interval (CI) for age and sex as confounders; other significant covariates accounted for the clustering effect in households. We also performed a subgroup analysis among the different combinations of symptoms to identify the inappropriate use of antibiotics. STATA version 13.1 was used for managing and analyzing data, and Python 3.6 was used for presenting data in interactive graphs.

Table 1. Demographic characteristics and antibiotic usage among sick children under five years of age during 2019 in Bangladesh.

Characteristics	Children in total		Sick children		Sick children with antibiotic used	
	n (%)	n (%)	95% CI	n (%)	95% CI	
In Total	23,099 (100)	8447 (36.7)	(35.8, 37.3)	2753 (32.6)	(31.4, 33.8)	
Age in month						
0-5	2414 (10.5)	874 (36.2)	(34.0, 38.4)	293 (33.5)	(30.0, 37.2)	
6-11	2194 (9.5)	1038 (47.3)	(44.9, 49.7)	392 (37.8)	(34.5, 41.2)	
12-23	4435 (19.2)	1986 (44.8)	(43.2, 46.4)	645 (32.5)	(30.2, 34.8)	
24-35	4606 (19.9)	1797 (39.0)	(37.4, 40.6)	594 (33.1)	(30.7, 35.6)	
36-47	4818 (20.9)	1508 (31.3)	(29.8, 32.9)	454 (30.1)	(27.5, 32.8)	
48-59	4632 (20.1)	1245 (26.9)	(25.4, 28.4)	377 (30.3)	(27.4, 33.4)	
Sex						
Male	12008 (52.0)	4508 (37.5)	(36.6, 38.5)	1530 (33.9)	(32.4, 35.5)	
Female	11091 (48.0)	3939 (35.5)	(34.5, 36.6)	1223 (31.0)	(29.4, 32.7)	
Area						
Rural	18196 (78.8)	6666 (36.6)	(35.8, 37.5)	2157 (32.4)	(31.1, 33.7)	
Urban	4903 (21.2)	1780 (36.3)	(34.5, 38.2)	596 (33.5)	(30.8, 36.3)	
Wealth index						
Poorest	5036 (21.8)	1804 (35.8)	(34.3, 37.4)	546 (30.2)	(27.9, 32.7)	
Poor	4534 (19.6)	1748 (38.6)	(36.9, 40.2)	544 (31.1)	(28.9, 33.6)	
Middle	4298 (18.6)	1593 (37.1)	(35.5, 38.7)	499 (31.3)	(28.9, 34.0)	
Upper-Middle	4511 (19.5)	1706 (37.8)	(36.1, 39.6)	609 (35.7)	(33.1, 38.5)	
Rich	4720 (20.4)	1596 (33.8)	(32.1, 35.5)	555 (34.8)	(31.9, 37.8)	
Mother’s education						
Pre-primary	2586 (11.2)	821 (31.7)	(29.7, 33.9)	252 (30.7)	(27.2, 34.3)	
Primary	5483 (23.7)	2062 (37.6)	(36.1, 39.1)	631 (30.6)	(28.3, 32.9)	
Secondary	11331 (49.1)	4225 (37.3)	(36.2, 38.3)	1395 (33.0)	(31.4, 34.6)	
Higher	3699 (16.0)	1339 (36.2)	(34.4, 38.0)	476 (35.5)	(32.6, 38.6)	
Improved toilet sanitation						
Yes	19209 (83.2)	6946 (36.2)	(35.3,37.0)	2309 (33.2)	(31.9, 34.6)	
No	3889 (16.8)	1499 (38.6)	(36.8,40.3)	444 (29.6)	(27.1, 32.3)	
Improved source of drinking water						
Yes	19960 (86.4)	7391 (37.0)	(36.2, 37.8)	2371 (32.1)	(30.9, 33.3)	
No	3139 (13.6)	1056 (33.6)	(31.4, 36.0)	382 (36.2)	(32.5, 40.1)	
Composite index of Anthropometric Failure (CIAF)						
Yes	8430 (36.5)	4878 (36.7)	(35.5,37.9)	1027 (33.2);	(31.3,35.1)	
No	14669 (63.5)	5276 (36.5)	(35.6, 37.4)	1726 (32.2);	(30.8, 33.7)	
Healthcare facilities (multiple responses)						
No advice or treatment sought		3233 (38.3)		0		
Public sector		878 (10.4)		235 (26.8)	(23.3, 30.2)	
Private sector		3443 (40.8)		1794 (52.1)	(50.1, 54.1)	
Recommended from relatives		132 (1.6)		6 (4.2)	(1.5, 10.7)	
Community health provider		149 (1.8)		17 (11.3)	(6.7, 18.3)	
Drug shops		254 (3.0)		183 (71.9)	(66.0, 77.1)	
Traditional healers		1320 (15.6)		324 (24.5)	(22.0, 27.3)	

Results

This analysis included 23,099 children under five years of age; 18,196 (78.8%) were enrolled from rural areas, and 12,008 (52%) were male. Among the children, the youngest children (0-11 months) was 20% (4608), and the oldest children (35-59 months) was 41% (9450). Most mothers/caregivers (65%) completed secondary and higher education and undernutrition was 36.5%.

