



## **A Systematic Review of Antibiotic Usage on Gastroenteritis**

<sup>1</sup>S.Anandkumar, <sup>2</sup>Abisha M, <sup>3</sup>Samuel I, <sup>4</sup>Naresh Kumar D, <sup>5</sup>Vaishakh V.

<sup>1</sup>Assistant professor, Department of Pharmacy Practice, The Erode College of Pharmacy and Research Institute, Erode, Tamil Nadu, India

<sup>2,3,4,5</sup>Doctor of Pharmacy, The Erode College of Pharmacy and Research Institute, Erode, Tamil Nadu, India

**Citation of this Article:** Dr. S. Anand Kumar, Abisha M, Samuel I, Naresh Kumar D, Vaishakh V., “A Systematic Review of Antibiotic Usage on Gastroenteritis,” IJMSAR – November – 2022, Vol. – 5, Issue - 6, Page No. 20-28.

**Copyright:** © 2022, Dr. S. Anand Kumar, et al. This is an open access journal and article distributed under the terms of the creative commons attribution noncommercial License. This allows others to remix, tweak, and build upon the work non commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**Corresponding Author:** Dr. S. Anand Kumar, Assistant professor, Department of Pharmacy Practice, The Erode College of Pharmacy and Research Institute, Erode, Tamil Nadu, India

**Type of Publication:** A Review Article

**Conflicts of Interest:** Nil

### **Abstract**

#### **Introduction**

Antibiotics are still widely used in general practice for the treatment of diarrhoea occurring in acute gastroenteritis, this disease is also caused by medications, viruses such as rotavirus and enteric adenovirus. The disease is self-limiting and there is no report regarding the efficacy of antibiotics in the treatment. The management of acute diarrhoea is mainly supportive: hydration and alteration of diet. Antibiotic treatment is usually preserved only for more severe cases. Our main aim in this study is to improve our knowledge in the antibiotics use for gastroenteritis and to find out the widely used antibiotics.

#### **Methodology**

A systematic review was conducted with 100 potentially relevant studies such as Descriptive, cross-sectional studies, prospective, or retrospective studies and case reports and series in which the prevalence of gastroenteritis were included. As a result, we considered that any observed difference between studies in treatment effect could not be confirmed to be an effect of sampling variation alone.

#### **Results and Discussion**

However we analysed the 100 studies, the results were obtained from finalised 30 articles which are more relevant to our criteria, hence the common use of antibiotics for adults is Metronidazole, Azithromycin, Ciprofloxacin, Ceftriaxone, Cotrimoxazole, Doxycycline, Amoxicillin/Ampicillin and commonly used antibiotics for paediatrics under the age group of 10 based on the study was Penicillin,

Aminoglycosides, Cephalosporin, Vancomycin, Macrolides, Sulphonamides.

### **Conclusion**

Gastroenteritis was mostly affected to the paediatric population and child population accordingly to the systematic review. Metronidazole was concurrently used antibiotic therapy and for adults. And Penicillin is widely used therapy for younger age peoples in gastroenteritis from the studies reviewed.

### **Introduction**

Antibiotics are still widely used in general practice for the treatment of diarrhoea occurring in acute gastroenteritis, despite evidence that their use is unnecessary and may be harmful.<sup>1</sup>

Antibiotics are the most commonly prescribed medications among nursing home residents, with approximately two thirds of residents receiving antibiotic treatment each year. Many of these prescriptions are inappropriate, unnecessary, or unnecessarily prolonged, thereby directly exposing individual recipients to *Clostridium difficile* infection and diarrhoea, antibiotic-resistant organisms, antibiotic allergies, and other medication toxic effect.<sup>2</sup> Acute gastroenteritis (AGE) presents a major burden to the global and the United States healthcare systems, as it is one of the most common diagnoses for emergency department visits and hospitalizations.<sup>3</sup> Although it is generally a self-limiting illness, it is the cause of a number of deaths each year, usually among patients with other underlying illnesses.<sup>4,5</sup> Diarrhoeal diseases remain a foremost public health burden in children under 5 years of age especially in low-resource settings. Every year diarrhoea kills around 525,000 children under 5 years of age and 25% of deaths in young children living in Africa and South-

east Asia are due to acute gastroenteritis.<sup>6</sup> Every year, around one in three persons experiences an episode of gastroenteritis (GE).<sup>7</sup>

