

Antibiotic prescribing practice in the management of cough or diarrhea among children attending hospitals in Addis Ababa: a cross-sectional study

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Background: Irrational use of antibiotics is a global problem. Failure to follow clinical guidelines is one of the main reasons for irrational use of antibiotics. Cough and/or diarrhea are the main childhood illnesses in Ethiopia, and health care providers are expected to follow the national guideline while managing these illnesses. This study tried to assess the extent of adherence to the guideline while managing cases of childhood diarrhea and/or cough.

Methods: The study was conducted in 23 hospitals in Addis Ababa. Data were collected prospectively from April to June 2016 using a structured questionnaire. A total of 1,073 children aged 2–59 months who visited the hospitals for cough or diarrhea during the study period were included in the study. Equal number of cases were allocated to each hospital and consecutive cases were included in the study until the calculated sample size was attained for each hospital. Data collectors approached cases after they were seen by the health care provider. SPSS version 20 was used to analyze the data.

Result: Of the total number of cases, an antibiotic was prescribed for 794 (74.0%) of the children. Cotrimoxazol 209 (26.3%), amoxicillin 185 (23.3%), and cephalosporines 174 (21.9%) were the three most commonly prescribed antibiotics. Six hundred eighty-eight (86.6%) of the prescriptions were determined to be inappropriate. Of the inappropriate prescriptions, 631 (91.7%) were for prescribing antibiotics when not necessary and 57 (8.3%) were for prescribing the wrong spectrum of antibiotics. Using multivariate analysis, a child not having diarrhea was independently associated with appropriate antibiotic prescription (adjusted odds ratio = 0.261, 95% confidence interval: 0.095–0.714). The prescriber being qualified as a pediatrician was an independent predictor of inappropriate antibiotic prescription (adjusted odds ratio = 9.967, 95% confidence interval: 4.221–23.532).

Conclusion: The magnitude of inappropriate antibiotic prescription while managing cough and/or diarrhea in our setting was high. It needs urgent action to prevent emergence of antibiotic-resistant microorganisms.

Keywords: diarrhea, cough, inappropriate antibiotic prescription, hospital, Addis Ababa

Introduction

Rational use of drugs implies prescribing the appropriate drug at the right dosage at the right time, with this all available at an affordable price to the people that need them.¹ Irrational use of antibiotics is an ongoing global public health problem that deserves more attention. The World Health Organization (WHO) estimates that globally more than 50% of all medicines are prescribed, dispensed, or sold inappropriately.² The problem of inappropriate prescribing affects developing countries more than developed countries. This is evidenced by the WHO report where it was demonstrated that

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in developing countries, half of all viral upper respiratory tract infections and viral diarrhea cases received antibiotics inappropriately while only 70% of all pneumonia cases, which warrant antibiotic treatment, receive antibiotics.³ This inappropriate antibiotic use has many consequences including serious morbidity and mortality resulting from incorrect dosage, adverse drug reaction, and increased antimicrobial resistance resulting from overuse of antibiotics. In 2011, the WHO stated “if no action today, no cure tomorrow”⁴ in an effort to emphasize to the consequence of the widespread and inadvertent use of antibiotics and the need for immediate action to preserve antibiotics for future use.

The extent of inappropriate use of antibiotics in Ethiopia is not well understood with only a few studies available, all of which were conducted based on retrospective data obtained from prescription records from hospital pharmacies.^{5–7} Previous studies also failed to show specifically to what extent prescribers follow the guideline when managing common childhood illnesses such as diarrhea and cough.

The use of antibiotics is recommended by the Ethiopian National Guideline and WHO guideline for the management of bacterial causes of diarrhea and pneumonia but not for presumed viral causes of such illnesses.^{8,9} Health care providers are expected to adhere to the guideline when antibiotics are prescribed for the management of these illnesses. There is a paucity of evidence in Ethiopia showing to what extent health care providers comply with guidelines when managing cough or diarrhea in children. Therefore, this study aimed to assess the extent of adherence to the guideline while managing cases of childhood diarrhea and/or cough in our setting.