The prevalence of infectious diseases among children under five was 36.6% (95% CI: 35.8-37.3%). Among sick children, the reported fever alone was one of the most common causes of illness (23.7%), followed by only fever with cough (18.1%), cough alone (16.3%), fever with cough, and rapid or difficult breathing (9.1%), only diarrhea (8.4%), diarrhea with fever (8.2%), cough with rapid or difficult breathing (6.1%), fever with ARI (3.3%), ARI alone (1.6%), fever with rapid or difficult breathing (1.3%) and fever with diarrhea and ARI (0.5%) (Figure 1). There was 61.7% of sick children aged under five years seeking healthcare facilities. The proportion of seeking healthcare from private healthcare facilities was 40.8%, public healthcare facilities (10.4%), community healthcare providers (1.6%), the recommendation from relatives/friends (1.6%), the drug received from shops without prescription (3.0%), and traditional healers (15.6%) (Table 1).

The proportion of reported antibiotic use among sick under-five children associated with infectious diseases was 32.6% (95% CI: 31.4, 33.8%). The prevalence of antibiotic usage was reported for fever

with ARI (69.8%), followed by fever with diarrhea and ARI alone (64.2%), fever with cough and rapid or difficult breathing (57.6%), ARI alone (51.0%), cough with rapid or difficult breathing (48.0%), fever with cough (47.6%), diarrhea with fever (42.2%), fever with rapid or difficult breathing (37.3%), fever alone (30.5%), and diarrhea alone (4.5%) (Figure 2). The reported cotrimoxazole and amoxicillin were 31.0% and 29.0% for fever with cough, respectively (Figure 3). The proportion of antibiotics usage was 52.1% among private healthcare facilities, public healthcare facilities (26.8%), community health providers (11.3%), the recommendation from relatives/friends (4.2%), drug stores (71.9%), and traditional healers (24.5%) (Table 1). About 3.6% of sick children received injectable antibiotics, which were used for fever with ARI (18.0%), only fever with cough (18.0%), fever with cough and rapid or difficult breathing (14.0%), ARI alone (10.0%), diarrhea with fever (12.0%), fever with diarrhea, and ARI (9.0%), fever alone (8.0%), cough with rapid or difficult

Figure 1. Distribution of clinical symptoms among children under five years of age in 2019, Bangladesh.

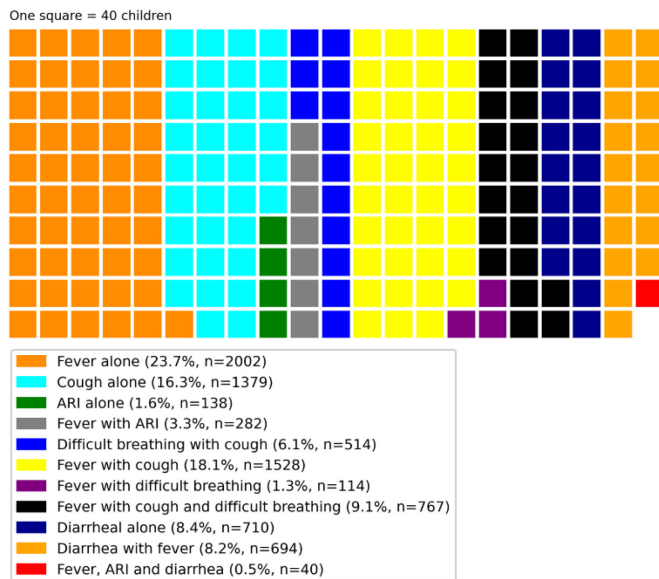


Figure 2. Proportion of antibiotic used among sick children under five years of age according to different clinical symptoms in 2019, Bangladesh.

