

## ORIGINAL ARTICLE

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# Prescribing practices of Antibiotics for acute diarrhea in children aged less than five years old in Pakistan

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## ABSTRACT

**Introduction:** Childhood diarrhea accounts for 16% of child deaths in Pakistan. Irrational prescribing of antibiotics, prescribing of antibiotics for viral infections, self-medication using antibiotics, prescription sharing, and refilling are very common practices in Pakistan. The aim of this study was to evaluate the prescribing practices of antibiotics for acute diarrhea in children less than five years of age at a Secondary Healthcare Hospital of Pakistan and to assess the compliance of prescribers with authentic clinical guidelines of treatment for childhood acute diarrhea.

**Method:** A cross-sectional study was conducted for a period of one year, from August 2020 to August 2021, at a Secondary Care Hospital of Karachi, Pakistan. It was based on the collection of outpatient clinic prescriptions of children aged less than five years and suffering from acute diarrhea. The regimens or suggested therapies by prescribers for acute diarrhea were assessed as per The National Institute of Care and Health Excellence and World Health Organization guidelines. A brief questionnaire was also distributed among prescribers, pharmacists, and caretakers of children to extract their opinions regarding antibiotic prescribing in acute diarrhea.

**Results & Discussion:** Antibiotics were inappropriately prescribed for acute diarrhea among children in Pakistan because p-value was less than 0.05 ( $p < 0.05$ ) as calculated by descriptive statistical tools using Z-test. More than 90% prescriptions of acute diarrhea in children less than five years of age failed to comply with the authentic treatment guidelines. Due to the limited knowledge of prescribers regarding treatment guidelines and compliance of parents with antibiotic prescribing for diseases in children, irrational prescribing of antibiotics for acute diarrhea in children less than five years of age is frequent in Pakistan. Healthcare professionals must be adequately trained to ensure the proper management of acute diarrhea by following authentic clinical guidelines.

**Conclusion:** Antibiotics are irrationally prescribed for acute diarrhea in children less than five years of age in Pakistan and prescriptions do not comply with authentic clinical guidelines.

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# JOP

## Introduction

Diarrhea is the frequent passage of three or more loose or watery stools per day which is more than normal for an individual. According to the World Health Organization (WHO), diarrhea is the second leading cause of death in children less than five years of age. Its causes may include infection by parasite, virus or bacteria, malnutrition, contaminated water, and unhygienic conditions (World Health Organization, 2017). When increased bowel movement terminates within three weeks, it is called acute diarrhea, but if it persists for more than three weeks it is called chronic diarrhea (Marsha & Anthony, 2012).

Symptoms of chronic diarrhea include uncontrollable bowel movements, nausea, abdominal pain, cramps, vomiting, shivering and fever. These symptoms can lead to severe dehydration and malabsorption (National Institute of Diabetes and Digestive and Kidney Diseases, 2017). Antibiotic-associated diarrhea is mild diarrhea that can occur in children and adults and does not cause decrease in weight or dehydration and terminates within one to two days of stopping the antibiotic (Fliesher & O’Ryan, 2017).

Childhood diarrhea under two years of age accounts for 72% deaths globally (Walker et al., 2013). It also leads to impairment in the growth of children as well as cognitive development (Checkley et al., 2008) (Lorntz et al., 2006). Diarrheal diseases in children below five years of age in low or middle-income countries need immediate treatment to reduce mortality rate (Ugboko et al., 2020).

In Pakistan, childhood diarrhea accounts for 16% of child deaths and it was suggested that a cost-effective, standardized, and accessible mode of treatment along with public education and awareness regarding childhood diarrhea must be established (Quadri et al., 2013). Diarrhea in children can be prevented up to major extent by vaccination against *Escherichia coli*, *Shigella* spp. and rotavirus, promoting health hygiene, consuming non-contaminated water and good sanitary conditions (Mokomane et al., 2018).

Acute diarrhea should not necessarily be treated by antibiotics in children because rehydration therapy is proven to be the mainstay treatment and usually the symptoms subside without requiring any specific therapy. In case of severe diarrhea, traveler’s diarrhea, antibiotic-associated diarrhea, or chronic diarrhea, one may opt to antibiotics or antimicrobial therapy. Oral doses of co-trimoxazole or metronidazole or parenteral doses of ceftriaxone or ciprofloxacin can be a choice for empiric therapy in severe cases of diarrhea (Bruzesse et al., 2018).