Methods and subjects

A cross-sectional prospective study design was used from April 2016 to June 2016 to assess the extent of inappropriate antibiotic use for the management of cough and/or diarrhea among children 2–59 months of age attending hospitals of Addis Ababa. At the time of the data collection, 6 public and 20 private-for-profit hospitals were providing clinical service for children in Addis Ababa. Three of the public and all of the private hospitals were included in our study. Three public hospitals were excluded from the study due to logistical reasons.

The calculated sample size was 1,066 children with the following assumption made while calculating the sample size: 50% prevalence of inappropriate antibiotic prescription which was determined from a study in Tanzania,¹⁰ 95% confidence level, and 3% confidence limit.

By allocating equal number of cases to the 23 hospitals, 47 children were recruited from each hospital for the study (a total of 1,081 cases). Eight cases were rejected during data entry due to incomplete information. Consecutive cases of children aged 2–59 months who visited the hospitals during the data collection time and who fulfilled the inclusion criteria were included in the study. Data collection continued until the calculated sample size for each hospital was met. Only self-referred cases of diarrhea and/or cough that were managed on an outpatient basis were included in the study. Children of age 2–59 months who had diarrhea and/or cough with comorbid illness were excluded from the study.

Data were collected by trained registered nurses on assessment of a child with diarrhea and/or cough based on the Ethiopian National Guideline. In each hospital, nurses who were performing triage were recruiters of cases for the study. These case recruiters inform the data collectors when a child with cough and/or diarrhea presented to the hospital. After the child was seen by the appropriate hospital health care provider, the child was then reevaluated by the data collector in a separate room.

Information pertaining to socio-demographic and clinical characteristics of the child were collected using a structured pretested questionnaire. Information including age, sex, address of the child, presence of cough or diarrhea, duration of the current episode of diarrhea or cough, stool consistency, and fever were obtained by interviewing the child's caretaker. The presence of crackles on chest auscultation, chest indrawing, stridor, signs of dehydration, prescriber qualification, type of antibiotics prescribed, dose, and coadministered medicines were extracted from the patient's file.

The definitions of empirical antibiotic prescribing for pneumonia or diarrhea were based on the recommendations by the Ethiopian National Guideline. The guideline recommends that antibiotics not be used for a child with acute (watery) diarrhea and nonpneumonia cough. The guideline defines pneumonia as cough with fast breathing or chest indrawing, and bloody diarrhea as visible blood in the stool.⁸ Inappropriate antibiotic prescription was defined as when the spectrum, dose, or duration of antibiotic prescribed was not in line with the Ethiopian National Guideline. Diagnosis of dehydration was made according to the WHO definition for the condition.⁹

Data were coded and entered in to a computer using SPSS for windows version 20.0 (IBM Corp., Armonk, NY, USA). Simple frequencies and proportions were determined using the independent variables. The dependent variable in this study was inappropriate antibiotic prescription for cough

or diarrhea. Odds ratio (OR) with 95% confidence interval (CI) was used to assess statistical association. *p*-value less than 0.05 was considered statistically significant. Variables with *p*-value <0.2 in the bivariate analysis were entered into multivariate (binary logistic regression) analysis to determine a model for it. During the data analysis, we considered pneumonia as a composite variable encompassing cough and fast breathing and/or presence of crackles or chest indrawing.

Ethical clearance was obtained from the Institutional Review Board of Saint Paul's Hospital Millennium Medical College and from Addis Ababa Regional Health Bureau. Written informed consent was also obtained from the parent or legal guardian of each child.