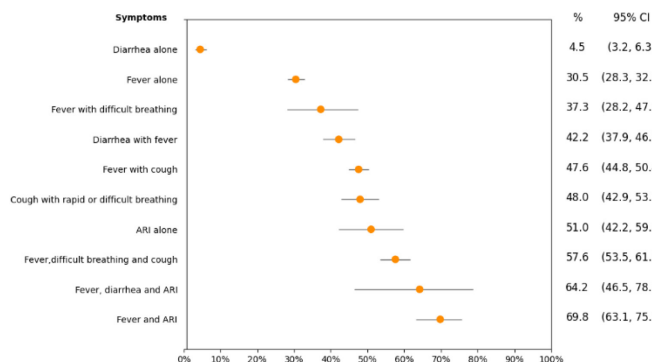
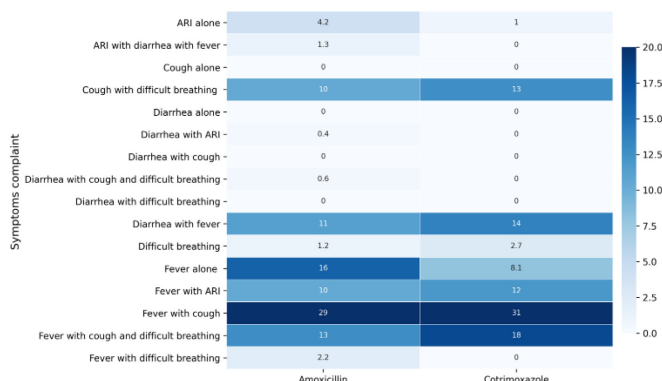


Figure 3. Use of antibiotics Amoxicillin and Cotrimoxazole among sick children under five years of age with different clinical symptoms in 2019, Bangladesh



breathing (5.0%), fever with rapid or difficult breathing (3.0%), and diarrhea alone (3%) (Figure 4).

Among the sick children under-five with fever alone, after adjusting for age, sex and account for clustering of households, the reported antibiotic usage was associated with wealth (poorest vs. poor: APR = 0.93; 95% CI: 0.79-1.11; middle: APR = 1.07; 95% CI: 0.86-1.32; Upper-middle: APR = 1.23; 95% CI: 1.1-1.50; rich: APR = 1.17; 95% CI: 0.93-1.47), unimproved drinking water source (APR = 1.26; 95% CI: 1.04-1.51) (Figure 5A). After adjusting for age, sex, and account for clustering of households among the sick children under five with diarrhea alone, the reported antibiotic use was associated with the mother’s education (pre-primary vs. higher: APR = 2.54; 95% CI: 1.04-6.19) (Figure 5B). The reported antibiotic use for the treatment of fever with cough alone was associated with wealth (poorest vs. poor: APR = 1.05; 95% CI: 0.94-1.18; middle: APR = 0.99; 95% CI: 0.86-1.16; upper-middle: APR = 1.15; 95% CI: 0.96-1.39; rich: APR = 1.25; 95% CI: 1.06-1.49) (Figure 5C).

Antibiotic usage for treating fever, diarrhea, and ARI was associated with wealth (poorest vs. poor: APR = 1.02; 95% CI: 0.92-1.15; middle: APR = 0.98; 95% CI: 1.01-1.23; rich: APR = 1.05; 95% CI: 0.92-1.22) and mother’s education (pre-primary vs. primary: APR = 1.05; 95% CI: 0.89-1.23; secondary: APR = 1.11; 95% CI: 1.01-1.24; higher: APR = 1.15; 95% CI: 1.03-1.27) (Figure 5D).

Discussion

Our analysis identified the present scenario of infectious diseases and antibiotics used for treating infectious diseases among under-five children. The results show that the prevalence of under-five sick children with fever, diarrhea, and ARI was available, and most mothers/caregivers used oral and injectable antibiotics for several symptoms in Bangladesh. Furthermore, the findings highlight that the high prevalence of excessive use of antibiotics was reported among children under five with symptom complaints. Our investigation also highlights that household wealth and the mother’s education were significantly associated with the reported excessive antibiotic usage.

Figure 4. Use of injectable antibiotics among sick children under five years of age received according to different clinical symptoms in 2019, Bangladesh

