MEDICINE

Antibiotic Use Among Children Under 5 Years of Age in a Tertiary Care Hospital, Bangladesh

Rajib Sarker[1] · Md Shafiqul Islam Khan[1] · Md Abu Tareq[1] · Sumon Ghosh[2] · Sukanta Chowdhury[2]

Abstract

Antimicrobial resistance is common in low-middle-income countries caused by inappropriate and irrational use of antibiotics in humans and animals. Bangladesh has very limited information on antibiotic use and associated resistance. This study explored the prescribing pattern of antibiotics uses among children visiting a tertiary care hospital in Bangladesh. We conducted a cross-sectional study among 400 hospitalized children less than 5 years of age from February to April, 2019, in a tertiary hospital in Bangladesh. Among the 400 children, >50% belonged to the age group for less than 1 year and >60% were male. The average hospital stay period was 3 days (range 1–14 days). The majority of the children had a history of respiratory illnesses (32.2%) and 31% had diarrhea. Most of the children (81.7%) were prescribed one or more antibiotics. The average number of antibiotics per child was 1.17. A combined form of antibiotics was prescribed in 17.43% of children. A total of 14 different antibiotics were prescribed. The most common antibiotic was ceftriaxone (62.39%), followed by azithromycin (18.65%). The parental route was mostly preferred (74.92%) for antibiotic administration. The antibiotic prescription was common in children less than 5 years of age visiting a tertiary level hospital. Most of the prescribed antibiotics were broad spectrum that can promote bacterial resistance. The study's finding is useful to draw attention to the public health policymakers for taking necessary actions on the appropriate use of antibiotics among children in Bangladesh.

Introduction

Antibiotics are commonly prescribed drugs treating children globally [1]. The effectiveness of an antibiotic against a particular disease depends on its' proper utilization [2]. Indiscriminate antibiotic use with the inappropriate prescribing, improper spectrum, suboptimal dosages, and prolonged administration led to antibiotic resistance [3]. This situation makes the first-line antibiotics less effective and frequently triggers the use of third-generation antibiotics [4, 5].

Appropriate use of antibiotics is necessary for early recovery and to prevent bacterial resistance. Developing countries are less conscious of the rational use of antibiotics than developed countries [6]. Antibiotics were prescribed more in Ethiopia (86%), Jordan (85%), and Sierra Leone (83%) compared to Australia (46%) and the UK (41%) [7–10]. In India, nearly about 64% of antibiotics were prescribed inappropriately with incorrect dosages [11]. Studies showed that ampicillin, amoxicillin, metronidazole, ciprofloxacin, and crystalline penicillin were the five most commonly prescribed antibiotics and there were serious lapses in antibiotic prescription patterns in patients referred from various healthcare settings in India [12, 13].

Children are at high risk of getting infections that contribute high morbidity and mortality. In every 2min, an infant dies due to antibiotic resistance in South Asia. Acute respiratory tract infection, diarrhea, and urinary tract infections due to bacteria are common in children [14, 15]. The high incidence of infectious diseases in low-resource countries leads to use of antibiotics very often.

Although the empirical use of antibiotics is recommended, antibiotics are overprescribed. In Bangladesh, antibiotics are widely available and people can purchase antibiotics very easily from the pharmacy without showing a prescription from a

