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REVIEW ARTICLE

# Antibiotic therapy in dysentery of infectious etiology in early childhood: a systematic scoping review

*Juan F. Guevara-Ramírez[1]*, Andrés F. Rodríguez-Gutiérrez[1], Ingrid S. Sánchez-Escobar[1], Samuel D. Bolaños-Rodríguez[1], Valentina Adames-Restrepo[1], Simón A. Ruiz-Galvis[1], Valentina Sánchez-Sánchez[1], Néstor A. De La Cruz-Torres[1], Erwin H. Hernández-Rincón[2], and Samuel D. Barbosa[3,4,5]*

*[1]Faculty of Medicine, Universidad de La Sabana, Chía, Cundinamarca, Colombia; [2]Department of Family Medicine and Public Health, School of Medicine, Faculty of Medicine, Universidad de La Sabana, Chía, Cundinamarca, Colombia; [3]Colegio Médico Colombiano, Bogotá, Colombia; [4]Universitat Oberta de Catalunya, Barcelona, Cataluña, España; [5]Sociedad Colombiana de Pediatría, Bogotá, Colombia*

## Abstract

*Acute diarrhea (AD) is one of the leading causes of child mortality, particularly in children under 5 years old. Dysentery, a severe form of AD characterized by blood and mucus in the stool, raises controversies regarding the appropriate use of antibiotics. The objective of this manuscript is to synthesize the available information on the indications, risks, and benefits of antibiotics used in infectious dysentery during early childhood. A scoping systematic review was conducted using international reference documents and the databases PubMed, Scopus, and Google Scholar, following the PRISMA-ScR guidelines. Studies from 2014 onwards that addressed antibiotic management in children under 5 years old with bacterial or parasitic dysentery were included. Among the 39 selected studies, the evidence shows limited benefits and significant risks associated with antibiotic use, with recommendations varying based on specific etiology and the patient's clinical conditions, where it is evident that the rational use of antibiotics in pediatric dysentery is crucial to avoid bacterial resistance and adverse effects. There is a need for future research to establish guidelines based on robust clinical trials, to optimize targeted treatment and improve clinical outcomes in this population.*

**Keywords:** *Dysentery. Antibiotics. Children. Diarrhea. Infantile. Drug Resistance. Microbial.*

## *Antibioticoterapia en la disentería de etiología infecciosa en la primera infancia: una revisión sistemática panorámica*

## Resumen

*La enfermedad diarreica aguda (EDA) es una de las principales causas de mortalidad infantil, especialmente en menores de 5 años. La disentería, una forma severa de EDA con sangre y moco en las heces, genera controversias sobre el uso adecuado de antibióticos. El objetivo de este manuscrito es sintetizar la información disponible sobre las indicaciones, riesgos y beneficios de los antibióticos en la disentería infecciosa en la primera infancia. Se realizó una revisión sistemática panorámica utilizando documentos de referencia internacional y las bases de datos PubMed, Scopus y Google Scholar, siguiendo los lineamientos PRISMA-ScR. Se incluyeron estudios desde 2014 que abordaran el manejo antibiótico en menores de 5 años con disentería*

***Correspondence:**
Juan F. Guevara-Ramírez
E-mail: juanguera@unisabana.edu.co

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*de origen bacteriano o parasitario. De 39 documentos seleccionados, la evidencia muestra beneficios limitados y riesgos significativos en el uso de antibióticos, con recomendaciones que varían según la etiología específica y las condiciones clínicas del paciente, donde se evidencia que el uso racional de antibióticos en disentería infantil es crucial para evitar la resistencia bacteriana y efectos adversos. Se destaca la necesidad de investigaciones futuras para establecer guías basadas en ensayos clínicos robustos, que optimicen el tratamiento dirigido y mejoren los resultados clínicos en esta población.*

***Palabras clave:*** *Disentería. Antibióticos. Niños. Diarrea Infantil. Farmacorresistencia. Microbiana.*

## Introduction

Acute diarrheal disease (ADD) accounts for 8.6% of infant mortality. It is one of the main reasons for medical consultation worldwide, primarily in children under 5 years of age (early childhood). It is the fourth leading cause of such outcomes in 499 thousand patients affected by this condition[1]. Most of these cases are due to complications such as dehydration from the number of stools, oral intolerance, and septic shock related to acute gastroenteritis, defined as any gastrointestinal infection lasting < 2 weeks[2], clinically identified by at least three episodes of liquid or watery stools within 24 h, usually associated with fever and emetic episodes[3].

One of its clinical manifestations is dysentery, characterized by the presence of blood and mucus in stools, which can occur due to different infectious agents and their biological toxins (Table 1), causing an intestinal inflammatory process with polymorphonuclear infiltrates leading to mucosal ulcers, hemorrhage, production of peptide cytokines that generate changes in metabolism, appetite, and loss of nutrients and body fluids, clinically referred to as a "dysenteric syndrome," which also includes certain associated symptoms such as fever, colic, tenesmus, and straining[2,3].

This phenomenon represents a major challenge in reaching consensus and institutional proposals, including those from international organizations such as the World Health Organization (WHO)[4], Pan American Health Organization (PAHO)[5], and the Infectious Diseases Society of America (IDSA)[6]. These bodies have not managed to align on universal proposals that would establish definitive and clear recommendations for standardized empirical management.

The lack of clear protocols for managing dysentery in early childhood has been a significant issue since the original 2005 WHO guidelines on ADD management, which remain current. This originates from their recommendation to empirically administer antibiotic therapy for dysentery in early childhood without demonstrating which studies at that time supported such a decision, along with the scarcity of specific studies in children under 5 years of age across indexed databases and grey literature. All of this has resulted in a lack of international consensus on adjunctive management beyond the rehydration inherent to conventional ADD treatment, which aims to reduce symptom intensity and duration regardless of etiology[7]. One of the key issues in this context is whether or not to administer antibiotic therapy to the affected patients.

**Table 1.** Relevant micro-organisms in early childhood dysentery

| Bacteria | Parasites |
|---|---|
| *Escherichia coli** | *Entamoeba histolytica* |
| *Salmonella* | *Cystoisospora* |
| *Shigella* | *Cyclospora cayetanensis* |
| *Campylobacter* | |
| *Clostridioides difficile* | |
| *Yersinia enterocolitica* | |

*Source: Authors' own elaboration based on information extracted from Kliegman et al.[1], Levy[27].*
*Includes Shiga toxin-producing bacteria (STEC).