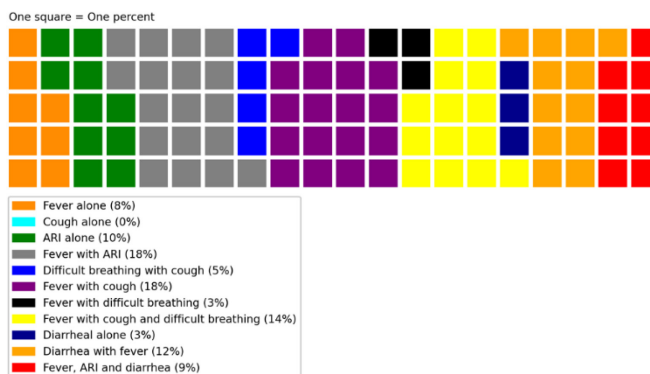
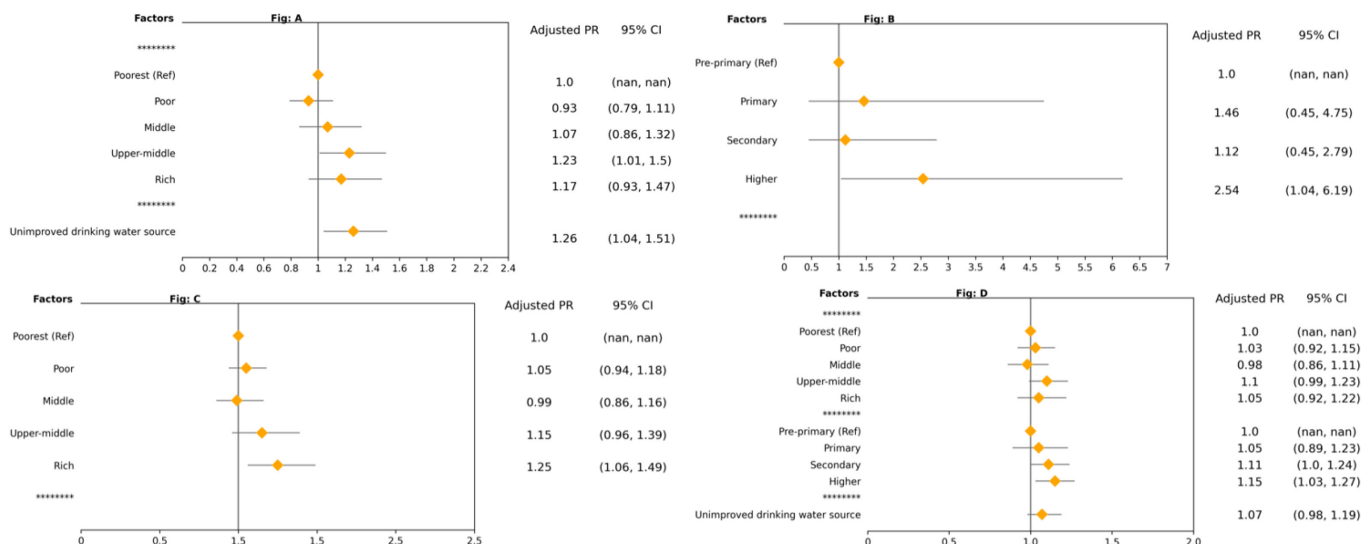


Figure 5. (A) Factors associated with antibiotic use among sick children under five years of age with only fever. (B) Factors associated with antibiotic use among sick children under five years of age with only diarrhea. (C) Factors associated with antibiotic use among sick children under five years of age with fever and cough. (D) Factors associated with antibiotic use among sick children under five years of age with fever, diarrhea, and ARI.



Additionally, access to private healthcare facilities, recommendations from relatives or friends, and available drug stores were crucial drivers of access to antibiotics.

This study's results show the factors of reported antibiotic usage similar to a previous systematic review study between 2005 and 2017 conducted on 132 surveys from 73 countries. Although they did not determine the associated factors of antibiotic usage in their study, they estimated the prevalence of antibiotic use in South Asia at 30.1% in 2017 among sick children under-five with fever, diarrhea, or ARI. The study identified the excessive use of amoxicillin and cotrimoxazole for fever and diarrhea alone, which is consistent with our findings. A population-based study in 2016 in Nepal on the reported antibiotics use among children under five years old [23] showed a similar pattern and determinants. Both studies revealed the importance of the non-government health sectors, wealthier households, and educated mothers in the use of antibiotics among children under five. A study was conducted among 2,144 children under-five with a similar methodology in the same community in Bangladesh in 2014 [24] which was performed among sick children under-five with only ARI irrespective of fever or diarrhea. The proportion of reported use of antibiotics among sick children under five with only ARI was approximately 11%, and the associated socio-demographic factors for antibiotic usage differed from our findings. These differences could be attributed to the distinct symptom complaints, study time and rapidly increased access to healthcare facilities across the country [25].

We found that every two in five children under five experienced illness in the preceding two weeks. Among the symptom complaints, the proportion of under-five sick children with fever alone was the highest reported compared with cough only, diarrhea, ARI, and cough with difficulty breathing. The non-government health sector in Bangladesh was the largest healthcare provider for children under five conditions. Our study findings highlight that one-third of sick children under five with symptom complaints reported using antibiotics for fever, diarrhea, or ARI. Our results showed that many young children in Bangladesh received an oral or injectable form of antibiotics for fever alone, diarrhea alone, diarrhea with fever alone, or fever with cough alone. We also found that many mothers or caregivers purchased antibiotics from traditional healers and drug sellers without prescriptions, some health professionals prescribed antibiotics for mild cases, and some mothers or