This article is part of the Topical Collection on *Medicine*

✉ Sukanta Chowdhury
    sukanta@icddrb.org

1   Department of Food Microbiology, Patuakhali Science and Technology University, Patuakhali, Bangladesh

2   International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh

registered physician. In most cases, antibiotics were not prescribed following the World Health Organization (WHO) guideline [16]. Antibiotics can cause adverse drug reactions (ADRs) to the patients [17]. Currently, no national guideline is available for antibiotic use. Many doctors in Bangladesh are prescribing antibiotics without taking into consideration of the clinical test in most cases. Despite the doctor's suggestion, many patients did not complete the full dosage regimen of antibiotics in cold and fever or even in other complicated infectious diseases [18]. Prescribing more than one antibiotic was not uncommon [19]. Cephalosporins, macrolides, quinolones, and carbapenem were commonly prescribed to treat patients [20]. Many patients (63%) are visited and treated by quacks known as "village doctors" and they have no or very limited understanding of antimicrobial resistance [17]. These factors together may promote antimicrobial resistance in humans in Bangladesh. Although many studies explored antibiotic use pattern in all age group of hospitalized patients, information about antibiotic practices in children under 5 years of age remains limited. More information about the pattern of antibiotics in children at high- and low-resource settings will help policymakers and health professionals to update and enforce antibiotic use guideline. This study explored the antibiotic use patterns among children under 5 years of age visiting a tertiary care hospital, Bangladesh.

Methods

We conducted a cross-sectional study in the Sher-E-Bangla Medical College Hospital in Barishal, Bangladesh, from February to April 2019 (Fig. 1). Barishal is located on the southwestern tip of Bangladesh and approximately 200 km away from the capital city Dhaka. This government hospital has 1000 beds, and around 1500 patients are getting treatment in the indoor daily and the bed occupancy rate is around 150% [21].

We enrolled a total of 400 children under 5 years of age conveniently who had a history of illnesses and visited the study hospital to get treatment. We visited the pediatric ward to select the study participants. Before data collection from children, we took written consent from their parents. A structured questionnaire was used to collect data on the demographics and clinical characteristics of selected children. We interviewed parents and observed prescription to collect data. The questionnaire included but was not limited to the type of antibiotic use, generic name, dosages, daily dosages, frequency, duration, strength, and route of administration. We reviewed the most recent prescription of each selected patient to collect information on antibiotic use. We considered a number of criteria for analyzing the prescriptions that include the following: the presence of antibiotics, the number of

prescriptions containing multiple antibiotics, class of antibiotics, dosage forms, and the combination of other drugs.

Statistical analysis

We performed a descriptive analysis to estimate the mean, standard deviations, and range values for continuous variables: percentage, 95% confidence interval, and p-value for categorical data. Fisher's exact test was used to measure the significant differences in the proportion of a variable among the groups. STATA 13 version was used for data analysis.

The research protocol was reviewed and approved by the Research Review Committee (RRC) of Department of Food Microbiology, Patuakhali Science and Technology University, Patuakhali, Bangladesh.

Results

All 400 selected children were sick and visited the hospital for treatment. Of the 400 children, 245 (61%) were male with the mean age of 20 months (range 1–59 months). The average body weight of children was 9 kg (range 2–30 kg). During the hospital visit, 129 (32.25%) children suffered from respiratory illnesses and 124 (31%) had diarrhea. The average hospital stay period was 3 days (range 1–14 days) (Table 1). The majority of the children's fathers' professions were day labor (45%) and 66% of their family income remained between 10,000 and 20,000 BDT (Bangladesh Taka). More than 70% of children went to a laboratory for diagnostic purposes.

All children were prescribed one or more medicines during our visit. Among the 400 children, 157 (40.78%) were suggested for three types of medicine, 104 (27%) were suggested for two types of medicine, and 15 (3.75%) were given only normal saline. At least an antibiotic was prescribed for 327 (81.75%) patients; 270 (82.56%) of them were suggested for a single type of antibiotic and 57 (17.43) of them were suggested for two types of antibiotics (Table 2). A total of 14 different antibiotics were prescribed. The average number of antibiotics per child was 1.17. The majority ($n=245$, 74.92%) of the prescribed antibiotics were injectable form. Ceftriaxone ($n=204$, 62.39%) was prescribed mostly followed by azithromycin ($n=61$, 18.65%), amikacin ($n=15$, 4.59%), cefepime ($n=15$, 4.59%), and ciprofloxacin ($n=14$, 4.28%) (Fig. 2). Among the children with diarrhea, azithromycin ($n=48$, 58.53%) was preferred mostly followed by ceftriaxone ($n=21$, 25.06%) and ciprofloxacin ($n=8$, 9.75%). Ceftriaxone was mostly prescribed to treat respiratory illness, fever, and other illnesses (Table 3). The variation of prescribed antibiotics to treat different clinical illnesses was statistically significant ($p < 0.0001$).