According to The National Institute for Care and Health Excellence (NICE) guidelines of 2009, acute diarrhea must be treated primarily by oral rehydration salt as 50ml/kg over 4 hours, diarrhea usually subsides within 2 weeks and if this duration is crossed then healthcare professional must be consulted (The National Institute for Care and Health Excellence, 2009). Oral Rehydration Salt

(ORS) is the primary element of care in children with acute gastroenteritis and acute diarrhea because it has been reported that the efficacy of oral rehydration is comparable to the IV rehydration in severe dehydration while severe dehydration may require IV rehydration therapy (Guarino et al., 2014).

According to WHO, patients must obtain medicines as per their clinical necessity in appropriate doses and frequency for adequate duration of therapy with the lowest possible expense to promote rational use of medications. Prescribing of medicines without authentic clinical guidelines, polypharmacy, preference of injections when oral dosage form of same drug could be used, irrational use of antibiotics, self-medication and non-compliance with prescribed regimen are some of the examples coming under irrational use of medications.

This worldwide concern can be resolved mainly by ensuring that the medications are prescribed according to clinical guidelines, public awareness about medications, enforcement of policies and regulations by multidisciplinary national body for rational use of medicines, essential drugs list, pharmacy and therapeutic committee in healthcare areas, problem-based training of pharmacotherapy, supervision, and audits (World Health Organization, 2002).

A diarrhea control plan was launched by World Health Organization (WHO) and United Nations International Children’s Emergency Fund (UNICEF) in 2009 and Global Action Plan for Pneumonia and Diarrhea (GAPPD) in 2013 realizing the increased prevalence of these diseases in children (World Health Organization & UNICEF, 2013). National Essential Medicines List (NEML) of Pakistan includes low osmolarity ORS, 250mg and 500mg oral amoxicillin trihydrate and 20mg zinc sulphate as recommended by UNICEF and WHO for pneumonia and diarrhea (Drug Regulatory Authority of Pakistan, 2016).

Government of Pakistan has provided this list at primary as well as secondary healthcare settings in the country. A study conducted in Pakistan revealed that healthcare education to communities, health interventions for children and intensive supervision or healthcare audits can improve mortality rate in children less than 5 years of age suffering from diarrhea and pneumonia. It also suggested promoting rational use of medicines, activities of healthcare workers in community, training of healthcare workers, surveillance, and improvement in socio-economic conditions of people to reduce the risks and deaths caused by diarrhea and pneumonia (Hansen et al., 2020).

Irrational prescribing of antibiotics, prescribing of antibiotics for viral infections, self-medication using antibiotics, prescription sharing, and refilling are very common practices in Pakistan (Hameed et al., 2016). Inappropriate prescribing of antibiotics in low and middle-income countries is highly prevalent (8% to 100%) at primary healthcare settings which needs strategies for proper prescribing practices and implementation of national prescribing guidelines or recommendations of treatment by

WHO (Sulis et al., 2020).

Healthcare professionals must be trained periodically upon the proper management of diarrhea along with prescribing or indication of antibiotics for children under five years of age (Udoh & Meremikwu, 2017). The aim of this study was to evaluate the prescribing practices of antibiotics for acute diarrhea in children less than five years of age at a Secondary Healthcare Hospital of Pakistan and to assess the compliance of prescribers with authentic clinical guidelines of treatment for childhood acute diarrhea.

## Methodology

This study was conducted for a period of one year at a Secondary Care Hospital of Karachi, Pakistan. It was a cross-sectional study based on the collection of outpatient clinic prescriptions at pharmacy from August 2020 to August 2021. The prescriptions were collected based on the inclusion and exclusion criteria such as pediatric prescriptions of acute diarrhea for both gender of children aged less than five years were included in the study while all such prescriptions of children greater than five years of age were excluded.