Gram-negative bacteria of the species *Salmonella* are a major cause of food-borne illness in mostly developed countries. Children in developing countries become infected with a diverse group of bacterial, viral and parasitic pathogens. *Salmonella* infections are recognized as one of the major causes of childhood diarrhoeal illness. It is generally transmitted to humans through consumption of contaminated food of animal origin, mainly meat, poultry, eggs, and milk.<sup>8</sup> It is also caused by medications, viruses such as rotavirus and enteric adenovirus. The disease is self-limiting and there is no report regarding the efficacy of antibiotics in the treatment, however, antibiotics are given to children younger than 5 years old.<sup>9</sup>

Most patients with acute diarrhoea are able to manage their illness, and do not seek medical attention. In patients with significant diarrhoeal illness, i.e. profuse, dehydrating, febrile or bloody diarrhoea needs medical management.<sup>10</sup>

The first step for managing any patient with diarrhoea is to determine the severity of dehydration according to the estimated volume loss and the symptoms and signs noted on physical examination. Children are managed differently. Oral rehydration is recommended to alleviate mild dehydration, which often causes minimal to no signs or symptoms. A few complicated cases may require antimicrobial therapy because of the severity of the clinical signs.<sup>11</sup> Inappropriate use of antibiotics may cause antibiotic-associated diarrhoea or other complications and may also lead to antibiotic resistance in the long term.<sup>12</sup>

If gastroenteritis is untreated the main complication can be dehydration — a severe loss of water and essential salts and minerals. If you're healthy and drink enough to replace fluids you lose from vomiting and diarrhoea, dehydration shouldn't be a problem. Infants, older adults and people with suppressed immune systems may become severely dehydrated when they lose more fluids than they can replace. Hospitalization might be needed so that lost fluids can be replaced intravenously. Dehydration can be fatal, but rarely.

Our goal in this detailed study is to identify the widely use of antibiotics for gastroenteritis and their effectiveness and their adverse drug reactions. This study deeply analysed and reported the common antibiotics use from the standard articles, case studies, international books and our skilful guidance from our beloved guide by doing our level best. Our main aim is to improve our knowledge in the antibiotics use for gastroenteritis and to find out the widely used antibiotics.

### **Methodology**

A systematic review was conducted according to Preferred Reporting Items for systematic reviews. Our predefined inclusion criteria included only randomized, blinded, clinical trials. Participants of all

ages were included; they all suffered from diarrhoea, and respected species was identified by stool culture for all. The clinical outcome measured was duration, in days, of diarrhoea after the start of therapy. We also tried to measure clearance of respected species in stool samples after therapy; however, studies presented these data in different ways and seldom with any measure of variance of the results, thereby making a meta-analysis difficult to perform. These data are, therefore, compiled in a descriptive table.

We searched the Medline, Web of Science, Embase, PubMed, Cochrane Central Register of Controlled Trials and Clinical Trials.gov databases for studies to include in our analysis. Both free text word searches and searches using medical subject heading (MeSH) terms were performed; details of the search strategy are listed in the appendix. All citations in the studies retained for detailed evaluation were also checked. Publications published from all standard journals were included.

Although all included studies were randomized, controlled trials, they differed in several aspects from each other (e.g., in age distribution, antibiotics administered, and time to first treatment dose). As a result, we considered that any observed difference between studies in treatment effect could not be confirmed to be an effect of sampling variation alone. Therefore, in addition to a fixed-effect meta-analysis, we also calculated a random-effect meta-analysis to allow for heterogeneity between studies.