caregivers did not use antibiotics for severe pneumonia cases. These findings indicate antibiotics are excessively used among children with fever, diarrhea, and ARI cases in Bangladesh regarding Integrated Management of Childhood Illness (IMCI) guidelines [26]. The resource-poor settings, where there are poor health systems, inadequate diagnosis, higher prevalence of infectious diseases, and childhood mortality, there may be excessive use of antibiotics among sick under-five children [27]. This result is almost uniform with the previous population-based survey in Bangladesh regarding the study design [24, 28], though results cannot be directly comparable due to different time periods case definitions, and program settings. Besides, our analysis focused on mutually exclusive symptom complaints, whereas the prior study was based on only ARI cases. We found that 4.5% - 69.8% of antibiotics were used for different symptom complaints. The proportion of antibiotic use among severe pneumonia cases was more than 51% among children under five higher than 39% in a previous study [24]. This result is not unexpected, as there have been rapidly increasing healthcare facilities across the country in the last five years [25], and a high portion of children were found to visit non-government healthcare facilities in our study. However, mothers or caregivers may inappropriately use antibiotics for their children under five because they do not have sufficient knowledge of doses for antibiotics and access to healthcare facilities [29–32].

Our study results showed that private healthcare facilities were a common place for treating infectious diseases in Bangladesh. There are more registered private hospitals and clinics than public healthcare facilities, along with many unregistered private hospitals or clinics in Bangladesh [25]. Many physicians of public sector practices in private sectors, difficult-to-reach healthcare facilities, limited services, and high cost of diagnostic tests, and medicines impeded access to the healthcare facilities in public sectors [32]. Consequently, most caregivers seek private healthcare facilities or self-medication for their children [33]. Prior studies showed that private healthcare facilities and self-medication are crucial factors in treating sick under-five children in low-income countries [23,34–36]. Our data is sufficient to indicate that antibiotics were more likely to be prescribed in private healthcare facilities compared with public healthcare sectors for sick children under five with fever, diarrhea, or ARI. The wide use of antibiotics may reflect that a large number of patients visited private healthcare facilities [23], limited access to appropriate diagnostics facilities [37], improper

diagnoses [38], patient preferences for antibiotics [39,40], and incentives for prescribing antibiotics [38]. Some mothers or caregivers decided to self-medication based on their children's illnesses which instigated them to seek inappropriate healthcare and take antibiotics from drug sellers and traditional healers [34,36,40–42]. Our data similarly indicates that drug stores and traditional healers are critical sources of excessive antibiotic usage for sick children under five with fever, diarrhea, and ARI. There is an urgent requirement to reduce inappropriate antibiotic prescribing in private healthcare sectors, drug shops, and traditional healers, particularly in limited-resource settings [43].

Our study found that the 95% CI of adjusted prevalence ratio (APR) for many distinct factors included the null value (1.0) but the APR apart from the null value. Nevertheless, our results showed a significantly lower prevalence of sick children under five in wealthier households, but the reported use of antibiotics among children under five was higher in more affluent households than in poor households. The highest percentage of access to private healthcare facilities explained this higher proportion of antibiotic usage among children under five in wealthier households. These similar findings have been found in many previous studies in LMICs [12,23]. Richest people are strongly associated with traveling to other areas, which can lead to the transmission of infectious diseases [44], which may contribute to the association between seeking private healthcare facilities and the excessive use of antibiotics for sick under-five children [5]. Many experimental and observational studies on antibiotic resistance showed that antibiotics among children under five in more affluent households are more likely to be consumed than in poor households [45–48]. A community-based cross-sectional study showed that the burden of excessive use of antibiotics among children under five in wealthy families was explained by using the recent antibiotics of other members [48]. It is anticipated that the low number of healthcare visits by sick children from low-income households and lack of proper diagnosis are more likely to receive antibiotics [49]. Hence, wealthier households are an important factor in the excessive use of antibiotics among under-five children.

One of the key results is that maternal education was strongly associated with antibiotic usage. Educated mothers/caregivers can manipulate the excessive use of antibiotics by influencing their knowledge, attitude, and behaviors. They seek healthcare with their children and consult with physicians or self-medication. They also

frequently classify their child's illness and expect to prescribe antibiotics. Therefore, many private practitioners seek information for prescribing antibiotics inappropriately [50], and some educated mothers unnecessarily take antibiotics by practicing self-medication [51]. This finding is consistent with the trend analysis of sick children under five with fever or diarrhea study in Nepal [23] and previous systematic review studies on respiratory infection in children under five [52].

The limitations of this study were that a high recall error occurred due to the data collection method in the MICS, as the primary outcome was self-reporting. The mothers or caregivers were asked about their children's illnesses in the preceding 14 days, health care facilities for each disease, type of health care seeking facilities, and the use of antibiotics for illness and did not verify medicines in the prescriptions. Due to the small samples in the sub-group, it is difficult to identify specific associations. The disease prevalence may be affected by seasonal bias because data collection was conducted within only the first two seasons of the year.