Total of 500 prescriptions were collected along-with the verbal consent and demography of children from their caretakers or attendants. The age, weight, duration of diarrhea, concomitant diseases, therapies given by caretakers at home for diarrhea and medications prescribed by prescribers were also noted. The compliance of prescribers with authentic clinical guidelines while prescribing treatment of acute diarrhea in children less than five years of age was evaluated.

The appropriateness and anti-microbial spectrum of prescribed antibiotics as per age of children, episodes of diarrhea and duration of diarrhea were noted. Regimens or suggested therapies by prescribers for acute diarrhea were also assessed as per NICE guidelines. Moreover, the opinions of prescribers, pharmacists, and caretakers of the children for prescribing antibiotics in children less than five years of age were also recorded through questionnaire.

The questionnaire contained some open-ended questions such as satisfaction with the prescribed regimen for acute diarrhea, episodes of diarrhea, nature of diarrhea, duration of diarrhea, knowledge about guidelines for childhood diarrhea and antibiotics, brief demography of case and concomitant diseases. The questionnaire contained scoring from 1 to 5 for each question. Descriptive statistics was used to describe the variables of the study. P values were calculated through Z-test using SPSS software and p-values less than 0.05 were considered as statistically significant.

## Results

Table 1 shows the antibiotics prescribed for children less than 5 years of age for acute diarrhea. The prescribed antibiotics did not comply with NICE guidelines when assessed on the basis of nature, duration and episodes of acute diarrhea. Although the prescribing practices of injectable preparations in acute diarrhea was less than that of oral dosage forms but 480 prescriptions out of total 500 prescriptions contained un-necessarily prescribed antibiotics that can lead to antibiotic resistance in pediatric population. The combination of diloxanide furoate and metronidazole as syrup dosage form was the most frequently prescribed antibiotic for childhood acute diarrhea because prescribers considered that the anti-microbial coverage of this combination would be more effective than other single generic formulae of antibiotics.

Table 1: Prescribed medications for acute diarrhea in children less than 5 years of age

Medications	Number of Prescriptions (n=500)	Percentage of prescriptions
Oral Diloxanide furoate + Metronidazole combination	187	37.4%
Oral Ciprofloxacin	75	15%
Cefixime suspension	125	25%
Oral Metronidazole	65	13%
Metronidazole infusion	5	1%
Ceftriaxone infusion	3	0.6%
Nitazoxanide suspension	15	3%
Ciprofloxacin infusion	5	1%

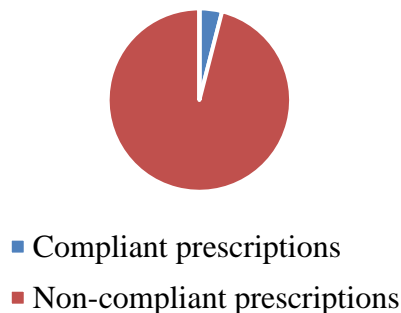
In Table 2, it is evident that the probability of inappropriate prescribing of antibiotics in childhood diarrhea was higher because p-value was less than 0.05 as calculated by descriptive statistical tools. P-value was highly significant as determined by Z-test using SPSS software. The main concomitant symptoms were dehydration; vomiting and abdominal pain but these symptoms did not need antibiotic prescribing. Most of the children suffering from acute diarrhea had normal body weight and the duration of diarrheal episodes was than 3 days. The prescriptions of general practitioners for childhood acute diarrhea deviated more from NICE guidelines than that of pediatricians.

Only 4% prescribers had compliance with clinical guidelines for acute diarrhea in children less than 5 years of age while 96% prescribers irrationally prescribed antibiotics as shown in Figure 1. A brief questionnaire distributed among prescribers, pharmacists and caretakers of children revealed their opinions for the rationale of prescribing antibiotics in children less than 5 years of age for acute diarrhea.

The rationale put forward by most of the prescribers for antibiotic prescribing in such cases was to prevent further risks and chances of chronic diarrhea while some of them documented that antibiotic prescribing was for the satisfaction of caretakers as 90% of the parents complied with antibiotic prescribing in acute diarrhea and considered it effective for treatment. Only 3% prescribers accepted it being due to limited knowledge of authentic and updated clinical guidelines. Some of the pharmacists considered these practices as blindly following the past practices of other prescribers while most of them had opinions that it is due to the information provided by medical representatives to the prescribers about the benefits of the prescribed medicine (Figure 2).