Fig. 1 Location of study hospital
in Bangladesh map

Sher-E-Bangla medical college hospital, Barishal

Discussion

This study explored the prescribing patterns of antibiotics among children in a tertiary care hospital, Bangladesh. Antibiotics were frequently prescribed to treat the children who were mostly suffered from respiratory illnesses, diarrhea, and fever. A similar pattern of antibiotics use was reported from India (91.6%), Ethiopia (86.4), Sierra Leone (74.8%), Papua New Guinea (53%), and South Africa (73.5%) [7, 8, 22–24]. However, the antibiotic prescription rate was decreased in children in the USA and Canada [25, 26]. In Bangladesh, previous studies also identified a high antibiotic use rate in pediatric patients to treat pneumonia and diarrhea [20, 27, 28]. In Bangladesh, physicians often do not prescribe antibiotics by adopting the antibiotics prescribing guidelines. Consequently, antibiotics are often irrationally administered here to give patients a fast relief without considering the state of the patient's illness [18]. The higher prescription rate of antibiotics in this study could be due to the patient's age, clinical characteristics, insufficient diagnostic facilities, poor awareness of antibiotic resistance, weak monitoring by drug authority, geographical location, and patient demand.

The average number of antibiotics per child was 1.17. Studies showed similar findings: the average number of antimicrobial 1.3 per pediatric patients in India and 1.82 antibiotics per patient in Iran [29, 30]. Though antibiotics prescription was common in Bangladesh, doctors prescribe a single antibiotic for most pediatric patients. The study did not study the specific reason for using a single antibiotic. We found that three-fourth of antibiotics were administered through a parental route which was similar to the findings in Nepal (75%), India (84.1%), and Ethiopia (86%) [7, 31, 32]. This preference

Table 1 Demographic and clinical characteristics of children, Sher-E-Bangla Medical College Hospital, Barishal, Bangladesh, 2019 (*n*=400)

Parameters	Category	Number of children (%)
Age	≤ 12 months	212 (53)
	13–24 months	66 (16.5)
	25–36 months	44 (11)
	37–48 months	35 (8.75)
	49–60 months	43 (10.75)
Gender	Male	245 (61.25)
Duration of hospital stay (day)	1 day	100 (25)
	2 days	114 (28.5)
	3 days	60 (15)
	4 days	50 (12.5)
	≥ 5 days	76 (19)
Clinical characteristics	Respiratory illnesses	129 (32.25)
	Diarrhea	124 (31)
	Only fever	81 (20.25)
	Others	66 (16.5)

happened because of the administrative difficulties of the oral form of antibiotics to children below 5 years of age. According to the WHO guideline, injectable forms of drugs should not be prescribed more than 10% of the total prescription [33].

Inappropriate use of antibiotics may continue the emergence of antimicrobial resistance globally [34–36]. Our study observed that doctors predominantly prescribed ceftriaxone to treat children. Doctors mostly preferred broad-spectrum antibiotics than narrow spectrum antibiotics. Multiple studies from Bangladesh also reported a high rate of ceftriaxone use to treat all age groups of patients [18, 20, 28, 37]. However, cephalosporins group antibiotics were less commonly prescribed in other countries. Penicillin G (20%) was prescribed mostly in Ethiopia and ceftriaxone (6%) was prescribed less

[7]. In developed countries, the pattern of antibiotic use was different. Narrow and broad-spectrum penicillins (41.54 %) were most frequently used to treat children in Germany [38]. In the USA, doctors recommended first-line penicillins as the agent of choice in children. In 2000, the use of penicillins was accounted for 59% of total antibiotics [25]. In Canada, the prescription rate of penicillins was highest for treating upper respiratory tract infections, acute otitis media, and bronchitis in children [26]. Another study reported similar findings in which physicians mostly prescribed first-line penicillins in Germany, Italy, South Korea, Norway, Spain, and the USA [39]. From this study, we found substantial differences in antibiotics use in Bangladesh and developed countries.