Conclusions

Overall, the results highlight the multiple significant factors leading to antibiotic use in the distinct symptom complaints among under-five children. The primary contributors to the high prevalence of antibiotic use for treating infectious diseases include socio-economic, maternal, and healthcare facilities. At the same time, the high prevalence of infectious diseases, non-prescribed antibiotic use and self-medication play a role in excessive use of antibiotic. Intervention programs in the community should be required to reduce excessive antibiotic use. At the same time, the most necessary children will likely use antibiotics, and strengthened surveillance systems for the use of antibiotics are required in resource-poor settings.

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References

1. Akova M (2016) Epidemiology of antimicrobial resistance in bloodstream infections. *Virulence* 7: 252–266. doi: 10.1080/21505594.2016.1159366.
2. Medina E, Pieper DH (2016) Tackling threats and future problems of multidrug-resistant bacteria. *Overcome Antibiot Crisis Facts Chall Technol Future Perspect* 398: 3–33. doi: 10.1007/82_2016_492.
3. Chokshi A, Sifri Z, Cennimo D, Horng H (2019) Global contributors to antibiotic resistance. *J Glob Infect Dis* 11: 36. doi: 10.4103/jgid.jgid_110_18.
4. Bell BG, Schellevis F, Stobberingh E, Goossens H, Pringle M (2014) A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. *BMC Infect Dis* 14: 1–25. doi: 10.1186/1471-2334-14-13.
5. Klein EY, Van Boeckel TP, Martinez EM, Pant S, Gandra S, Levin SA, Goossens H, Laxminarayan R (2018) Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. *Proc Natl Acad Sci* 115: E3463–E3470. doi: 10.1073/pnas.1717295115.
6. Khameneh B, Diab R, Ghazvini K, Bazzaz BSF (2016) Breakthroughs in bacterial resistance mechanisms and the potential ways to combat them. *Microb Pathog* 95: 32–42. doi: 10.1016/j.micpath.2016.02.009.
7. Chisti MJ, Harris JB, Carroll RW, Shahunja K, Shahid AS, Moschovis PP, Schenkel SR, Hasibur Rahman ASMM, Shahrin L, Faruk T (2021) Antibiotic-resistant bacteremia in young children hospitalized with pneumonia in bangladesh is associated with a high mortality rate. *Oxford University Press US*, p ofab260. doi: 10.1093/ofid/ofab260.
8. Sharma A, Luvsansharav U-O, Paul P, Lutgring JD, Call DR, Omulo S, Laserson K, Araos R, Munita JM, Verani J (2021) Multi-country cross-sectional study of colonization with multidrug-resistant organisms: protocol and methods for the Antibiotic Resistance in Communities and Hospitals (ARCH) studies. *BMC Public Health* 21: 1–9. doi: 10.1186/s12889-021-11451-y.
9. Chellat MF, Raguž L, Riedl R (2016) Targeting antibiotic resistance. *Angew Chem Int Ed* 55: 6600–6626. doi: 10.1002/anie.201506818.
10. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, Lawn JE, Cousens S, Mathers C, Black RE (2016) Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the sustainable development goals. *Lancet* 388: 3027–3035. doi: 10.1016/S0140-6736(16)31593-8.
11. Laxminarayan R, Amabile-Cuevas CF, Cars O, Evans T, Heymann DL, Hoffman S, Holmes A, Mendelson M, Sridhar D, Woolhouse M (2016) UN High-Level Meeting on antimicrobials—what do we need? *Lancet* 388: 218–220. doi: 10.1016/S0140-6736(16)31079-0.