Figure 1: Prescribers' compliance with guidance for childhood acute diarrhea

### Prescribers' compliance with guidelines for acute diarrhea



### Discussion

The frequent passage of three or more loose or watery stools per day is referred to as diarrhea and when this increased bowel movement ends within three weeks, it is called acute diarrhea. As per the authentic treatment guidelines for acute diarrhea in children under five years of age, oral rehydration therapy is the mainstay of treatment. Irrespective of etiology, treatment with diosmectite and probiotic powders or solutions must continue along with rehydration therapy. Clinical conditions of child and host-related aspects must be considered while prescribing treatment for acute diarrhea.

Antibiotic therapy must not be started when clear indications for the need of antibiotic therapy are absent because symptoms of acute diarrhea usually subside with oral rehydration therapy and probiotics. Antibiotics can be considered for treatment if diarrhea becomes chronic, child is at risk or is severely ill but microbiological investigations are necessary. World Health Organization does not recommend the use of antibiotics in children for acute diarrhea except for those with severe clinically identified

cases. Antibiotics can be considered for acute diarrhea with bloody stool, severe traveler's diarrhea, diarrhea with some other super-imposed infection for which antibiotic is essential, diarrhea with high grade fever and for immunocompromised children. Oral zinc in the form of zinc sulphate suspension can also be prescribed as zinc is severely lost from the body during diarrheal condition.

Childhood diarrhea accounts for 16% of child deaths in Pakistan. The prescribing practices of injectable preparations in acute diarrhea is although less than that of oral dosage forms in Secondary Healthcare setting of Pakistan but irrational prescribing of antibiotics for diarrhea in pediatric population is common. This study revealed that the combination of diloxanide furoate and metronidazole was the most frequently prescribed antibiotic for childhood acute diarrhea.

The two major reasons told by most of the prescribers for prescribing antibiotics were to prevent the transformation of acute diarrhea to chronic diarrhea and the compliance of parents with antibiotics for resolution of diarrheal condition. Pharmacists considered that the prescribing of antibiotics in acute diarrhea to children less than five years of age was due to the limited knowledge of prescribers for clinical guidelines, following the past practices of other prescribers or due to the information provided by the medical representatives from different pharmaceutical industries for their products.