This article aims to synthesize the available evidence from the last 10 years addressing the following question: in early childhood children with dysentery of infectious etiology, what are the indications, risks, and benefits of antibiotic therapy compared to non-administration? Given the limited available information, conducting a panoramic systematic review was deemed appropriate to gather information from various sources, obtaining an overview of the topic with emphasis on available information and identifiable knowledge gaps for each possible bacterial and parasitic micro-organism.

This has been viewed as an opportunity for rational antibiotic use in the everyday clinical setting of pediatricians and primary care physicians, calling attention to a critical and updated perspective due to its clinical impact in a world striving to reduce bacterial resistance through clear indications and correct dosing. In addition, it aims to avoid unfavorable outcomes when antibiotics are not indicated, which affect not only the individual and their family but also the community at large[1].

## Method

### Study design

A scoping review of medical literature was conducted to evaluate the available evidence on the indications, risks, and benefits of antibiotic therapy in infectious dysentery during early childhood. This review followed international guidelines established by the Enhancing the Quality and Transparency of Health Research network, using their PRISMA Extension for Scoping Reviews (PRISMA-ScR)[8] guidance.

### Search strategy

The search was conducted in PubMed, Scopus, UpToDate, and Google Scholar databases, as well as in gray literature, using the following search terms in English and their Spanish equivalents: ("Antibiotics" OR "Antibiotic therapy") AND "Dysentery" AND ("Bacteria" OR "Parasite" NOT "Virus") AND ("Infant" OR "Children" NOT "Adults"). The search strategy was designed to capture the largest possible number of relevant studies, ensuring a comprehensive and transparent evaluation of the studies found and available for review.

### Study selection

Studies were selected based on the following predefined criteria:

- Inclusion criteria: Publication from 2014 onwards, complete document with available access, studies including children under 5 years with dysentery of bacterial or parasitic origin, written in Spanish or English. Study types had to be meta-analyses, review articles, analytical and experimental studies, guideline documents, or management references
- Exclusion criteria: Publications before 2014, studies on prophylactic antibiotic management, or non-scientific sources.

### Selection process

Search results were managed bibliographically using Mendeley reference software after duplicate studies were removed. Titles and abstracts of identified manuscripts were evaluated to determine their eligibility for full-text review and subsequent extraction of their analyses and conclusions for synthesis and comparison with other sources found in the text, according to each infectious etiology. This allowed for identifying common patterns and discrepancies among recommendations regarding antibiotic use in our target population.

### Data extraction and analysis

Relevant data regarding recommendations, population characteristics, isolates, and association measures were extracted from the selected studies, identifying possible indications, risks, and benefits of antibiotic use in infectious dysentery in children under 5 years of age.

Study characteristics, design, sample size, main outcomes, and recommendations were considered in writing this article as a practical aid for primary care physicians and general pediatricians who face this clinical challenge. This information is presented through synthesis tables and sections in the subsequent discussion of the article. In addition, secondary references from the main articles contributing to the development were included.

## Results

Following the described processes, 39 documents were selected for complete review. These included 18 reference articles and consensus statements and 15 additional studies discussed in detail (Fig. 1).

The analysis proceeded from an initial general approach toward identifying specific etiologies and particular situations of infectious dysentery in early childhood. From the selected documents, the following types of studies were identified:

- Two narrative reviews
- Two cross-sectional studies
- Two cohort studies
- One case–control study
- Three systematic reviews
- One meta-analysis
- One clinical trial.

Table 2 synthesizes the main findings from these studies, providing a comprehensive overview of the different perspectives and available data.

### Antibiotic therapy regimens

The respective dosing schedules found for each indication are summarized in table 3. This table provides a detailed summary of the different antibiotic regimens currently recommended by international expert societies in this field of study, along with those used in intervention articles identified after the search process,

