Appropriateness of Antibiotic use for the Management of Acute Diarrhea Among Under-Five Children Treated at Primary Care Centers in Northwest Ethiopia: A Cross-Sectional Study

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Research Article

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Abstract

Background Acute diarrhea management is solely aimed at fluid replacement and nutritional support while antibiotics have a very limited role. Antibiotic treatment is recommended only for bloody diarrhea (dysentery), cholera and invasive bacterial diarrhea. This study is launched to assess the appropriateness of antibiotic use for the management of acute diarrhea among under-five children in Gondar town primary care centers.

Methods Institutional based cross-sectional study was conducted in three primary care centers located in Gondar town, Northwest Ethiopia. Children aged from 2–59 months who visited the three primary care centers from September 12, 2015 to September 10, 2016 and received treatment for acute diarrhea were included in the study. We selected 176 cases from Azezo Health Center, 166 from Poly Health Center and 80 from Woleka Health Center. Cases were drawn using systematic random sampling technique. The findings of the study were summarized using tables and figures; binary logistic analysis was used to identify association between the independent and outcome variables at 95% confidence level where $p < 0.05$ was considered as statistically significant.

Results The mean age of the study participants was 19.1 ± 12.8 months. The majority (60.8%) were males. Appropriate antibiotic use was recorded in less than half (47.2%) of the study subjects. Almost all (98.1%) of children subjected to inappropriate antibiotic use were those with watery diarrhea treated with antibiotics. Out of 253 children who received antidiarrheal antibiotics 202 (79.8%) had acute watery diarrhea which should not be treated with antibiotics. Children diagnosed with acute watery diarrhea were less likely to receive treatment qualified as appropriate antibiotic use [AOR: 0.003 (0.001,0.017)]. Conversely, receiving no antibiotic [AOR: 391.00 (92.46, 1653.37)] and prescriber's profession of Clinical Nurse [AOR: 3.57 (1.02, 12.51)] were positive predictors for appropriate antibiotic use.

Conclusion The findings of the study confirm the prevalence of widespread inappropriate antibiotic use on under-five children presenting with acute diarrhea. The findings can be used by stakeholders as input for promoting appropriate antibiotic use in the healthcare system as well as to deter antimicrobial resistance.

Background

Acute infectious diarrheal disease is common public health problem worldwide. It is the second leading cause of mortality in under-five children [1–3]. It accounts 1.8 million deaths annually. Majority of these death happen in South Asia and Africa [4]. In Ethiopia, diarrhea remains a serious public health problem as it is the major killer of children with an estimated 73,700 deaths of under-five children. This accounts for an estimated 20% of the deaths among children under five years of age in the country [5].

Acute diarrhea management is solely aimed at fluid replacement and nutritional support while antibiotics have a very limited role. Guidelines recommended the use of oral rehydration solution (ORS) along with

zinc as the mainstay of treatment of acute diarrhea in children. Antibiotic treatment is recommended only for bloody diarrhea (dysentery), cholera and invasive bacterial diarrhea [6, 7].

While it is important to use antibiotics appropriately ensure best use of resources, effective therapy, reducing the rising rate of antibiotics resistance pathogens, increasing quality and efficiency of healthcare and minimization of potential side effects, it is common to encounter inappropriate antibiotic use in diarrheal patients, especially in developing countries [8–10]. Inappropriate antibiotic use takes many different forms like poly-pharmacy, over-use/misuse of antibiotics and injections, failure to prescribe in accordance with guidelines and inappropriate self-medication [11, 12]. Inappropriate use of antibiotics in the treatment of acute diarrhea results in an increased risk of adverse effects, higher rates of antimicrobial resistance by enteric pathogens, inappropriate patient demand, and increase healthcare cost [8–12]. In addition to these, all oral antibiotics are capable of causing, or worsening diarrhea due to their effect on gut microflora [2, 9].