Results

A total of 1,073 children aged 2–59 months were surveyed during the study period. Of the total, 936 (87.2%) children were seen at private-for-profit hospitals and the rest at public hospitals. Five hundred seventy-one (53.2%) of the children were male. The majority of the children lived in Addis Ababa (96.2%), with the rest coming from nearby towns and villages. Out of the total, 490 (45.7%) attendants claimed that the reason for hospital visitation was because the child was having diarrhea and 653 (60.9%) reported the reason as cough. Only 72 (6.7%) attendants claimed the reason for bringing their child to hospital was because the child had both cough and diarrhea. Half of the children, 536 (50.0%), were reported to have fever in addition to cough and/or diarrhea. Antibiotics were prescribed for 794 (74.0%) children, and the rest were sent home after receiving counseling or symptomatic treatment with cough syrup and/or analgesics. Cotrimoxazol, 209 (26.3%), amoxicillin, 185 (23.3%), and cephalosporines (ceftriaxone [16.0%], cefixime [4.5%] cephalaxine [1.4%]), 174 (21.9%), were the three most commonly prescribed antibiotics. Based on the national guideline for managing cough and/or diarrhea, of those children for whom antibiotic were prescribed 688 (86.6%) of the prescriptions were inappropriate. Of the inappropriate prescriptions, 631 (91.7%) were for prescribing when not necessary and 57 (8.3%) were for prescribing the wrong spectrum of antibiotics. Dosages of the prescribed antibiotics were within the recommended range by the national guideline. The prescribers were pediatricians, pediatric resident doctors, interns, and general practitioners. Most of the children, 894 (83.3%), were seen by a pediatrician (Table 1).

Bivariate analysis showed that the odds of prescribing antibiotics inappropriately for a child with cough and/or diarrhea was higher when the child was treated at private-for-profit

Table 1 Demographic and clinical characteristics of the children, Addis Ababa, 2016

Characteristics		N (%)
Age (months)	2–11	386 (36.0)
	12–23	260 (24.2)
	24–35	147 (13.7)
	36–59	280 (26.1)
Sex	Male	571 (53.2)
	Female	502 (46.8)
Type of facility (hospital)	Public	137 (12.8)
	Private-for-profit	936 (87.2)
Fever	Yes	536 (50.0)
	No	537 (50.0)
Diarrhea	Yes	490 (45.7)
	No	583 (54.3)
Duration of diarrhea	<3 days	285 (58.2)
	3–11 days	205 (41.8)
Consistency of diarrhea	Watery	475 (96.9)
	Bloody	15 (3.1)
Presence of dehydration	Yes	119 (24.3)
	No	371 (34.6)
Cough	Yes	653 (60.9)
	No	420 (39.1)
Duration of cough	<3 days	273 (41.7)
	3–14 days	382 (58.3)
Chest indrawing	Yes	33 (5.0)
	No	622 (95.0)
Fast breathing	Yes	152 (23.2)
	No	503 (76.8)
Stridor	Yes	48 (7.3)
	No	607 (92.7)
Crackles on auscultation	Yes	50 (7.6)
	No	605 (92.4)
Antibiotic prescribed	Yes	794 (74.0)
	No	279 (26.0)
Inappropriate prescription	Yes	688 (86.6)
	No	106 (13.4)
Reason to say inappropriate prescription	Prescribed while not needed	631 (91.7)
	Wrong spectrum prescribed	57 (8.3)
Type of antibiotics prescribed	Cotrimoxazol	209 (26.3)
	Amoxicillin	185 (23.3)
	Cephalosporines (cephalexine, ceftriaxone, cefixime)	174 (21.9)
	Amoxicillin–clavulanic acid	129 (16.2)
	Others	97 (12.2)
		97 (12.2)
Prescriber qualification	Intern	110 (10.3)
	General practitioner	10 (0.9)
	Pediatric resident doctor	59 (5.5)
	Pediatrician	894 (83.3)

hospital ($p=0.000$), when the child had fever in addition to cough and/or diarrhea ($p=0.027$), when the child had diarrhea ($p=0.000$), when the child had cough ($p=0.000$), and when the child was treated by an intern/general practitioner ($p=0.000$) or a pediatrician ($p=0.000$) (Table 2).