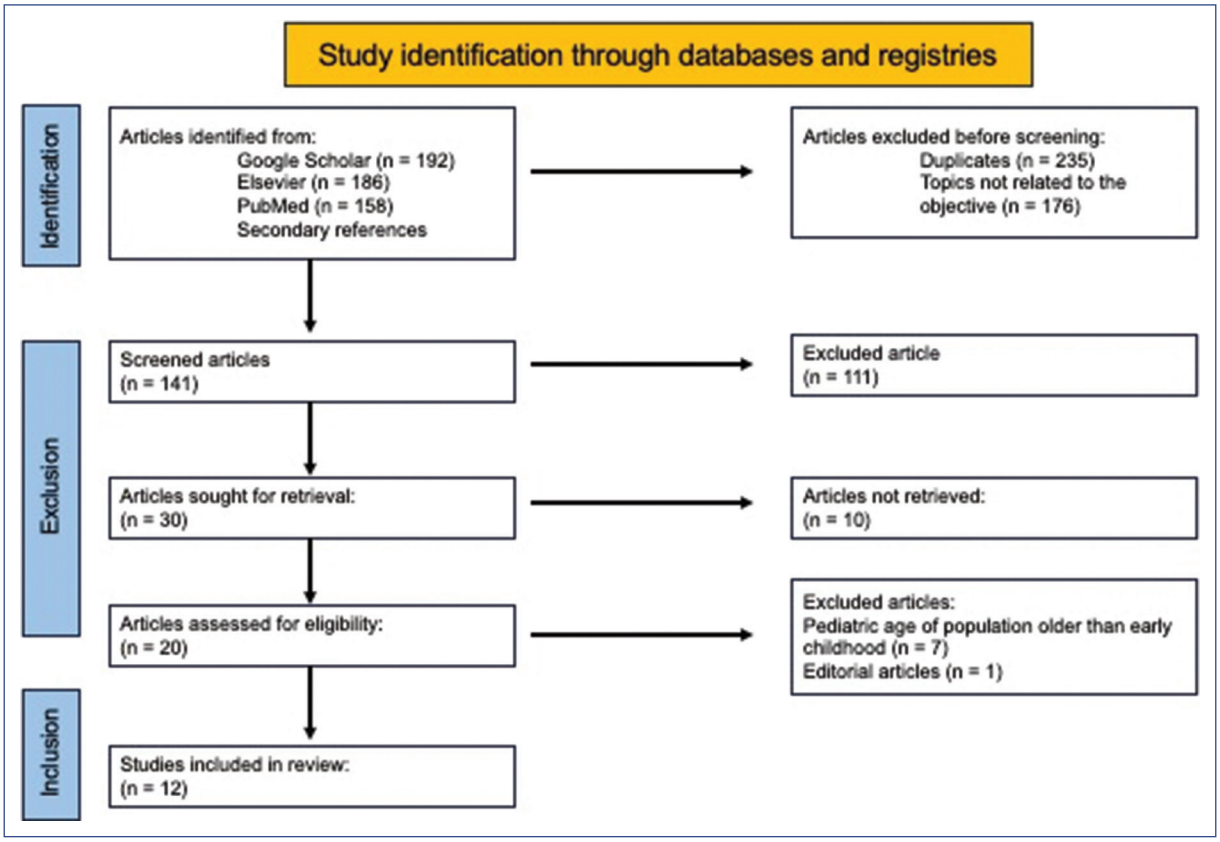


**Figure 1.** PRISMA flow chart for study selection.

based on specific etiology and the patient's clinical conditions as appropriate.

## Discussion

### *Isolates and empirical management*

Implementing new technologies for diagnosing and isolating specific pathogens in dysentery has undergone multiple changes, facilitating the identification of causative micro-organisms. Despite this, at the international level, no consensus indicates how to direct antimicrobial therapy in the pediatric population with infectious dysentery[7].

The only current international guideline on empirical management of dysentery in early childhood is WHO's fourth edition recommendations from 2005, which suggests 3 days of ciprofloxacin or 5 days of another antimicrobial effective against local *Shigella* strains[4]. Although this controversial point was mentioned without supporting clinical trials or studies, the use of nalidixic acid is discouraged, apparently due to increased antibiotic resistance against this antimicrobial[4]. In contrast, the Procedures Manual for the Integrated Management of Childhood Illness written by PAHO does recommend it as the first-line treatment based on expert consensus due to the risk of complications from dysenteric syndrome, given the difficulty in patient follow-up and limited resources in the areas where it is applied[5]. However, considering the recent changes in international antibiotic resistance patterns, it coincides with the WHO reference document in not citing studies supporting this decision.

In 2017, IDSA initiated an approach not previously mentioned by these two prior organizations, which was to give precedence to microbiological diagnosis before deciding on antibiotic treatment in cases of clinical significance, especially for identifying infections caused by *Salmonella enterica*, *Shigella*, *Campylobacter*, *Yersinia*, Shiga toxin-producing bacteria (STEC), and other local parasites[6].

Thus, they acknowledge the importance of microbiological technology use in clinical decision-making, prioritizing the clinical scenarios outlined in table 4, where they consider the need for immediate antimicrobial treatment with azithromycin or third-generation cephalosporins[6]. However, the results of the studies

**Table 2.** Evidence from studies included in the text

| Study data | Study type | Objectives and/or type of intervention | Results and Conclusions |
|---|---|---|---|
| Authors: Bruzzese et al., 2018[7] Country: Italy | Narrative review | Based on 57 published articles without a specific population, this study aims to describe the indications and antibiotic regimens used internationally for the treatment of acute gastroenteritis, including in South America, Europe, Asia, and Africa, based on the microbiological isolates reported in these studies. | The authors conclude that the administration of antibiotic therapy in the context of acute gastroenteritis may be justified under the following factors: Clinical conditions: dysenteric diarrhea, fever, increased inflammatory markers, prolonged diarrhea, small intestinal bacterial overgrowth, antibiotic-associated diarrhea, and toxic state. Host-related risk factors: age under<3 or 6 months, severity of clinical presentation, malnutrition, underlying chronic disease, and immunodeficiency. Environmental factors: daycare centers, hospitals, institutions, and traveler's diarrhea. |
| Authors: Kotloff et al., 2018[23] Country: United States | Narrative review | A total of 139 articles and clinical trials were reviewed to establish a standardized definition, pathogenesis, and epidemiology of *Shigella* dysentery, considering its clinical manifestations, diagnostic tests, treatment, and environmental prevention. | First- and second-line treatments for managing shigellosis in both adults and children have been established. However, the presence of Shiga toxin does not always guarantee pharmacological success in patients. Consequently, preventive measures, such as hygiene, proper nutrition, and environmental contamination prevention, have been suggested and progressively implemented. |
| Authors: O'Ryan et al., 2014[21] Country: United States | Narrative review | A review was conducted analyzing the rationale and potential pathogen-specific benefits of antimicrobials and empirical management based on 75 articles. | Underlying malnutrition and diseases such as AIDS increase the severity and risk of unfavorable outcomes. Evidence showed that early hospitalization in severely malnourished children reduces mortality. In addition, the review emphasizes the importance of limiting antibiotic use exclusively to patients at high risk of complications, rather than employing it as a routine practice. |
| Authors: Morán et al., 2023[34] Country: Mexico | Narrative review | Current concepts in the pathogenesis, diagnosis, treatment, and interactions with the microbiota during *Entamoeba* infection were reviewed across 115 articles, comparing amebicide management in international guidelines. | The study suggests the importance of reliable diagnostic tools, such as molecular tests, to guide treatment. A proposed approach includes luminal treatments (paromomycin, diloxanide furoate, iodoquinol, and nitazoxanide) and extraluminal amebicides (chloroquine, tinidazole, and metronidazole) to reduce morbidity and mortality and ensure appropriate management. However, these tests are high-cost and may be challenging to implement in certain contexts. |
| Authors: Somji et al., 2024[15] Country: Bangladesh, India, Kenya, Malawi, Mali, Pakistan, and Tanzania | Cross-sectional analysis | A total of 6,692 children under 2 years of age with moderate-to-severe diarrhea and available qPCR isolates were analyzed to identify clinical characteristics associated with a likely bacterial etiology. The findings revealed correlations with more than six stools in the previous 24 h (OR 1.20, 95% CI 1.05–1.36), moderate acute malnutrition (OR 1.56, 95% CI 1.18–2.08, $p = 0.002$), dehydration (OR 1.66, 95% CI 1.25–2.22, $p < 0.001$), and the combination of these two conditions (OR 2.21, 95% CI 1.61–3.06, $p < 0.001$). No clinical correlation was found with reports of fever or prolonged diarrhea duration. | It was concluded that the presence of moderate acute malnutrition, dehydration, or high stool frequency can help identify children with moderate-to-severe diarrhea who may benefit from antibiotic treatment. |
| Authors: Zachariah et al., 2021[29] Country: Kenya | Cross-sectional study | The study aimed to determine the prevalence of antibiotic resistance and sensitivity profiles of *Shigella* and *Campylobacter* in fecal samples from 139 children with diarrhea at a hospital in Kenya. | High resistance to common antibiotics was found in *Shigella spp.* and *Campylobacter jejuni*, with 33.1% of samples testing positive for enteric pathogens. *Shigella spp.* exhibited resistance to erythromycin (91.7%), doxycycline (83.3%), ampicillin (82.1%), cotrimoxazole (73.1%), minocycline (66.7%), and cefuroxime (54.2%). *Campylobacter jejuni* also showed resistance to erythromycin (87.5%), doxycycline (75%), ampicillin (73.7%), cotrimoxazole (73.3%), and minocycline (68.8%). These findings underscore the importance of appropriate antibiotic use. |