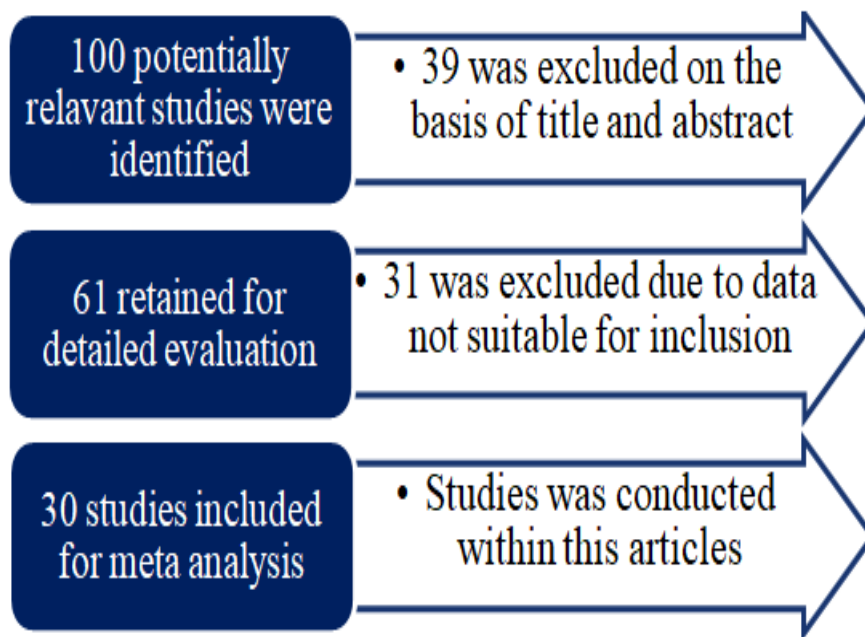


Figure 1: Study Design

### Inclusion Criteria

- Descriptive, cross-sectional studies, prospective, or retrospective studies and case reports and series in which the prevalence of gastroenteritis were included.
- Conference abstracts
- Only studies published since 2000.

### Exclusion Criteria

- Articles with co-morbidities conditions were excluded
- Review articles

### Data extraction (selection and coding)

Titles and abstracts were screened for location, study population and general correlation with the research objectives. Full versions of potentially relevant articles were obtained to assess eligibility. Two researchers (DFH and SMSA)

screened independently studies and determined study eligibility. Cross-references of the full text retrieved articles were also searched. Data were collected independently from each publication and captured using a standardized Word document form. Data were extracted from text, tables and figures.

### Results and Discussion

The Table.1&2 contains demographics classification based on the information from the 30 articles. The average percentage of demographics distributions according to the studies and the data are calculated by means of average from all the studies included in inclusion criteria. The average total population from reviewed article shows that males were 425 patients and female were 375 patients and age wise distribution shows that 25-35 years-54.5%, 35-40 years - 19.2%, 40-45 years -12.37%, 45-50 years - 7.9%, Above 50 years - 6.1% respectively.<sup>10,11.</sup>

1. Gender wise classification

Table 1: Gender Wise Classification

Gender	Average (%)
Male	53.1
Female	46.9

2. Age-wise classification

Table 2: Age-Wise Classification

Age(years)	Average (%)
5-15	9.1
15-25	20.2
25-35	34.3
35-40	10.1
40-45	12.37
45-50	7.93
Above 50	6.1

3. Etiological factors

Since possible pathogens can be estimated based on epidemiological characteristics in patients with suspected acute gastroenteritis (Table.3), food consumption (undercooked meat, eggs, shellfish, and milk), consumption of unsterilized water, contact with pets, contact with other infected individuals, history of stay at group facility, travel history, underlying diseases, sexual history, and occupation should be confirmed. *Vibrio* spp. and norovirus are common causes of diarrhoea after consumption of uncooked seafood or shellfish, and diarrhoea after consumption of uncooked meat or poultry may be caused by Shiga toxin-producing *Escherichia coli* (STEC) (beef), *C.*

*perfringens* (beef and poultry), *Salmonella* (poultry), *Campylobacter* (poultry), *Yersinia* (pork and pork intestine), *Staphylococcus aureus* (poultry). When patients consumed unpasteurized milk, their diarrhoea may be accountable to *Salmonella*, *Campylobacter*, *Yersinia enterocolitica*, *S. aureus* toxin, *Cryptosporidium*, or *STEC*, and *Salmonella* or *Shigella* contamination is common in eggs.