Lack of national policies and strategies related to antibiotic use is associated with increased antibiotic use in acute diarrhea [13]. Factors that influence appropriateness of antibiotics use in acute acute diarrhea include diagnostic uncertainty, giving something more than just ORS to satisfy the patient, insufficient number of qualified and competent staff, caregiver preference, source of updating knowledge, experience of the prescriber, age of the child, lack of specific medicines' information (e.g., clinical guidelines and drug bulletins), lack of continuing medical education and supervision, peer pressure (where senior staff may set inappropriate prescribing practices that are followed by junior staff), lack of diagnostic support services (e.g., laboratory services), poor infrastructure [14–16].

Ethiopia is one of developing countries where the healthcare system at a low level of development, factors that predispose to inappropriate antibiotic use are common futures of its most primary healthcare institutions [17]. Despite this fact, there has been limited data on the pattern of antibiotic use in the management of acute diarrhea in pediatric patients treated at primary healthcare facilities in the country. This study is launched to assess the appropriateness of antibiotic use for the management of acute diarrhea among under-five children in Gondar town health centers.

Methods

Institutional based cross-sectional study was conducted in three primary care centers (Azezo Health Center, Poly Health Center and Weleka Health Center) located in Gondar town, Northwest Ethiopia. Children aged from 2–59 months who visited the three primary care centers from September 12, 2015 to September 10, 2016 and received treatment for acute diarrhea were included in the study. Children whose diarrheal illness lasted more than 14 days, children who were referred to hospitals and children who were immunocompromised or had other comorbidities were excluded from the study.

The sample size was determined using single population proportion formula by assuming 95% confidence level, 5% margin of error, estimated proportion of appropriate use of antibiotics (0.5) and 10% sample size was 422, which is then proportionally distributed

over the three primary care centers based on the number of under-five children acute diarrheal cases in each center. Thus, we selected 176 cases from Azezo Health Center, 166 from Poly Health Center and 80 from Woleka Health Center. Cases were drawn using systematic random sampling technique.

Data was collected by review of patient medical cards and entered into IBM SPSS Statistics 24® software for analysis. The findings of the study were summarized using tables and figures. Furthermore, binary logistic analysis was used to identify association between the independent and outcome variables at 95% confidence level where $p < 0.05$ was considered as statistically significant.

Ethical clearance was obtained from School of Pharmacy, University of Gondar, Research and Ethics Review Committee. The study followed the principles outlined in the Declaration of Helsinki. The requirement of participants' written informed consent was waived by the ethical review committee of the University of Gondar because this was a retrospective study through document review. Anonymity of study participants was assured by neglecting the personal identifiers such as patients' name and address. The information from patients' cards was kept confidentially, only data collectors and investigator have access to them.

Results

Socio-demographic and clinical characteristics

A total of 422 children presenting with acute diarrhea between the age of 2 and 59 months were enrolled in this study from HCs of Gondar town. However, data of 32 children were excluded from the study due to incompleteness, giving the card retrieval rate of 92.4%.

The mean age of the study participants was 19.1 ± 12.8 months. The majority (60.8%) were males while 80.9% were vaccinated. Height and body temperature records were found only on few patients' medical files, thus these variables were excluded from our analyses. Less than a fifth (19.7%) of the study subjects visited health facilities within a day of symptom onset. The majority (85.9%) of the children presented with watery diarrhea (Table 1).

Table 1

Socio-demographic and clinical characteristics of under-five children presented with acute diarrhea

Variables	Frequency (%)
Age (months)	153(39.2)
2–12	143 (36.7)
13–24	94 (24.1)
25–59	
Sex	237 (60.8)
Male	153 (39.2)
Female	
Vaccination status (n = 383)*	310 (80.9)
Completed	68 (17.8)
Up to date	5 (1.3)
Defaulted	
Weight in Kilograms (n = 363)*	2 (0.6)
< 5	187 (51.5)
5–9	140 (38.6)
9–14	34 (9.4)
15–20	
Chief complaint	209 (53.6)
Diarrhea	43 (11.0)
Diarrhea with fever	59 (15.1)
Diarrhea with vomiting	23 (5.9)
Diarrhea with cough	20 (5.1)
Diarrhea with fever and vomiting	22 (5.6)
Diarrhea with fever and cough	10 (2.6)
Diarrhea with vomiting and cough	4 (1.0)
Diarrhea with fever, vomiting and cough	

Note: * 'n' represents total number of children for which data regarding the respective variables was

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Variables	Frequency (%)
Time from onset to visiting health center (n = 381)	75 (19.7)
Less than 24 hours	96 (25.2)
24–72 hours	210 (55.1)
73 hours – 14 days	
Stool characteristics	355 (85.9)
Watery diarrhea	55 (14.1)
Bloody diarrhea	
Note: * 'n' represents total number of children for which data regarding the respective variables was found recorded in their medical files.	