The association between antibiotic prescribing and resistance is complex. In Bangladesh, Enterobacteriaceae isolates

Table 2 Pattern of antibiotic prescribed by age and illnesses in children, Sher-E-Bangla Medical College Hospital, Barishal, Bangladesh, 2019 (*n*=400)

Parameters	Number of children suggested for antibiotic (%)		*p*
	Yes	No	
Age			
≤ 12 months	175 (43.75)	37 (9.25)	0.809
13–24 months	51 (12.75)	15 (3.75)	
25–36 months	35 (8.75)	9 (2.25)	
37–48 months	30 (7.5)	5 (1.25)	
49–60 months	36 (9)	7 (1.75)	
Clinical characteristics			
Respiratory illnesses	125 (31.25)	5 (1.25)	<0.0001
Diarrhea	82 (20.5)	42 (10.5)	
Only fever	67 (16.75)	14 (3.5)	
Others	53 (13.25)	12 (3)	

Table 3 Name of the prescribed antibiotics by clinical illnesses, Sher-E-Bangla Medical College Hospital, Barishal, Bangladesh, 2019 (n=327)

| Types of antibiotic	Number of children with respiratory illnesses (%)	Number of children with diarrhea (%)	Number of children with only fever (%)	Number of children with other illnesses (%)	Total number (%)	Overall p value
Ceftriaxone	103 (31.49)	21 (6.42)	47 (14.37)	33 (10.09)	204 (62.38)	<0.0001
Amikacin	5 (1.52)	-	4 (1.22)	6 (1.83)	15 (4.58)	
Azithromycin	4 (1.22)	48 (14.67)	5 (1.52)	4 (1.22)	61 (18.65)	
Cefepime	7 (2.14)	2 (0.61)	6 (1.83)	-	15 (4.58)	
Ciprofloxacin	1 (0.3)	8 (2.44)	1 (0.3)	4 (1.22)	14 (4.28)	
Flucloxacillin	2 (0.61)	-	2 (0.61)	-	4 (1.22)	
Cefixime	1 (0.3)	-	1 (0.3)	3 (0.91)	5 (1.52)	
Ceftazidime	2 (0.61)	-	-	-	2 (0.61)	
Vancomycin	-	-	1 (0.3)	-	1 (0.3)	
Cefuroxime	-	1 (0.3)	-	-	1 (0.3)	
Metronidazole	-	2 (0.61)	-	-	2 (0.61)	
Gentamicin	-	-	-	3 (0.91)	3 (0.91)	

showed higher resistance against streptomycin (78%) and ampicillin (72%) in children [40]. *Escherichia coli* showed high resistance against ampicillin (95%), amoxiclav (67%), ciprofloxacin (65%), and co-trimoxazole (72%). Penicillin (90%), ampicillin (84%), co-trimoxazole (43%), and amoxicillin (64.3%) developed resistance against *Staphylococcus aureus* [4]. The excessive use of broad-spectrum antibiotics in children may increase the risk of antimicrobial resistance in Bangladesh. Regular monitoring is necessary to obtain updated information on the prevalence of antibiotic use and drug resistance.

This study has a few limitations. Due to the limited resources, we conducted this study for a short period of time with small sample size. We collected data only from a government hospital located south-central part of Bangladesh and we used convenient sampling for patient enrollment.

Therefore, this study finding might not be generalized for other private and general hospitals.