Water can cause infectious diseases directly through consumption or indirectly through contamination of food or dishes. Consumption of unsterilized water may lead to *Campylobacter*, *Cryptosporidium*, *Giardia*, *Shigella*, *Salmonella*, or

STEC infection, and Cryptosporidium or other water-borne infections are possible after swimming at pools. In Korea, there was an outbreak of acute diarrhoea in 67 patients that used a pool in 2008; in six patients with severe diarrhoea, norovirus was identified in three patients.

Since norovirus with a similar RNA sequence was also detected in samples of groundwater, the outbreak was reported to have been caused by contaminated groundwater. Diarrhoea in prisons can be accounted for by norovirus, *C. difficile*, *Shigella*, *Cryptosporidium*, *Giardia*, *Salmonella*, *STEC*, and *rotavirus*, and diarrhoea in childcare services may have been caused by *rotavirus*, *Cryptosporidium*, *Giardia*, *Shigella*, or *STEC*. *C. difficile* may be

accountable if the patient has recent history of antibiotic use.

Infectious diarrhoea is caused by different common bacteria in patients of different ages; for infants of 6 - 18 months, *rotavirus* is common, whereas nontyphoidal *Salmonella* is common for patients younger than 3 months or patients older than 50 with atherosclerosis.

*Shigella* should be considered first for patients aged 1 - 7 years, and *Campylobacter* should be considered for young adults. Traveller's diarrhoea is a common disease associated with travelling and is observed in 30 - 70% of travellers depending on the area and season; it is most commonly caused by *E. coli*, *Campylobacter jejuni*, *Shigella*, and *Salmonella*.<sup>12</sup>