(*Continues*)

**Table 2.** Evidence from studies included in the text *(continued)*

| Study data | Study type | Objectives and/or type of intervention | Results and Conclusions |
|---|---|---|---|
| Authors: Yehonatan et al., 2023[11] Country: Israel | Retrospective cohort study | The study included 281 patients aged 0-18 years with a clinical diagnosis of dysentery, of whom 247 (88%) were under 7 years old, and only 234 (83%) received antibiotic treatment. Cultures were positive in 162 cases (58%), showing that among children receiving empirical treatment, only 134 (57%) had a positive culture, whereas 28 children (60%) were not empirically treated despite having a positive culture. | No correlation was found between microbiological isolation and initiation of antibiotic therapy (p = 0.77) or patient age (under 5 years, p = 0.314). However, there was an association between the initiation of antibiotic therapy and the presence of fever (p = 0.004), leukocytosis (> 15×10≥/uL, p = 0.026), and neutrophilia (> 15×10≥/uL, p = 0.002). Finally, 34 children (16.7%) with positive isolates for *Shigella spp.*, *Salmonella spp.*, or *Campylobacter spp.* did not receive antibiotics and did not require emergency readmission. |
| Authors: Wong et al., 2012[13] Country: United States | Prospective cohort study | From 1997 to 2006, a population of 259 children under 10 years old and older than 7 days, infected with *E. coli* O157:H7 and presenting with diarrhea, was included in a clinical and paraclinical follow-up to monitor their hematological and renal function until diarrhea resolved or hemolytic uremic syndrome (HUS) developed. HUS was defined as a hematocrit < 30% with evidence of hemolysis in a peripheral blood smear, platelet count < 150,000/µL, and serum creatinine above the age-specific normal limit with oligoanuria. Of the total population, 36 children (14%) developed HUS, showing that children who received antibiotics during the diarrheal episode were more likely to develop HUS compared to those who did not (13%, p = 0.001). This increased risk was observed across all classes of antibiotics used (TMP/SMX, beta-lactams, metronidazole, azithromycin). A multivariate analysis demonstrated that elevated leukocyte count (OR 1.10, 95% CI 1.03–1.19), emesis (OR 3.05, 95% CI 1.23–7.56), and antibiotic exposure (OR 3.62, 95% CI 1.23–10.6) during the 1st week of illness were independently associated with the development of HUS. | In children with diarrhea caused by *E. coli* O157:H7, emesis, elevated leukocyte counts, and antibiotic use during the 1st week of illness independently increased the risk of developing HUS. |
| Authors: Zamanlou et al., 2022[26] Country: Iran | Case–control study | A total of 89 fecal samples were collected from children under 12 years old with diarrhea or dysentery, comprising 56 samples of *Shigella flexneri* and 33 of *Shigella sonnei*. These samples underwent disk diffusion testing, agar dilution methods, and detection of class 1 or 2 extended-spectrum beta-lactamase (ESBL) integrons through PCR. | Antimicrobial resistance mechanisms were detected, complicating the selection of appropriate antimicrobial agents for children with shigellosis. These mechanisms included the presence of ESBL genes in 60 samples (67.4%) and azithromycin resistance in 16 isolates. In addition, 71.24% of the strains harbored class 1 integrons, whereas 95.82% carried class 2 integrons. |