Conclusions

The findings of our study suggest that antibiotics were frequently prescribed in children visiting the hospital. Increased prescription of antibiotics may occur due to the higher incidence of bacterial infection among children. Increased use of third-generation cephalosporin can lead to develop resistance against extended spectrum beta lactamase (ESBL)-producing organisms. Physicians should be more careful about using of first-line antibiotics among children considering the increasing antimicrobial resistance pattern. This study's findings may
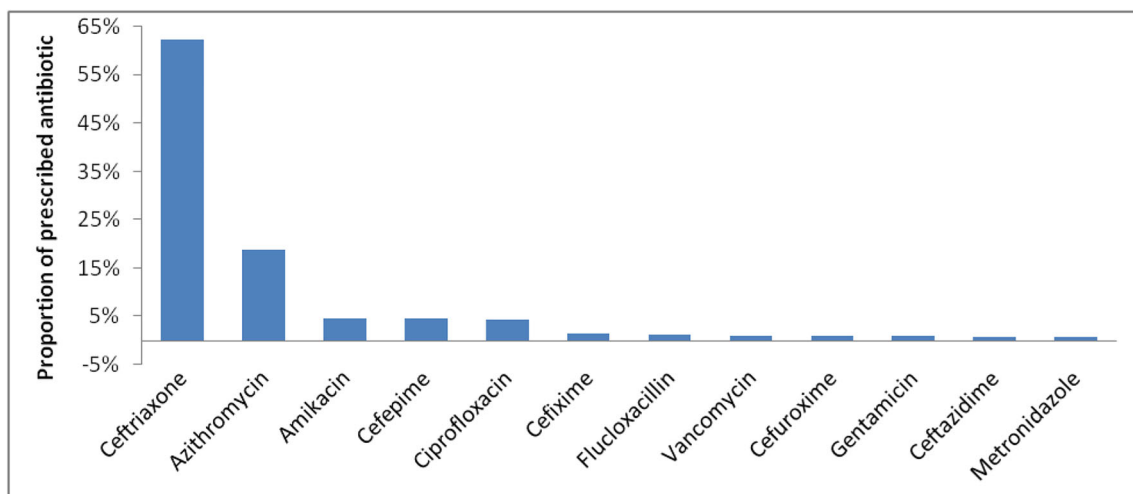
Fig. 2 Proportion of prescribed antibiotics among children under 5 years of age (n=327)

be useful to the policymakers and health professionals in developing a national antibiotic use guideline in Bangladesh.

Authors' contribution Rajib Sarker, Md Shafiqul Islam Khan, and Sukanta Chowdhury have made substantial contributions to the conception or design of the work, or the acquisition, analysis, and interpretation of data for the research work. Rajib Sarker, Md Shafiqul Islam Khan, Md Abu Tareq, Sumon Ghosh, and Sukanta Chowdhury have drafted and revised the manuscript.

Data Availability All data are available and can be shared upon request with proper justification.

Declarations

Ethics approval and consent to participate The Research Review Committee of Department of Food Microbiology, Patuakhali Science and Technology University, reviewed and approved the protocol.

Written consent was obtained from parents of the selected children.

Consent for publication All authors approved the manuscript for publication.

Conflict of interest The authors declare no competing interests.

References

1. Gwimile JJ, Shekalaghe SA, Kapanda GN, Kisanga ER. Antibiotic prescribing practice in management of cough and/or diarrhoea in Moshi Municipality, Northern Tanzania: cross-sectional descriptive study. Pan Afr Med J. 2012;12(1).

2. Gandra S, Singh SK, Jinka DR, Kanithi R, Chikkappa AK, Sharma A, et al. Point prevalence surveys of antimicrobial use among hospitalized children in six hospitals in India in 2016. Antibiotics. 2017;6(3):19.

3. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. Pharm Ther. 2015;40(4):277–83.

4. Ahmed I, Rabbi MB, Sultana S. Antibiotic resistance in Bangladesh: a systematic review. Int J Infect Dis. 2019;80:54–61.

5. Williams DJ, Edwards KM, Self WH, Zhu Y, Ampofo K, Pavia AT, et al. Antibiotic choice for children hospitalized with pneumonia and adherence to national guidelines. Pediatrics. 2015;136(1):44–52.

6. Bartoloni A, Gotuzzo E. Bacterial-resistant infections in resource-limited countries. Antimicrobial Resistance in Developing Countries: Springer; 2010. p. 199–231.