**Table 3: Etiological factors**

Etiological factors		Possible pathogens
Food-related	Food at hotel or restaurant	Norovirus, nontyphoidal <i>Salmonella</i> , <i>Clostridium perfringens</i> , <i>Bacillus cereus</i> , <i>Staphylococcus aureus</i> , <i>Campylobacter</i> , <i>ETEC</i> , <i>STEC</i> , <i>Listeria</i> , <i>Shigella</i> , <i>Cyclospora cayetanensis</i> , <i>Cryptosporidium</i>
	Unpasteurized milk	<i>Salmonella</i> , <i>Campylobacter</i> , <i>Yersinia enterocolitica</i> , <i>S. aureus</i> toxin, <i>Cryptosporidium</i> , <i>STEC</i> , <i>Brucella</i> (goat milk products), <i>Mycobacterium bovis</i> , <i>Coxiella burnetii</i>
	Raw or uncooked meat or poultry	<i>STEC</i> (meat), <i>C. perfringens</i> (meat, poultry), <i>Salmonella</i> (poultry), <i>Campylobacter</i> (poultry), <i>Yersinia</i> (pork, pork intestine), <i>S. aureus</i> (poultry), <i>Trichinella</i> (pork, wild animal meat)
	Fruits or vegetables	<i>STEC</i> , nontyphoidal <i>Salmonella</i> , <i>Cyclospora</i> , <i>Cryptosporidium</i> , <i>Norovirus</i> , <i>Hepatitis A</i> , <i>Listeria monocytogenes</i>
	Uncooked eggs	<i>Salmonella</i> , <i>Shigella</i>
	Shellfish	<i>Vibrio</i> , <i>Norovirus</i> , <i>Hepatitis A</i> , <i>Plesiomonas</i>
Exposure or contact	Consumption of unsterilized water	<i>Campylobacter</i> , <i>Cryptosporidium</i> , <i>Giardia</i> , <i>Shigella</i> , <i>Salmonella</i> , <i>STEC</i> , <i>Plesiomonas shigelloides</i>
	Swimming at a pool	<i>Cryptosporidium</i>
	Prisons	<i>Norovirus</i> , <i>C. difficile</i> , <i>Shigella</i> , <i>Cryptosporidium</i> , <i>Giardia</i> , <i>STEC</i> , <i>Rotavirus</i>
	Childcare services	<i>Rotavirus</i> , <i>Cryptosporidium</i> , <i>Giardia</i> , <i>Shigella</i> , <i>STEC</i>
	Recent antibiotic use	<i>C. difficile</i> , multi-drug-resistant <i>Salmonella</i>
	Travel history to areas with poor public health	<i>Escherichia coli</i> (enteroaggregative, enterotoxigenic, enteroinvasive), <i>Shigella</i> , <i>Salmonella Typhi</i> , nontyphoidal <i>Salmonella</i> , <i>Campylobacter</i> , <i>Vibrio cholerae</i> , <i>Entamoeba histolytica</i> , <i>Giardia</i> , <i>Blastocystis</i> , <i>Cyclospora</i> , <i>Cystoisospora</i> , <i>Cryptosporidium</i>
	Contact with pets that have diarrhoea	<i>Campylobacter</i> , <i>Yersinia</i>
	Contact with pig stool	<i>Balantidium coli</i>
	Contact with poultry	Non-typhoidal <i>Salmonella</i>
	Visits to farms or zoos	<i>STEC</i> , <i>Cryptosporidium</i> , <i>Campylobacter</i>

#### 4. Average Percentage of Antibiotics Used in Children

The average percentage of antibiotics used for children under the age of 10. From the study it was deeply analysed and concluded the average percentage of antibiotics used from the studies taken, it also

compiles the exclusion criteria and recorded as mentioned. The average percentage of antibiotics used is Penicillins-33% Aminoglycosides-31% Cephalosporin-16% Vancomycin-9% Macrolides-2% Sulphonamides-1% others -8% as mentioned in Table.4.<sup>8-12.</sup>

**Table 4: Average Percentage of antibiotics used in children**

Antibiotic	Average (%)
Penicillins	33
Aminoglycosides	31
Cephalosporin	16
Vancomycin	9
Macrolides	2
Sulphonamides	1
Others	8

#### 5. Average Dose and Duration of therapy

Table.5 contains the average dose and duration of therapy. From the studies included in the inclusion criteria, the data was collected such as the

dose and duration of antibiotics used and from the studies some common antibiotics dose and duration of therapy as follows.<sup>12</sup>

**Table 5: Average Dose and Duration of therapy**

Antibiotic	Dose	Duration
Ciprofloxacin	500 mg PO twice daily or	3 days
	500 mg PO once daily	3 days
	750 mg PO	Single dose
Levofloxacin	500 mg PO	3 days
Azithromycin	500 mg PO	3 days
	1,000 mg PO	Single dose
Metronidazole	400 mg PO two times daily	3 days
Cefixime	400 mg PO two times daily	3 days
TMP-SMX	400 mg PO two times daily	3 days
	800mg PO once a day	3 days
Ampicillin	500 mg PO two times daily	3 days

## 6. Average percentage of Antibiotics used in adults

Table.6 contains the average percentage of antibiotics used from the studies included in inclusion criteria for the adults. From the studies the average percentage of antibiotics for gastroenteritis was

analysed from the last finalised 30 studies which also complies the inclusion criteria are Metronidazole, 28% Azithromycin, 19% Ciprofloxacin, 15% Ceftriaxone, 11% Co-trimoxazole, 13% Doxycycline, 8% Amoxicillin/Ampicillin, 6%.<sup>8-12,19,20.</sup>

**Table 6: Average percentage of Antibiotics used in adults**

<b>Antibiotic</b>	<b>Average (%)</b>
Metronidazole	28
Azithromycin	19
Ciprofloxacin	15
Ceftriaxone	11
Co-trimoxazole	13
Doxycycline	8
Amoxicillin/Ampicillin	6

## Conclusion

Gastroenteritis was the common problem for both paediatrics and adults mainly for low socio economic status countries. The etiology of gastroenteritis was also assessed.