12. Allwell-Brown G, Hussain-Alkhateeb L, Kitutu FE, Strömdahl S, Mårtensson A, Johansson EW (2020) Trends in reported antibiotic use among children under 5 years of age with fever, diarrhoea, or cough with fast or difficult breathing across low-income and middle-income countries in 2005–17: a systematic analysis of 132 national surveys from 73 countries. *Lancet Glob Health* 8: e799–e807. doi: 10.1016/S2214-109X(20)30079-6.
13. Bielicki J, Lundin R, Patel S, Paulus S (2015) Antimicrobial stewardship for neonates and children: a global approach. *Pediatr Infect Dis J* 34: 311–313. doi: 10.1097/INF.0000000000000621.
14. World Health Organization (2019) Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015. Available: https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf. Accessed: 20 Aug 2022.
15. Padgett M, Guillemot D, Delarocque-Astagneau E (2016) Measuring antibiotic consumption in low-income countries: a systematic review and integrative approach. *Int J Antimicrob Agents* 48: 27–32. doi: 10.1016/j.ijantimicag.2016.04.024.
16. UNICEF (2019) Bangladesh mics report: key findings. Available: https://mics.unicef.org/news_entries/152/BANGLADESH-MICS-2019-REPORT:-KEY-FINDINGS. Accessed: 23 Jul 2021.
17. UNICEF (2005) Handbook imci: integrated management of childhood illness. World Health Organization, Geneva. Available: <https://apps.who.int/iris/handle/10665/42939>. Accessed: 21 Jul 2021.
18. Vyas S, Kumaranayake L (2006) Constructing socio-economic status indices: how to use principal components analysis. *Health Policy Plan* 21: 459–468. doi: 10.1093/heapol/czl029.
19. Ghosh PK, Das P, Goswami DR, Islam A, Chowdhury S, Mollah MM, Harun GD, Akhtar Z, Chowdhury F (2021) Maternal determinants mediating the impact of household poverty on the nutritional status of children under 5 years of age in Bangladesh. *Food Nutr Bull* 42: 389–398. doi: 10.1177/0379572121999016.
20. Nandy S, Svedberg P (2012) The composite index of anthropometric failure (ciaf): an alternative indicator for malnutrition in young children. In: *Handbook of anthropometry*. Springer, pp 127–137. doi: 10.1007/978-1-4419-1788-1_6.
21. Devereux S (2001) Poverty and undernutrition: theory, measurement, and policy. *J Dev Stud* 38: 189. doi:10.1093/0198292686.001.0001.
22. Zheng C, Karkey A, Wang T, Makuka G, van Doorn HR, Lewycka S (2021) Determinants and patterns of antibiotic consumption for children under five in Nepal: analysis and modelling of Demographic Health Survey data from 2006 to 2016. *Trop Med Int Health* 26: 397–409. doi: 10.1111/tmi.13540.
23. Hassan MZ, Monjur MR, Biswas MAAJ, Chowdhury F, Kafi MAH, Braithwaite J, Jaffe A, Homaira N (2021) Antibiotic use for acute respiratory infections among under-5 children in Bangladesh: a population-based survey. *BMJ Glob Health* 6: e004010. doi: 10.1136/bmjgh-2020-004010.
24. Directorate General of Health Services, Government of Peoples Republic of Bangladesh (2021) DGHS Health Bulletin. Available: <https://dghs.gov.bd/index.php/en/publications/health-bulletin/dghs-health-bulletin>. Accessed: 10 Aug 2021
25. Johansson EW, Kitutu FE, Mayora C, Awor P, Peterson SS, Wamani H, Hildenwall H (2016) It could be viral but you don't know, you have not diagnosed it: health worker challenges in managing non-malaria paediatric fevers in the low transmission area of Mbarara District, Uganda. *Malar J* 15: 1–13. doi: 10.1186/s12936-016-1257-y.
26. NIPORT/Bangladesh NI of PR and T-, Associates M, International ICF (2016) Bangladesh Demographic and Health Survey 2014. available: <https://dhsprogram.com/pubs/pdf/fr311/fr311.pdf>. Accessed: 21 Jul 2021.