*(Continues)*

**Table 2.** Evidence from studies included in the text *(continued)*

| Study data | Study type | Objectives and/or type of intervention | Results and Conclusions |
|---|---|---|---|
| Authors: Gonzales et al., 20193[5] Country: Philippines | Systematic review | The effectiveness of tinidazole and metronidazole for amebic colitis was compared across 41 trials involving a total of 4,999 participants. Only one trial met the criteria for random allocation, blinding, and analysis of all participants. | Tinidazole may be more effective than metronidazole in reducing clinical failure (RR 0.28; 95% CI 0.15–0.51, low-certainty evidence) and is probably associated with fewer adverse events (RR 0.65; 95% CI 0.46–0.92, moderate-certainty evidence). Compared to metronidazole, combination therapy may result in fewer parasitological failures (RR 0.36; 95% CI 0.15–0.86, low-certainty evidence). However, no conclusive findings suggested that combination therapy is superior to other treatments. Nevertheless, the evidence is based on small and outdated studies, highlighting the need for updated and robust research. |
| Authors: Khademi et al., 2019[25] Country: Iran | Meta-analysis | Data from 25 published articles on antibiotic resistance in *Shigella* among individuals under 18 years old were collected from various databases. All included studies utilized the disk diffusion test as the sole susceptibility testing method. | Across the included studies, ciprofloxacin can still be used as a first-line treatment, whereas antimicrobials like ceftriaxone and azithromycin are not recommended for treatment. Resistance was found as follows:<br>Ciprofloxacin: *S. dysenteriae* 7%, *S. flexneri* 3.8%, S. boydii 6.9%, and *S. sonnei* 2.6%.<br>Ceftriaxone: *S. dysenteriae* 27.9%, *S. flexneri* 19.3%, S. boydii 15.7%, and *S. sonnei* 9.5%.<br>Azithromycin: *S. dysenteriae* 91.7%, *S. flexneri* 20.7%, S. boydii 46.7%, and *S. sonnei* 32.3%. |
| Authors: Ahmed et al.[12] Year: 2021 Country: Bangladesh, India, Kenya, Malawi, Mali, Pakistán y Tanzania. | Randomized Clinical Trial | The study aimed to determine whether adding azithromycin to standard treatment for acute non-bloody watery diarrhea in 8,598 dehydrated or malnourished children aged 2-23 months could reduce mortality and improve linear growth. Participants were randomly assigned to receive either oral azithromycin 10 mg/kg or placebo once daily for 3 days in cases of acute watery diarrhea. The study included children with mild and/or severe dehydration, or moderate malnutrition, and/or severe growth retardation. Primary outcomes were all-cause mortality within 180 days of enrollment and change in linear growth measured as change in length-for-age z-score at 90 days.<br>The antibiotic was administered to 4,463 children (54.0%), with a mean age of 11.6 months. In this group, 0.5% (20) died, compared to 0.7% (28) of 4,135 children in the placebo group (RR 0.72; 95% CI, 0.40-1.27; p = 0.25). The azithromycin group had 170 hospitalizations by day 90 compared to 211 in the placebo group (4.1% vs. 5.1%; RR 0.81; 95% CI, 0.66-0.98). The change in standard deviations in length-for-age z-scores at 90 days was –0.16 (0.59) in the azithromycin group and –0.19 (0.60) in the placebo group (risk difference, 0.03; 95% CI, 0.01-0.06; p = 0.007). | The study found no survival benefit from adding azithromycin to WHO standard treatment for acute watery diarrhea cases in low-resource settings. There was a small reduction in linear growth retardation, though it was not considered clinically significant. The trial was ultimately stopped for futility at the pre-specified interim analysis, concluding that expanding antibiotic use in low-resource settings is not justified. |

qPCR: quantitative polymerase chain reaction; RR: relative risk; CI: confidence interval; *S. dysenteriae: Shigella dysenteriae; S. flexneri: Shigella flexneri; S. boydii: Shigella boydii; S. sonnei: Shigella sonnei.*

**Table 3.** Summary of antibiotic dosing for infectious dysentery in early childhood according to etiology

| Note: Isolation of any of these micro-organisms is not an absolute indication for antibiotic therapy. Review indications and susceptibility for each case before prescription. | |
|---|---|
| **Micro-organism** | **Dosage and duration** |
| *Salmonella* | Typhoid:<br>Ceftriaxone 75-80 mg/kg (maximum 2 g/dose) or 1 g/day (HIV) IV as single dose for 5-14 days, or cefotaxime 150-200 mg/kg/day IV divided every 6-8 h for 10-14 days, or azithromycin 10-20 mg/kg PO as single dose (maximum 1 g/day) for 5-7 days, or *ciprofloxacin 30 mg/kg/day (maximum 1 g/day) PO divided every 12 h for 7-10 days, or *ciprofloxacin 20 mg/kg/day (maximum 800 mg/day) IV divided every 12 h for 7-10 days, or *cefixime 20 mg/kg/day (maximum 400 mg/day) PO divided every 12 h for 10-14 days, or *meropenem 20 mg/kg/dose IV (maximum 1 g/dose) every 8 h.<br>Non-typhoid:<br>Azithromycin 10 mg/kg PO as single dose on day one, followed by 5 mg/kg PO as single dose to complete 5-10 days of treatment, or ceftriaxone 50 or 75-100 mg/kg IV as single dose for 5-14 days, or *ciprofloxacin 15 or 20-30 mg/kg/dose (maximum 500 mg/dose) PO divided every 12 h for 3-7 days, or *TMP/SMX at 8-10 mg/kg/day of TMP PO divided every 12 h for 3-7 days.<br>Salmonellosis in immunocompromised cases should be treated for at least 14 days, whereas meningitis cases should extend treatment to 4 weeks, or 4-6 weeks in cases of osteomyelitis or other metastatic focal lesions. |
| *Shigella* | Ceftriaxone 50 mg/kg/day (maximum 1.5 g/day) IV or IM as a single dose for 2-5 (usually 3) days, or ciprofloxacin 15 mg/kg/dose (maximum 400 mg/dose) PO divided every 12 h for 3-5 days, or azithromycin 12 mg/kg (maximum 500 mg/dose) PO as a single dose on day one. Complete regimen with 3-4 more days at 5-6 mg/kg (maximum 250 mg/dose) PO as single dose, or azithromycin 10 mg/kg (maximum 500 mg/dose) PO as single dose for 3 days, or *cefixime 8 mg/kg PO as a single dose for 3 days, or *TMP/SMX at 4 or 8-10 mg/kg/day of TMP PO divided every 12 h for 3-5 days. |
| *Campylobacter* | Azithromycin 10 mg/kg PO as a single dose for 3 days (5 days in HIV cases), or erythromycin 40 mg/kg/day PO divided every 8 h for 5 days, or *azithromycin 30 mg/kg PO as a single dose. *ciprofloxacin 10-15 mg/kg/dose (maximum 750 mg/dose) PO every 12 h for 3-5 days. HIV cases may require 7-10 days. |
| *Clostridioides difficile* | Mild-or-moderate disease:<br>Metronidazole 30 mg/kg/day PO divided every 6 h (maximum 500 mg/dose) for 10 days, or *vancomycin 40 mg/kg/day PO divided every 6 h (maximum 125 mg/dose) for 10 days.<br>Severe disease:<br>Consider in cases of leukocytosis, leukopenia, or clinical deterioration. Vancomycin 40 mg/kg/day PO divided every 6 h for 10 days, or the same vancomycin dose PR in a ratio of 500 mg/100 ml NS as enema. Either option +/- metronidazole 30 mg/kg/day IV divided every 8 h for 10 days.<br>Severe and complicated disease:<br>Intensive care admission, hypotension, shock, endoscopy with pseudomembranous colitis, ileus, or toxic megacolon. Vancomycin 40 mg/kg/day PO divided every 6 h for 10 days, with metronidazole 30 mg/kg/day IV divided every 6 h for 10 days. In cases of distention, ileus, or toxic megacolon, add vancomycin enema until improvement (see above).<br>Second or additional episodes:<br>Vancomycin 10 mg/kg/dose (maximum 125 mg/dose) PO every 6 h for 7 days, then every 8 h for 7 days, then every 12 h for 7 days, then every 24 h for 7 days, then every 48 h for 7 days, then every 72 h for 7 days, or vancomycin 10 mg/kg/dose (maximum 125 mg/dose) PO every 6 h for 14 days, then every 12 h for 7-14 days, then every 24 h for 7-14 days, then every 24-72 h for 2-8 weeks, or vancomycin 10 mg/kg/dose (maximum 125 mg/dose) PO every 6 h for 14 days, followed by rifaximin 400 mg PO as single dose every 8 h for 14 days, or fidaxomicin with weight-based dosing** PO every 12 h for 10 days. |
| *Yersinia enterocolitica* | TMP/SMX at 8-10 mg/kg/day of TMP PO divided every 12 h for 7 days, or cefotaxime 150-200 mg/kg/day IV divided every 6-8 h. No defined duration period. |
| *Entamoeba histolytica* | Cyst carrier:<br>Iodoquinol 30-40 mg/kg/day PO divided every 6-8 h (maximum 650 mg/dose) for 20 days, or paromomycin 25-35 mg/kg/day PO divided every 8 h for 7-10 days, or diloxanide furoate 20 mg/kg/day PO divided every 8 h (maximum 500 mg/dose) for 10 days.<br>Invasive disease:<br>Metronidazole 30-40 or 50 mg/kg/day PO divided every 8 h for 7-10 days, or tinidazole 50 mg/kg PO as a single dose (maximum 2 g/day) for 3 days. Consider 5 or even 10 days in severe cases. Either option should be followed by one of the treatments used for cyst carriers at those doses. |
| *Cystoisospora* | TMP/SMX at 8-10 mg/kg/day of TMP or 15-20 mg/kg/day (HIV) (maximum 160 mg/dose) PO or IV divided every 12 h for 7-10 days or up to 3-4 weeks in HIV cases. |
| *Cyclospora cayetanensis* | TMP/SMX at 8-10 mg/kg/day of TMP PO divided every 12 h for 7-10 days. |