7. Kebede HK, Gesesew HA, Woldehaimanot TE, Goro KK. Antimicrobial use in paediatric patients in a teaching hospital in Ethiopia. PLoS One. 2017;12(3):e0173290.

8. Cole CP, James PB, Kargbo AT. An evaluation of the prescribing patterns for under-five patients at a Tertiary Paediatric Hospital in Sierra Leone. J Basic Clin Pharm. 2015;6(4):109–14.

9. Osowicki J, Gwee A, Noronha J, Palasanthiran P, McMullan B, Britton PN, et al. Australia-wide point prevalence survey of the use and appropriateness of antimicrobial prescribing for children in hospital. Med J Aust. 2014;201(11):657–62.

10. Gharbi M, Doerholt K, Vergnano S, Bielicki JA, Paulus S, Menson E, et al. Using a simple point-prevalence survey to define appropriate antibiotic prescribing in hospitalised children across the UK. BMJ Open. 2016;6(11).

11. Ahmad A, Parimalakrishnan S, Mohanta GP, Patel I, Manna P. A study on utilization pattern of higher generation antibiotics among patients visiting community pharmacies in Chidambaram, Tamil Nadu at South India. Int J Pharm. 2012;2(3):466–71.

12. Padmaja U, Adhikari P, Pereira P. A prospective analysis of adverse drug reactions in a South Indian Hospital. Online J Health Allied Sci. 2009;8(3).

13. Kaur A, Bhagat R, Kaur N, Shafiq N, Gautam V, Malhotra S, et al. A study of antibiotic prescription pattern in patients referred to tertiary care center in Northern India. Ther Adv Infect Dis. 2018;5(4):63–8.

14. Cars O, Högberg L. Innovating for antibacterial resistance. Professional affairs [2007] Available from: https://www.reactgroup.org/uploads/publications/react-publications/innovating-for-bacterial-resistance.pdf. Accessed 4 February 2018. 2008.

15. Ilić K, Jakovljević E, Škodrić-Trifunović V. Social-economic factors and irrational antibiotic use as reasons for antibiotic resistance of bacteria causing common childhood infections in primary healthcare. Eur J Pediatr. 2012;171(5):767–77.

16. Ara F, Alam MK, Momen A. Prescribing pattern of antimicrobials in acute watery diarrhea in children below five years in the tertiary hospitals in Dhaka city. J Dhaka Natl Med Coll Hosp. 2011;17(1):22–4.

17. Laizu J, Parvin R, Sultana N, Ahmed M, Sharmin R, Sharmin Z. Prescribing practice of antibiotics for outpatients in Bangladesh: rationality analysis. Am J Pharm. 2018;1(1):1008.

18. Biswas M, Roy DN, Tajmim A, Rajib SS, Hossain M, Farzana F, et al. Prescription antibiotics for outpatients in Bangladesh: a cross-sectional health survey conducted in three cities. Ann Clin Microbiol Antimicrob. 2014;13(1):15.

19. Begum MM, Uddin MS, Rahman MS, Nure MA, Saha RR, Begum T, et al. Analysis of prescription pattern of antibiotic drugs on patients suffering from ENT infection within Dhaka Metropolis, Bangladesh. Int J Basic Clin Pharmacol. 2017;6(2):257–64.

20. Rashid MM, Chisti MJ, Akter D, Sarkar M, Chowdhury F. Antibiotic use for pneumonia among children under-five at a pediatric hospital in Dhaka city, Bangladesh. Patient Prefer Adher. 2017;11:1335–42.

21. MOHFW. Ministry of Health and Family Welfare, Bangladesh. Sher-e-bangla Medical College Hospital. https://app.dghs.gov.bd/localhealthBulletin2016/publish/publish.php?org=10001978&year=2016&lvl=5 (accessed on 30 March 2020). HEALTH BULLETIN 2016. 2016.

22. Kanish R, Gupta K, Juneja S, Bains H, Kaushal S. Prescribing pattern of antibiotics in the department of pediatrics in a tertiary care medical college hospital in Northern India. Asian J Med Sci. 2014;5(4):69–72.