28. Bari A, Sadruddin S, Khan A, Khan A, Lehri IA, Macleod WB, Fox MP, Thea DM, Qazi SA (2011) Community case management of severe pneumonia with oral amoxicillin in children aged 2–59 months in Haripur district, Pakistan: a cluster randomised trial. *The Lancet* 378: 1796–1803. doi: 10.1016/S0140-6736(11)61140-9.
29. World Health Organization (2018) Antimicrobial resistance and primary health care. World Health Organization. Available at: <https://www.who.int/docs/default-source/primary-health-care-conference/amr.pdf>. Accessed: 9 Sep 2023.
30. Smieszek T, Pouwels KB, Dolk FCK, Smith DR, Hopkins S, Sharland M, Hay AD, Moore MV, Robotham JV (2018) Potential for reducing inappropriate antibiotic prescribing in English primary care. *J Antimicrob Chemother* 73: ii36–ii43. doi: 10.1093/jac/dkx500.
31. Auta A, Ogbonna BO, Adewuyi EO, Adeloye D, Strickland-Hodge B (2019) Prevalence and factors associated with the use of antibiotics in non-bloody diarrhoea in children under 5 years of age in sub-Saharan Africa. *Arch Dis Child* 104 :518–521. doi: 10.1136/archdischild-2017-314228.
32. Gruen R, Anwar R, Begum T, Killingsworth JR, Normand C (2002) Dual job holding practitioners in Bangladesh: an exploration. *Soc Sci Med* 54: 267–279. doi: 10.1016/S0277-9536(01)00026-0.
33. Islam A, Biswas T (2014) Health system in Bangladesh: challenges and opportunities. *Am J Health Res* 2: 366–374. doi: 10.11648/j.ajhr.20140206.18.
34. Awor P, Wamani H, Tylleskar T, Jagoe G, Peterson S (2014) Increased access to care and appropriateness of treatment at private sector drug shops with integrated management of malaria, pneumonia and diarrhoea: a quasi-experimental study in Uganda. *PLoS One* 9: e115440. doi: 10.1371/journal.pone.0115440.
35. Fink G, D’Acremont V, Leslie HH, Cohen J (2020) Antibiotic exposure among children younger than 5 years in low-income and middle-income countries: a cross-sectional study of nationally representative facility-based and household-based surveys. *Lancet Infect Dis* 20: 179–187. doi: 10.1016/S1473-3099(19)30572-9.
36. Amuyunzu-Nyamongo M, Nyamongo IK (2006) Health seeking behaviour of mothers of under-five-year-old children in the slum communities of Nairobi, Kenya. *Anthropol Med* 13: 25–40. doi: 10.1080/13648470500516261.
37. World Health Organization (2010) Increasing access to health workers in remote and rural areas through improved retention: global policy recommendations. Available: <https://books.google.com.bd/books>. Accessed: 18 Aug 2022.
38. Nepal A, Hendrie D, Selvey LA, Robinson S (2021) Factors influencing the inappropriate use of antibiotics in the Rupandehi district of Nepal. *Int J Health Plann Manage* 36: 42–59. doi: 10.1002/hpm.3061.
39. Reynolds L, McKee M (2009) Factors influencing antibiotic prescribing in China: an exploratory analysis. *Health Policy* 90: 32–36. doi: 10.1016/j.healthpol.2008.09.002.
40. Wang NC, Liu Y (2021) Going shopping or consulting in medical visits: caregivers’ roles in pediatric antibiotic prescribing in China. *Soc Sci Med* 290: 114075. doi: 10.1016/j.socscimed.2021.114075.
41. Kitutu FE, Kalyango JN, Mayora C, Selling KE, Peterson S, Wamani H (2017) Integrated community case management by drug sellers influences appropriate treatment of paediatric febrile illness in South Western Uganda: a quasi-experimental study. *Malar J* 16: 1–18. doi: 10.1186/s12936-017-2072-9.
42. Singh P (2017) A universal good: how increased health coverage can help beat back antimicrobial resistance. *World Health Organ Reg Off South-East Asia*. Available: <https://www.who.int/southeastasia/news/opinion-editorials/detail/a-universal-good-how-increased-health-coverage-can-help-beat-back-antimicrobial-resistance>. Accessed: 18 Aug 2022.
43. Le Doare K, Barker CI, Irwin A, Sharland M (2015) Improving antibiotic prescribing for children in the resource-poor setting. *Br J Clin Pharmacol* 79: 446–455. doi: 10.1111/bcp.12320.
44. Alirol E, Getaz L, Stoll B, Chappuis F, Loutan L (2011) Urbanisation and infectious diseases in a globalised world. *Lancet Infect Dis* 11: 131–141. doi: 10.1016/S1473-3099(10)70223-1.
45. Metlay JP, Strom BL, Asch DA (2003) Prior antimicrobial drug exposure: a risk factor for trimethoprim–sulfamethoxazole-resistant urinary tract infections. *J Antimicrob Chemother* 51: 963–970. doi: 10.1093/jac/dkg146.
46. Huovinen P, Cars O (1998) Control of antimicrobial resistance: time for action: the essentials of control are already well known. doi: 10.1136/bmj.317.7159.613.
47. Nilsson P, Laurell MH (2005) Impact of socioeconomic factors and antibiotic prescribing on penicillin-non-susceptible *Streptococcus pneumoniae* in the city of Malmö. *Scand J Infect Dis* 37: 436–441. doi: 10.1080/00365540510037795.
48. Kristiansson C, Grape M, Gotuzzo E, Samalvides F, Chauca J, Larsson M, Bartoloni A, Pallecchi L, Kronvall G, Petzold M (2009) Socioeconomic factors and antibiotic use in relation to antimicrobial resistance in the Amazonian area of Peru. *Scand J Infect Dis* 41: 303–312. doi: 10.1080/00365540902783301.
49. Ahmed NU, Alam MM, Sultana F, Sayeed SN, Pressman AM, Powers MB (2006) Reaching the unreachable: barriers of the poorest to accessing NGO healthcare services in Bangladesh. *J Health Popul Nutr* 24: 456–466.
50. Cabral C, Horwood J, Hay AD, Lucas PJ (2014) How communication affects prescription decisions in consultations for acute illness in children: a systematic review and meta-ethnography. *BMC Fam Pract* 15: 1–13. doi: 1471-2296/15/63.
51. Kariyawasam S, Nanayakkara D, Mohottiarachchi M, Nandasena Y (2005) A descriptive cross-sectional study on mothers self-medicating children. *Sri Lanka J Child Health* 34: 7–12. doi: 10.4038/sljch.v34i1.563.
52. Cantarero-Arévalo L, Hallas MP, Kaae S (2017) Parental knowledge of antibiotic use in children with respiratory infections: a systematic review. *Int J Pharm Pract* 25: 31–49. doi: 10.1039/ijpp.12337.

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