IM: intramuscular; IV: intravenous; NS: normal saline; PO: oral route; PR: intrarectal route; *alternative second-line regimens; **4 kg to < 7 kg, 80 mg; 7 kg to < 9 kg, 120 mg; 9 kg to < 12.5 kg, 160 mg; ≥ 12.5 kg, 200 mg.

*Source: Authors' own elaboration based on extracted information from Kliegman[1], World Health Organization[4], Shane et al.[6], American Academy of Pediatrics[18], Hohmann[19], Andrews et al.[20], American Academy of Pediatrics[22], Crews and Nicholson[30], McDonald et al.[31], Kotloff[37], American Academy of Pediatrics[38-45].*

supporting such a suggestion show that the benefits are modest, reducing symptomatic duration by only 1 day. Furthermore, they declare inconsistencies in the clinical trials they found without specifying particulars of study design or population characteristics.

A middle ground among these three important international entities could be found in an interesting recommendation from a Colombian expert panel in 2015. They recommend empirical antibiotic administration in infectious dysentery during early childhood in cases of symptomatic persistence, clinical deterioration (partially following IDSA's approach), or if *Shigella* is found in the patient's stool culture, aligning with WHO's emphasis on its presence and the potential deterioration that occurs when antibiotic therapy is not provided[9].

This was also found in a cohort study conducted in Botswana, where the presence of *Shigella*, *Campylobacter*, or enterotoxigenic *Escherichia coli* was documented and associated with higher mortality in patients with severe acute malnutrition or human immunodeficiency virus (HIV) infection when empirical antibiotic therapy was not administered[10]. However, they related this as a possible confounding factor due to the patients' critical underlying condition, beyond the use of antibiotics, due to limitations in the logistic regression analysis of their results.

However, this contrasts with an Israeli retrospective study of 281 participants with a mean age of 2 years, in which clinical criteria for initiating empirical antibiotic therapy (fever, leukocytosis, and neutrophilia) were applied, but this did not correlate with positive stool cultures, hospitalization requirements, or clinical worsening[11]. They noted that 17.7% of children who presented with dysentery positive for *Shigella* or *Campylobacter* did not receive antibiotics and did not require hospital readmission, questioning the need for empirical treatment. However, it is important to understand the cultural and social differences compared to low-income countries, from which most available information comes regarding early childhood morbidity and mortality from this disease.

On the other hand, a clinical trial published in the *Journal of the American Medical Association*, which included 8,266 participants aged between 2 and 23 months with watery diarrhea, found no significant differences in mortality and weight-for-height growth delay between patients empirically treated with azithromycin and those treated with placebo[12]. Although this study did not specifically address dysentery, it did document positive isolates for *E. coli* among its participants.

**Table 4.** IDSA recommendations for immediate antimicrobial treatment initiation in patients with dysentery

| |
|---|
| Sepsis and septic shock. |
| Children under 3 months with suspected bacterial infection. |
| Fever in cases of immunocompromise or recent international travel. |
| Acute abdomen. |
| Suspected *Shigella* infection. |

*Source: Authors' own elaboration based on information extracted from Shane et al.[6].*
IDSA: Infectious Diseases Society of America.

## *Escherichia coli*

The presence of STEC, whether O157:H7 or regardless of its toxin genotype[6], is a known reason to avoid antibiotic use due to the release of intracellular Shiga toxin at the tissue level and its impact on the development of hemolytic-uremic syndrome (HUS)[13]. This complication is especially relevant in regions such as Latin America, where microbiological panels are limited, and the enteroinvasive strain can be clinically similar, with no clear benefits from antibiotic administration. At present, no studies demonstrate the benefits of antibiotic therapy in cases of dysentery, except in cases of persistent traveler's watery diarrhea, treated with ciprofloxacin, azithromycin, and rifaximin[1].