With regard to the level of profession and experience of practitioners, 58.2% of the patients were examined by Clinical Nurses (holding BSc Degree) while the rest (41.8%) were examined by Assistant Nurses (holding technical level diploma). The practitioner examining a patient took full responsibility of selecting treatment regimens. Antibiotics were prescribed to 66.2% of the children. Trimethoprim-sulfamethoxazole (TMP-SMZ) was the predominant antibiotic prescribed (Fig. 1).

Appropriateness of antibiotic use

We determined appropriateness of antibiotic use in acute diarrheal patients using the World Health Organization (WHO) manual for treatment of diarrhea. According to the manual, antimicrobial therapy should only be given for the following cases: 1) in cases of bloody diarrhea; 2) for suspected cholera cases; 3) for proven cases of giardiasis. The guideline provides that cholera should be suspected if there is diarrhea with severe dehydration in children over five years of age or in cholera endemic areas. It also states that acute diarrhea should not be treated for giardiasis. Since our study is on acute diarrheal cases of under five children in an area with no cholera incidence in preceding three years, only the first case for antimicrobial therapy applies for this study. Thus, antibiotic use is designated appropriate if antibiotic was administered to a bloody diarrhea case or if no antibiotic was administered for watery diarrhea case; and considered inappropriate otherwise. Antibiotics prescribed for other coinfections were also taken into consideration.

Accordingly, appropriate antibiotic use was recorded in less than half (47.2%) of the study subjects. Almost all (98.1%) of children subjected to inappropriate antibiotic use were those with watery diarrhea treated with antibiotics. Out of 253 children who received antidiarrheal antibiotics 202 (79.8%) had acute watery diarrhea which should not be treated with antibiotics (Fig. 2).

Factors associated with appropriateness of antibiotic use

Results of binary logistic analysis indicate that patients’ demographic characteristics do not have association with appropriateness of antibiotic use while some clinical features have been found to be predictors. For instance, children diagnosed with acute watery diarrhea were less likely to receive treatment qualified as appropriate antibiotic use [AOR: 0.003 (0.001,0.017)]. Conversely, receiving no antibiotic [AOR: 391.00 (92.46, 1653.37)] and prescriber’s profession of Clinical Nurse [AOR: 3.57 (1.02, 12.51)] were positive predictors for appropriate antibiotic use (Table 2).

Table 2

Factors associated with appropriateness of antibiotic use in under-five children with acute diarrhea

Variables	Antibiotic use		Odds ratio (95% CI)	
	Appropriate	Not appropriate	COR	AOR *
Primary care center where treatment was obtained				
Azezo	65	101	1.00	1.00
Poli	109	40	4.23 (2.63, 6.83)	1.15 (0.30, 4.42)
Weleka	10	65	0.24 (0.16, 0.50)	0.35 (0.07, 1.90)
Weight in Kg				

Discussion

The main aim in the treatment of acute diarrhea is treating and prevention of dehydration. Proper nutritional support, fluid management and early medical intervention are essential for successful management of acute diarrhea [18]. More than half of patients in our study (53.8%) visited healthcare facilities 72 plus hours after the onset of symptoms. This may be related to lack of health-seeking behavior and low awareness about diarrhea and its risk in the community.