23. Paruk F, Richards G, Scribante J, Bhagwanjee S, Mer M, Perrie H. Antibiotic prescription practices and their relationship to outcome in South Africa: findings of the prevalence of infection in South African intensive care units (PISA) study. S Afr Med J. 2012;102(7):613–6.

24. Senn N, Rarau P, Salib M, Manong D, Siba P, Rogerson S, et al. Use of antibiotics within the IMCI guidelines in outpatient settings in Papua New Guinean children: an observational and effectiveness study. PLoS One. 2014;9(3):e90990.

25. Finkelstein JA, Stille C, Nordin J, Davis R, Raebel MA, Roblin D, et al. Reduction in antibiotic use among US children, 1996–2000. Pediatrics. 2003;112(3):620–7.

26. Marra F, Patrick DM, Chong M, Bowie WR. Antibiotic use among children in British Columbia, Canada. J Antimicrob Chemother. 2006;58(4):830–9.

27. Datta SK, Paul TR, Monwar M, Khatun A, Islam MR, Ali MA, et al. Patterns of prescription and antibiotic use among outpatients in a tertiary care teaching hospital of Bangladesh. Int J Pharm Pharm Sci. 2016;8(11):54.

28. Fahad B, Matin A, Shill M, Asish K. Antibiotic usage at a primary health care unit in Bangladesh. Australas Med J (Online). 2010;3(7):414.

29. Pise HN, Padwal SL, Jadhav RR, Deshmukh VS, Jadhav AD, Kolhe AM. Drug prescribing and dispensing pattern in pediatrics outpatient clinic of a rural tertiary-care teaching hospital. Natl J Physiol Pharm Pharmacol. 2015;5(4):313–7.

30. Shiva F, Ghanaie R, Shirvani F, Armin S, Tabatabaei SR, Fahimzad SA, et al. Pattern of antibiotic usage in children hospitalized for common infectious diseases. Arch Pediatr Infect Dis. 2018;6(1).

31. Palikhe N. Prescribing pattern of antibiotics in pediatric hospital of Kathmandu valley. J Nepal Health Res Counc. 2004.

32. Baidya S, Hazra A, Datta S, Das AK. A study of antimicrobial use in children admitted to pediatric medicine ward of a tertiary care hospital. Indian J Pharm. 2017;49(1):10–5.

33. Isah A, Ross-Degnan D, Quick J, Laing R, Mabadeje A. The development of standard values for the WHO drug use prescribing indicators.: International Conferences on Improving Use of Medicines. WHO, Essential Medicines and Policy Department 2008. 2008.

34. Thrane N, Steffensen FH, Mortensen JT, Schønheyder HC, Sørensen HT. A population-based study of antibiotic prescriptions for Danish children. Pediatr Infect Dis J. 1999;18(4):333–7.

35. Jan D. Antibiotic resistance in Australia. Health Issues. 2001;69:1–5.

36. Resi D, Milandri M, Moro M. Emilia Romana Study Group on the Use of Antibiotics in Children. Antibiotic prescriptions in children. J Antimicrob Chemother. 2003;52.

37. Hasan SR, Hossain MM, Akter R, Karim SH, Haque S, Kamaluddin M, et al. Pattern of antibiotics use at the primary health care level of Bangladesh: survey report-1. Stamford J Pharm Sci. 2009;2(1):1–7.

38. Holstiege J, Garbe E. Systemic antibiotic use among children and adolescents in Germany: a population-based study. Eur J Pediatr. 2013;172(6):787–95.

39. Youngster I, Avorn J, Belleudi V, Cantarutti A, Díez-Domingo J, Kirchmayer U, et al. Antibiotic use in children–a cross-national analysis of 6 countries. J Pediatr. 2017;182:239–44. e1.

40. Mamun KZ, Shears P, Hart C. The prevalence and genetics of resistance to commonly used antimicrobial agents in faecal Enterobacteriaceae from children in Bangladesh. Epidemiol Infect. 1993;110(3):447–58.