A study performed by the Washington Department of Health analyzing 405 cases of O157:H7, including adults and children, among whom 211 were under 18 years and received antibiotic treatment with nitroimidazoles, fluoroquinolones, or beta-lactams, found that the presence of *E. coli* in children under 5 years is more frequent than in adults. Furthermore, it found that antibiotic use in this population may be harmful and slightly increase the risk of STEC-associated HUS[14]. However, given the wide confidence intervals, they did not propose a specific conclusion, limiting clinically or statistically significant indications, in addition to the heterogeneity of HUS definitions used in the article. Thus, the patient's context and clinical manifestations determine the appropriateness of antibiotic therapy administration.

A cross-sectional study conducted across seven countries in Asia and Africa with 6,692 children found that in scenarios of moderate or severe diarrhea with factors such as moderate acute malnutrition, dehydration, and high fecal output are associated with bacterial agents and could benefit from antibiotics[15]. However, in reviewing this manuscript, no suggestions of protective effects were found for any strains.

## *Salmonella*

In its latest 2024 report, WHO identified typhoid and non-typhoid *Salmonella* species as a high-risk public health concern due to their antibiotic multi-resistance, especially to fluoroquinolones[16]. This is another reason to reconsider the widespread use of antibiotics in ADD and dysentery, where their inappropriate use may increase the possibility of becoming a chronic carrier[1].

This problem has been seen with an increasing frequency, so much so that the Cochrane Collaboration, since 2011, has insisted on the importance of regulation according to local patterns despite their utility[17]. In contrast, there are no specific studies of this etiology in children, and there is an urgent need for such studies due to the health emergency it represents. The only international reference entity specifically addressing the topic through expert committees is the American Academy of Pediatrics (AAP), which dedicates a section to the disease in this population group.

Initially, recommendations for typhoid fever in this population group mention the use of fluoroquinolones due to the high risk of complications, as the historically mentioned osteoarticular adverse effects which have not been substantiated in subsequent studies. However, azithromycin and third-generation cephalosporins should be considered alternatives to quinolones given the indiscriminate use of the latter in adults, which has produced resistance as documented in different regions of the world such as Pakistan or Iraq[1].

Regarding non-typhoid fever, some experts recommend the use of ciprofloxacin or, according to the AAP, a single dose of ceftriaxone followed by an azithromycin regimen[18], including alternatives such as cefixime or trimethoprim/sulfamethoxazole (TMP/SMX). However, based on adult studies and expert opinions in the field of pediatrics, it should be reserved for cases of disseminated and high-risk disease, with special emphasis on HIV/acquired immunodeficiency syndrome (AIDS), and other immunosuppressive states, hemoglobinopathies, high-output diarrhea, infants under 3 months, chronic gastrointestinal disease, or significant heart and joint diseases[1,19,20]. Relapse rates have been shown to be lower with ciprofloxacin or oral azithromycin compared to oral TMP/SMX, amoxicillin, or parenteral ceftriaxone[18].

## *Shigella*

This is a controversial agent due to WHO's 2005 recommendation to use antibiotic therapy in all cases of dysentery, considering that most cases are caused by this bacterium, which, along with *E. coli*, are the main responsible agents for this clinical presentation[6], as well as considering dysentery as a criterion for initiating antibiotic therapy in *Shigella* infection[1].

However, recommendations have changed again according to the AAP's 2024 guidelines, now recommending antibiotic therapy for immunocompromised patients, those with severe disease, those requiring hospitalization, attending daycare or living in institutions, or those involved in food handling, as it reduces transmission and leads to faster pathogen eradication, shortening diarrhea duration, preventing clinical deterioration, and the development of chronic symptoms and malnutrition[21-23]. This recommendation aligns with findings from a review published by Kotloff et al. in *The Lancet*[23] in 2017, and the findings from the previously mentioned Botswana cohort study, where 671 participants had a mean age of 8.3 months. The study documented that *Shigella* had a strong association with bloody diarrhea, although a high proportion (37%) did not present with dysentery despite positive pathogen cultures, and there was a high diarrhea-related mortality rate (3.7%)[11]. Similarly, in cases where *Shigella dysenteriae* type 1 is isolated, there is a higher risk of invasive infection and intestinal complications when associated with malnutrition, and an increased mortality risk when there is a higher number of bowel movements before hospital admission, hyponatremia, altered consciousness, and seizures[23].

Treatment guidelines are similar to those for *Salmonella*, with differences in treatment duration[23]. The previously mentioned clinical considerations should be considered given the increasing resistance to azithromycin, fluoroquinolones, ampicillin, TMP/SMX[21], and even the possibility of HUS. A systematic review from Pediatrics and International Child Health found that ciprofloxacin, pivmecillinam, and ceftriaxone reduce the clinical failure rate by 82% in cases of shigellosis. Ciprofloxacin resistance increased in Asia and Africa while remaining low in Europe and America, with higher rates in children than adults globally[24]. Regarding alternatives, macrolides, cephalosporins, and aminoglycosides showed higher resistance in children, limiting their usefulness. Gatifloxacin showed poorer clinical outcomes compared to ciprofloxacin[24].

Cephalosporins, especially cefixime, demonstrated high effectiveness as an alternative when fluoroquinolone resistance is present; however, studies have been conducted in hospital settings, limiting extrapolation to outpatient contexts where future research may be

needed[24]. This contrasts with findings from an Iranian meta-analysis, which showed low *Shigella* resistance to ciprofloxacin (*S. dysenteriae* 7%, *Shigella flexneri* 3.8%, *Shigella boydii* 6.9%, and *Shigella sonnei* 2.6%) and high resistance to ceftriaxone and azithromycin, recommending reevaluation of these antibiotics' use based on the population and local resistance patterns[25,26].

## *Campylobacter*

Considered one of the main causes of food poisoning, it still shows 95% sensitivity to macrolides, fluoroquinolones, and aminoglycosides[27]. In the few studies on treatment efficacy in this population, azithromycin has been the drug of choice, reducing symptom duration by 1.3 days according to a 2007 meta-analysis[28], suggesting its use in all cases of dysentery, as this is considered a marker of disease severity.