Table 2 Inappropriateness of prescribed antibiotics versus demographic, clinical, and prescriber qualification, Addis Ababa, 2016

Characteristics	Inappropriateness of prescription		p-value	Crude OR (95% CI)	Adjusted OR (95% CI)
	Yes	No			
Age, months (n=794)					
2–11	221 (32.1)	39 (36.8)	0.680	1	–
12–23	177 (25.7)	25 (23.6)	0.419	1.249 (0.728–2.143)	
24–35	108 (15.2)	13 (12.3)	0.262	1.466 (0.751–2.861)	
36–59	182 (26.5)	29 (27.4)	0.700	1.108 (0.659–1.861)	
Type of facility (n=794)					
Public	65 (9.4)	32 (30.2)	0.000	1	1
Private-for-profit	623 (90.6)	74 (69.8)		4.145 (2.547–6.746)	0.545 (0.240–1.236)
Fever (n=794)					
Yes	355 (51.6)	67 (63.2)	0.027	1	1
No	333 (48.4)	39 (36.8)		1.611 (1.057–2.458)	1.093 (0.676–1.767)
Diarrhea (n=794)					
Yes	353 (51.3)	22 (20.8)	0.000	1	1
No	335 (48.7)	84 (79.2)		0.249 (0.152–0.407)	0.261 (0.095–0.714)
Duration of diarrhea (n=375)					
<3 days	196 (55.5)	13 (59.1)	0.744	1	–
3–14 days	157 (44.5)	9 (40.9)		1.157 (0.482–2.777)	
Dehydration (n=375)					
Yes	87 (24.6)	7 (31.8)	0.453	1	–
No	266 (75.4)	15 (68.2)		1.427 (0.563–3.614)	
Cough (n=794)					
Yes	396 (57.6)	89 (84.0)	0.000	1	1
No	292 (42.4)	17 (16.0)		3.860 (2.249–6.627)	1.148 (0.374–3.521)
Prescriber qualification (n=794)					
Intern/GP	45 (6.5)	27 (25.5)	0.000	1	1
Resident doctor	22 (3.2)	25 (23.6)	0.093	0.528 (0.251–1.113)	0.476 (0.205–1.107)
Pediatrician	621 (90.3)	54 (50.9)	0.000	6.9 (3.972–11.986)	9.967 (4.221–23.532)

Abbreviations: CI, confidence interval; GP, general practitioner.

Binary logistic regression model was used to look for factors associated with prescribing antibiotics inappropriately while managing cough and/or diarrhea. Variables with *p*-value less than 0.2 in the bivariate analysis were included in the model. Under multivariate analysis, child not having diarrhea was independently associated with appropriate antibiotic prescription (adjusted OR =0.261, 95% CI: 0.095–0.714), while prescriber qualified as a pediatrician was an independent predictor of inappropriate antibiotic prescription (adjusted OR =9.967, 95% CI: 4.221–23.532) (Table 2).

Discussion

This study aimed to assess the extent of inappropriate antibiotic prescription among children managed for cough and/or diarrhea. Our finding that antibiotic was prescribed for the majority of the children (74.0%) who visited hospital for cough and/or diarrhea was consistent with the reports of other investigators.^{10–12} Our study identified that, based on the Ethiopian national management guideline for cough and diarrhea, 86.6% of the prescriptions were inappropriate.

According to the WHO estimate, 50% of the global antibiotic use is inappropriate.² In developing countries, only less than half of the patients seen in private sectors and public primary care centers are treated according to the standard guidelines.³ Gwimile et al reported that in Tanzania 80% of children with diarrhea and 68.9% of children with common cold were given antibiotics inappropriately.¹⁰ Also, a study conducted by Hashemi et al¹¹ in Tehran showed 68.9% of prescriptions were irrational. Similarly, Wang et al¹² revealed that antibiotics were prescribed for 78% of cold cases which are assumed to be caused by viruses.

The national and WHO guidelines recommend use of antibiotics for pneumonia and bloody diarrhea.^{8,9} In our study, we found that all cases that fulfilled these criteria for the diagnosis of pneumonia and bloody diarrhea were prescribed antibiotics. Importantly though, the spectrums of the prescribed antibiotics was not according to the national guideline. The Ethiopian National Guideline recommends the use of amoxicillin for the management of childhood pneumonia and cotrimoxazol for a child affected with bloody diarrhea.