Characteristics of diarrhea, especially low proportion of patients with bloody diarrhea (14.1%) suggests that the majority of cases of acute diarrhea were mild and self-limiting. Despite this, at least one antibiotic was prescribed to 66.2% of children. Widely ranging findings were reported on similar studies conducted elsewhere; an Indian study reporting antibiotic use lower than our study (43%) [9] while higher antibiotic use (84.9%) was reported on a study from Tanzania [19]. The differences in the prevalence of antibiotic use across different studies may be due to many factors such as difference in the epidemiology of diarrhea between the areas, difference in resources or treatment approaches.

The overall proportion of appropriate use of antibiotics for acute diarrheal treatment in our study was Loading [MathJax]/jax/output/CommonHTML/jax.js p that reported in a hospital based cross-sectional study in

Southern Thailand (44%), but less than that of a study conducted in Gambia, West Africa (63.4%) [1, 8]. Out of children identified with inappropriate antibiotic use 98.1% had watery diarrhea and of all patients who received antidiarrheal antibiotics 79.8% had watery diarrhea which should not be treated with antibiotics. This indicates prescribers' widespread deviation from WHO recommendations particularly, high tendency to prescribe antibiotics for acute watery diarrhea in under-five children. Prescribers' lack of sufficient knowledge, diagnostic uncertainty and easy accessibility of antibiotics may be contributing factors for this wrongful practice.

In our study, TMP-SMZ was the most inappropriately prescribed antibiotic which is consistent with Southern Thailand [1]. However, this result is not supported by other studies conducted in Tanzania and India where cephalosporins, metronidazole and ciprofloxacin were frequently inappropriately prescribed antibiotics [9, 19, 20]. The possible reason may be the fact that TMP-SMZ was more available than other drugs (cephalosporins, ciprofloxacin) in our setup.

There was no association between appropriateness of antibiotic use and patients' age, weight, chief complaint as well as health center where they got treatment. In contrast, diagnosis of bloody diarrhea, treatment regimen with no antibiotics and having clinical nurses as prescriber were found to be predictors of appropriate antibiotic use. Similarly, higher level professionals were associated with appropriate antibiotic use as reported by studies conducted in India and Tanzania [9, 19].

Recommendations on use of antibiotics in the management of acute watery diarrhea should be followed strictly, since indiscriminate use of antibiotics results in development of resistance. In addition to this, giving unnecessary antibiotics means addition of unnecessary cost to the community. Especially in our setup where available antibiotics are limited, we do not have second line antibiotics for diseases caused by resistant strains of microorganisms. Thus, appropriate use of antibiotics is crucial to maintain effective treatment and prevention of infectious diseases in a community.

Conclusion

The findings of the study confirm the prevalence of widespread inappropriate antibiotic use on under-five children presenting with acute diarrhea. The study shows how parameters such as stool characteristic, medication regimens and prescribers' profile affect the appropriateness of antibiotic use. The findings can be used by stakeholders as input for promoting appropriate antibiotic use in the healthcare system as well as to deter antimicrobial resistance.

List Of Abbreviations

AOR adjusted odds ratio

CI: confidence interval

COR: crude odds ratio

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ORS: oral rehydration solution

TMP-SMZ: Trimethoprim-Sulfamethoxazole

WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Ethical clearance was obtained from School of Pharmacy, University of Gondar, Research and Ethics Review Committee. The study followed the principles outlined in the Declaration of Helsinki. The requirement of participants' written informed consent was waived by the ethical review committee of the University of Gondar because this was a retrospective study through document review. Anonymity of study participants was assured by neglecting the personal identifiers such as patients' name and address. The information from patients' cards was kept confidentially, only data collectors and investigator have access to them.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

STA participated in conceptualization, design of the study, data acquisition and analysis, writing original draft and funding acquisition. AJZ contributed in design, data analysis, supervision, review and editing of the manuscript. ZTT provided contribution in conceptualization and design of the study, data analysis, supervision, review and editing of the manuscript. All authors read and approved the final manuscript.

Not applicable.