There are no subsequent articles reassessing this result, and this therapeutic concept has persisted until today, with a lengthy period without evidence regarding this etiology, except for the AAP expert panel in 2024[18], which recommends limiting antibiotic use to invasive cases, such as bacteremia or in patients at risk of severe disease, preferring azithromycin and erythromycin[18]. While their efficacy has been preserved over time, there is an increasing incidence of antimicrobial resistance of *Campylobacter jejuni* to ampicillin, cotrimoxazole, and erythromycin[29], compromising therapeutic options in areas with limited access to ciprofloxacin and norfloxacin, presenting a serious threat to global public health.

## *Clostridioides difficile*

It can be rarely defined as a pathogen causing dysentery. IDSA indicates that it is not expected to cause dysentery[6], although it can be found in up to 15% of cases[30]. When isolated, basic treatment should follow the same approach as a conventional case of pseudomembranous colitis, requiring discontinuation of all non-essential antibiotics, and administration of oral metronidazole in mild-to-moderate cases.

In patients with risk factors such as oncological conditions, immunosuppression, transplants, or cystic fibrosis, severe complications may occur more frequently, including pseudomembranous colitis, intestinal pneumatosis, toxic megacolon, perforation, peritonitis, and shock with multisystem failure, as well as in recurrent infection, requiring combined use of oral vancomycin[31] with intravenous metronidazole[32].

Unlike adults, children require clinical analysis of each scenario to define disease severity and specific therapy in fulminant cases. In these cases, intrarectal vancomycin administration and ileostomies have been attempted in surgical emergencies, with mortality rates reaching 2-4%[32]. In 2020, the Food and Drug Administration approved the use of the macrolide fidaxomicin in children from 6 months of age based on retrospective studies, and according to the AAP in 2024, its utility has been considered in recurrent cases with concomitant hematological-oncological diseases[32,33].

## *Yersinia enterocolitica*

There have been no recent trials on antibiotic therapy, apparently because most cases are self-limited. However, the AAP[18], through its 2024 expert panel, recommends antibiotic use in neonates due to their higher risk of sepsis[1], immunocompromised patients, and cases of enterocolitis, pseudoappendicitis syndrome, or mesenteric adenitis. Suggested treatments include third-generation cephalosporins, TMP/SMX, aminoglycosides, fluoroquinolones, chloramphenicol, tetracyclines, or doxycycline[18].

## *Entamoeba histolytica*

There are various complex aspects of amebiasis at the medical care level and even of a cultural nature. One of the most relevant medical errors is failing to recognize the trophozoite as its infective form, and considering that cysts, its stationary form, require urgent antibiotic management and cause dysentery when found in an isolated coproparasitological sample; this is why, when requesting a coproparasitological test, antimicrobial decisions in emergency services can become confused and should be reserved only for persistent cases or therapeutic failures[9].

It is common to find inappropriate antimicrobial administration for this condition, making it necessary to clarify its indications, which have been defined by guideline documents and secondary references. These indications are hepatic abscesses or invasive disease characterized by a rapidly progressive dysenteric phenomenon in infants. In such cases, metronidazole or tinidazole is suggested, followed by a luminal agent such as iodoquinol or paromomycin for the eradication of intestinal cysts and prevention of recurrence[1], with these last two being indicated when treating an asymptomatic cyst carrier[34,35].

### *Cystoisospora and Cyclospora cayetanensis*

Although dysentery is rare, most evidence comes from cases with HIV/AIDS. Some suggest universal management with TMP/SMX in all symptomatic children[1,36]. In contrast, others posit that it should only be given in immunocompromised situations to reduce the possibility of chronification in these cases[18], which reconsiders its true benefit in immunocompetent patients as it is self-limited. Results show lower effectiveness with ciprofloxacin or nitazoxanide, which could be useful in cases of sulfa intolerance in cystoisosporiasis[1,18].

## Conclusions

At present, infectious dysentery in early childhood presents a clinical decision challenge with an unresolved issue that represents its most relevant adjunct management: antimicrobial therapy. This controversy arises from the lack of standardized management protocols, limitations in building clinical evidence due to ethical dilemmas in clinical trial development, and the coexistence of the pathogen to be treated in the microbiome rather than its true eradication, which in some scenarios becomes a chronic carrier state.

According to the literature review, indications for antibiotic therapy vary depending on clinical compromise, relevant individual susceptibility factors, and the possibility of specific microbiological isolation, potentially being more useful in scenarios of infections produced by *Shigella*, *Campylobacter*, *C. difficile*, and *E. histolytica*, while being limited to specific scenarios with *Y. enterocolitica*, and avoided when isolating Shiga toxin-producing *E. coli* O157:H7.

With the technological advancement of medicine, it was found that a problem arises from the lack of precise microbiological diagnosis before the physician's decision, particularly in regions with limited resources. The absence of advanced diagnostic tools limits therapeutic management, promoting indiscriminate use of antibiotics and contributing to growing bacterial resistance. Moreover, the fact that much of the information found is extrapolated from adults or comes from expert panels further reflects the critical gap in knowledge and management of infectious dysentery in children under 5 years of age. This area has been insufficiently addressed in the existing literature.

The advancement toward greater coverage in the use of molecular diagnostics offers a promising path to improve precision in pathogen identification, supporting clinical practice, and guiding specific treatment, which could transform antibiotic therapy. While it is clear that the widespread implementation of these technologies still faces barriers, their potential for precision medicine is evident.

In addition, it is necessary to implement and develop continuing education programs for pediatricians, primary care physicians, and the general community, focusing on rational antibiotic management, prevention of bacterial resistance, primary prevention measures, and local epidemiological knowledge to promote informed therapeutic decision-making following the best scientific evidence to significantly improve the clinical management of infectious dysentery in early childhood and contribute to the global fight against microbial resistance.

Finally, although the management of infectious dysentery in early childhood remains an area of controversy and challenge, with microbiological identification and susceptibility along with patient comorbidity assessment being today's key to antibiotic decision-making, the integration of advanced diagnostics and implementation of robust research strategies are the true gateway of understanding the real indications and risks of administering antibiotic therapy in the near future.

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The authors declare no conflicts of interest.

## Ethical considerations

**Protection of humans and animals.** The authors declare that no experiments involving humans or animals were conducted for this research.

**Confidentiality, informed consent, and ethical approval.** The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

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