In our study, we found out that prescribers use different spectrums of antibiotics not recommended by the national guideline to treat pneumonia (amoxicillin–clavulanic acid, cephalosporines, and azithromycin) and diarrhea (amoxicillin and ceftriaxone). The WHO guideline recommends ceftriaxone as alternative therapy for bloody diarrhea.⁹ In summary, though prescribers were ordering antibiotics to treat pneumonia and bloody diarrhea, which is in accordance to both the national and WHO guidelines, they were not following the national guideline in terms of the chosen antibiotic coverage spectrum. On the other hand, prescribers were using antibiotics for watery diarrhea and cough with no pneumonia, ie, in causes that are mostly assumed to be viral. The antibiotics prescribed were amoxicillin, amoxicillin–clavulanic acid, ceftriaxone, cephalexine, azithromycin, and cefixime. Hence, not only was the use of antibiotics not in accordance with the national guideline, but also the use of such broad-spectrum antibiotics has the potential for additional harm. Antibiotics such as ceftriaxone and cefixime are considered second-line therapy for most of the infectious causes of illnesses by the Ethiopian National Guidelines. The widespread use of these antibiotics as first-line therapy as well as the inadvertent use of them for nonbacterial causes of illnesses has the potential to make these “second-line” antibiotics to fail soon and become ineffective. Sometimes, drugs can cause life-threatening adverse effects like anaphylaxis and Stevens–Johnson syndrome; hence, the unnecessary use of antibiotics exposes the patient to substantial morbidity due to its adverse effect in addition to the unnecessary cost incursion.¹³ Therefore, prescribers should order antibiotics only when it is necessary to prevent emergence of antibiotic-resistant bacteria, so as to not risk the patient to life-threatening side effects and to avoid unnecessary drug cost.¹⁴ A Cochrane systematic review showed educational interventions designed to address the physician, the patient, and the public in a variety of ways are successful interventions in reducing inappropriate prescription.¹⁵

The unexpected finding in our study was that the likelihood of inappropriate antibiotic prescription was more likely to be done by pediatricians compared to the other health professionals. In an observational study conducted in Karachi, Nizami et al¹⁶ reported the proportion of antibacterials prescribed for childhood diarrhea by pediatricians was lesser compared to the prescription of similar agents done by the general practitioners. In our setting, the reason why pediatricians were making more inappropriate prescription than the other health care providers needs further investigation. This could be because prescription practice can be

affected by different factors such as economic incentives from pharmaceutical companies and weak regulation over prescription in addition to knowledge gap from providers and consumers.¹⁷

In our study, we found that there was no significant difference with regard to inappropriateness of prescriptions given by health care providers who were working in the private-for-profit hospitals compared to those working in the public health facility. Previous studies reported mixed findings, with South African health care providers in public hospitals prescribing higher number of drugs per patient than those working in private hospitals.¹⁸ But in the Attock District of Pakistan, inappropriate prescription was done more commonly by the health care providers who were working in the private sector than their counterparts in public health facility.¹⁹

A limitation of our study was that only hospitals were included in the study and other health facilities such as clinics and health centers were not included. The study also failed to explore the driving factors for inappropriate prescription by prescribers, such as prescribers' knowledge, attitude, drug availability, and perceived prevalence of antibiotic sensitivity pattern of bacterial diarrhea and pneumonia by prescribers. The role of attendants as well as hospital administrators and drug companies was also not addressed by our study.

Conclusion

In conclusion, the magnitude of inappropriate antibiotic prescription while managing cough and/or diarrhea among children aged 2–59 months in our setting was high. This study has shown the extent of antibiotics overuse for presumed viral infection and the choice of antibiotics for bacterial infections in our setting. We recommend urgent action to be taken to halt such widespread inappropriate antibiotic prescription practice in our setting, as this can lead to emergence of drug-resistant microorganisms. Policymakers and planners can address the problem through providing continuous medical education or refresher training for prescribers on the one hand and through teaching the public through broadcasting, distributing brochures, and using the press on the other hand. We also recommend researches to further explore the driving factors for inappropriate prescription of antibiotics in our setting.

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Author contributions

All the authors have participated in writing the proposal, data collection, writing the manuscript, and have read and approved the manuscript. Additionally Atnafu Mekonnen Tekleab conceived the study and performed data analysis.

Disclosure

The authors report no conflicts of interest in this work.

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