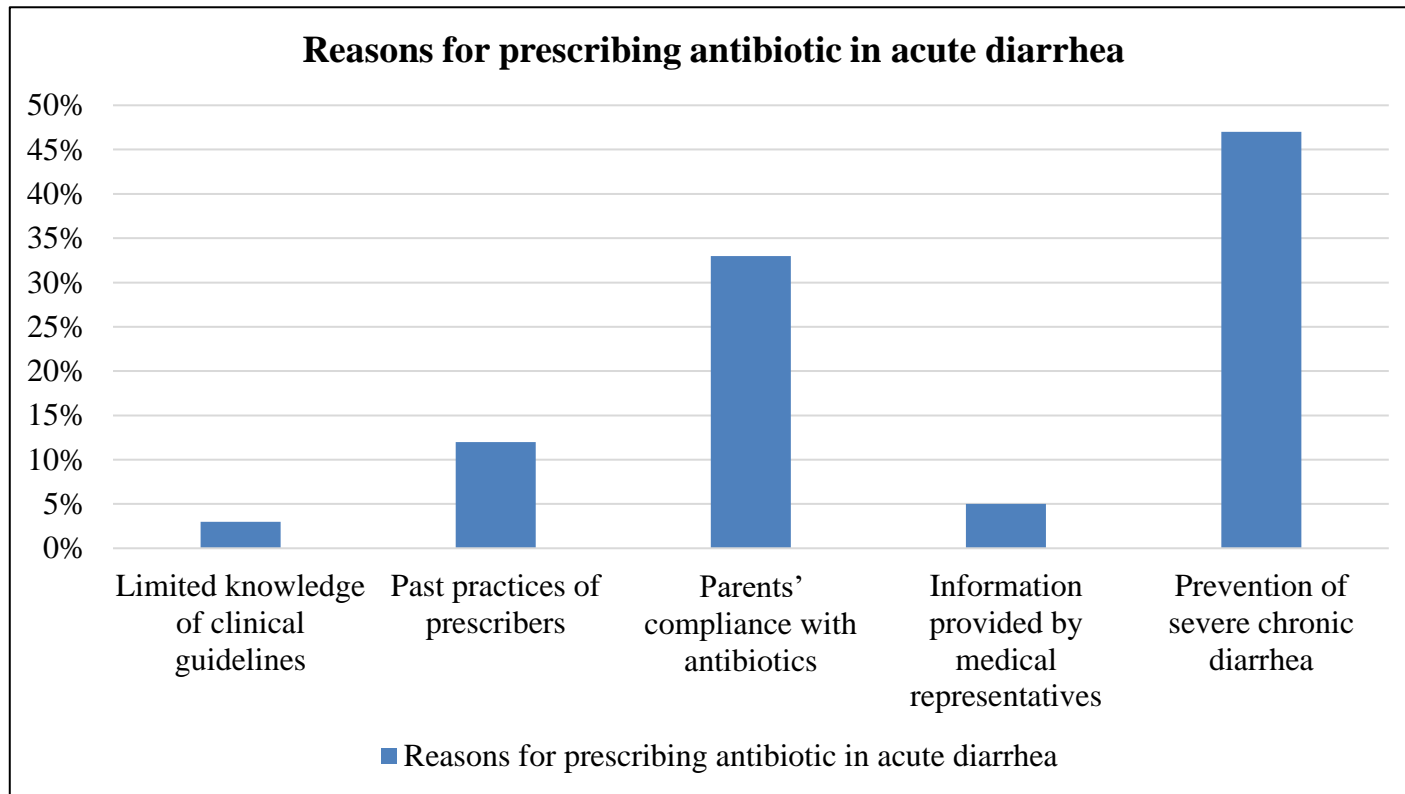
More than 90% prescriptions of acute diarrhea in children less than five years of age failed to comply with the authentic treatment guidelines. Healthcare professionals must be adequately trained to ensure the proper management of acute diarrhea by following authentic clinical guidelines, such as guidelines by WHO or NICE. Healthcare education and awareness programs, health interventions and healthcare audits are necessary to promote rational use of medications in childhood acute diarrhea.

Vaccinations of children against *Escherichia coli*, *Shigella* spp. and rotavirus must be regarded mandatory by the government. Presence of NEML must be assured at all the healthcare settings and all the medications mentioned in it for diarrhea must be available at every healthcare area of Pakistan. The therapy for acute diarrhea in children less than five years of age must be according to the severity of clinical condition and oral rehydration therapy must be ensured. Parents or caretakers of children must be convinced by healthcare professionals to discourage the irrational use or prescribing of antibiotics for acute diarrhea in children less than five years of age in Pakistan.

Table 2: Demography, concomitant symptoms, and prescribers' qualification

Characteristics	Number of prescriptions	Inappropriate prescriptions	Percentage of inappropriate prescriptions	p value
Diarrhea	500			p<0.05
Age (months)				
1-12	130	125	96%	
13-24	142	140	98%	
25-36	107	106	99%	
37-46	52	49	94%	
47-60	69	60	86%	
Fever	60			
Dehydration	456			
Vomiting	391			
Abdominal pain	442			
Weight				
Under-weight	113			
Normal weight	387			
Overweight	0			
Duration of diarrhea				
Less than 3 days	289			
3-7 days	200			
8-14 days	11			
Prescribers' qualifications				p<0.05
General practitioners	215	208	96%	
Pediatricians	285	272	95%	

Figure 2: Reasons for prescribing antibiotics for acute diarrhea in children aged less than 5 years



## Conclusion

Antibiotics are irrationally prescribed for acute diarrhea in children less than five years of age at Secondary Healthcare Hospital of Pakistan and prescriptions do not comply with the authentic clinical guidelines due to the limited knowledge of prescribers regarding treatment guidelines and compliance of parents with antibiotic prescribing for diseases in children.

## Conflict of Interest

The author has no conflicts of interest to report.

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