References

1. Osatakul S, Puetpaiboon A. Appropriate use of empirical antibiotics in acute diarrhoea: a cross-sectional survey in southern Thailand. *Ann Trop Paediatr*. 2007;27(2):115-22.
2. Diniz-Santos DR, Silva LR, Silva N. Antibiotics for the empirical treatment of acute infectious diarrhea in children. *Braz J Infect Dis*. 2006;10(3):217-27.
3. Rahman AE, Moinuddin M, Molla M, Worku A, Hurt L, Kirkwood B, et al. Childhood diarrhoeal deaths in seven low- and middle-income countries. *Bull World Health Organ*. 2014;92(9):664-71.
4. Löfgren J, Tao W, Larsson E, Kyakulaga F, Forsberg BC. Treatment patterns of childhood diarrhoea in rural Uganda: a cross-sectional survey. *BMC Int Health Hum Right*. 2012;12(1):19.
5. Atnafe H. Under-five street children diarrheal home treatment: The case of mothers residing on streets of selected sub-cities in Addis Ababa, Ethiopia 2016. [Thesis]. In press 2016.
6. World Health Organization. Clinical management of acute diarrhoea: WHO. Geneva: World Health Organization; 2004.
7. Duggan C, Santosham M, Glass R. The management of acute diarrhea in children: oral rehydration, maintenance, and nutritional therapy. Centers for Disease Control and Prevention. *MMWR*. 1992;41(16):1-20.
8. Risk R, Naismith H, Burnett A, Moore SE, Cham M, Unger S. Rational prescribing in paediatrics in a resource-limited setting. *Arch Dis Child*. 2013;98(7):503.
9. Kotwani A, Chaudhury RR, Holloway K. Antibiotic-Prescribing Practices of Primary Care Prescribers for Acute Diarrhea in New Delhi, India. *Value in Health*. 2012;15(1, Supplement):S116-S9.
10. Chareonkul C, Luong Khun V, Boonshuyar C. Rational drug use in Cambodia: study of three pilot health centers in Kampong Thom Province. *Southeast Asian J Trop Med Public Health*. 2002;33(2):418-24.
11. Awad AI, Ball DE, Eltayeb IB. Improving rational drug use in Africa: the example of Sudan. *Est Mediterranean Health J*. 2007;13(5):1202-11.
12. Kar SS, Pradhan HS, Mohanta GP. Concept of essential medicines and rational use in public health. *Indian J Community Med*. 2010;35(1):10-3.
13. Holloway KA, Rosella L, Henry D. The impact of WHO essential medicines policies on inappropriate use of antibiotics. *PLoS One*. 2016;11(3):e0152020.
14. Bharathiraja R, Sridharan S, Chelliah LR, Suresh S, Senguttuvan M. Factors affecting antibiotic prescribing pattern in pediatric practice. *Indian J Pediatr*. 2005;72(10):877-9.
15. Gebeyehu E, Bantie L, Azage M. Inappropriate Use of Antibiotics and Its Associated Factors among Urban and Rural Communities of Bahir Dar City Administration, Northwest Ethiopia. *PLoS One*. 2015;10(9):e0138179.

16. Mahapatra T, Mahapatra S, Banerjee B, Mahapatra U, Samanta S, Pal D, et al. Predictors of rational management of diarrhea in an endemic setting: observation from India. PLoS One. 2015;10(4):e0123479-e.
17. World Health Organization. Ethiopia: Health Workforce - The Health System: WHO Regional Office for Africa; 2018.
http://www.aho.afro.who.int/profiles_information/index.php/Ethiopia:Health_workforce_-_The_Health_System. Accessed 29 May 2019.
18. Franceschi F, Scaldaferri F, Riccioni ME, Casagrande I, Forte E, Gerardi V, et al. Management of acute diarrhea: current and future trends. Eur Rev Med Pharmacol Sci. 2014;18(14):2065-9.
19. 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;12:103.
20. Ahmad A, Khan MU, Malik S, Mohanta GP, Parimalakrishnan S, Patel I, et al. Prescription patterns and appropriateness of antibiotics in the management of cough/cold and diarrhea in a rural tertiary care teaching hospital. J Pharm Bioallied Sci. 2016;8(4):335-40.

Figures

Figure 1

Frequency of antibiotic prescription and types of antibiotics prescribed for under-five children with acute diarrhea

Figure 2

Appropriateness of antibiotic use in under-five children with acute diarrhea