From the Systematic review common use of antibiotics for adults is Metronidazole, Azithromycin, Ciprofloxacin, Ceftriaxone, Co-trimoxazole, Doxycycline, Amoxicillin/Ampicillin.

And commonly used antibiotics for paediatrics under the age group of 10 based on the study was Penicillin, Aminoglycosides, Cephalosporin, Vancomycin, Macrolides, Sulphonamides.

Gastroenteritis was mostly affected to the paediatric population and child population accordingly to the systematic review.

This study highlighted the need for development and implementation of relevant, diagnosis-specific antibiotic prescribing guidelines for paediatric patients and need for the development of evidence-based treatment protocols for common clinical conditions to rationalize the use of antibiotics.

Metronidazole was concurrently used antibiotic therapy and for adults. And Penicillin is widely used therapy for younger age peoples in gastroenteritis from the studies reviewed.

## Reference

1. M. T. Everett, Plymouth et al. The place of antibiotics in the treatment of acute gastroenteritis in general practice: a controlled clinical trial. 2021.
2. Daneman N, Bronskill S, Gruneir A, Newman A, Fischer H, Rochon P et al. Variability in



- Antibiotic Use Across Nursing Homes and the Risk of Antibiotic-Related Adverse Outcomes for Individual Residents.
3. Homsy M. Antibiotic therapy in acute gastroenteritis: a single-center retrospective cohort study.
  4. Gastroenteritis in Children: Part II. Prevention and Management. [www.aafp.org/afp](http://www.aafp.org/afp); 2012.
  5. Dryden M, Gabb R, Wright S. Empirical Treatment of Severe Acute Community-Acquired Gastroenteritis with Ciprofloxacin.
  6. Qureshi S, Resham S, Hashmi M, Naveed A, Haq Z, Ali S. A retrospective review on antibiotic use in acute watery diarrhoea in children in a tertiary care hospital of Karachi, Pakistan.
  7. Schierenberg A, Bruijning-Verhagen P, van Delft S, Bonten M, de Wit N. Antibiotic treatment of gastroenteritis in primary care.
  8. Salmonella gastroenteritis in children (clinical characteristics and antibiotic susceptibility): comparison of the years 1995- 2001 and 2002-2008
  9. Adeyemi O, Alabi A, Adeyemi O, Talabi O, Abidakun O, Joel I et al. Acute gastroenteritis and the usage pattern of antibiotics and traditional herbal medications for its management in a Nigerian community.
  10. Zollner-Schwetz I, Krause R. Therapy of acute gastroenteritis: role of antibiotics. 2021.
  11. Abdulhadi H Almazroea, Shatha Ibrahim Almagheerbi, Mousa Atqan Alamri, Muath Musallam Alloqmani, Ghaida'a Saleh Almohammadi, AnharAbdulmannanBazarbayand et al.,(2019), "Prevalence of Antibiotic Use For Pediatric Acute Viral Gastroenteritis in Madinah Almunwarah, KSA".
  12. Kim Y, Park K, Park D, Park J, Bang B, Lee S et al. Guideline for the Antibiotic Use in Acute Gastroenteritis.
  13. Al Jassas B, Khayat M, Alzahrani H, Asali A, Alsohaimi S, ALHarbi H et al. Gastroenteritis in adults. 2021.
  14. Friesema I, Boer R, Duizer E, Kortbeek L, Notermans D, Norbruis O et al. Etiology of acute gastroenteritis in children requiring hospitalization in the Netherlands.
  15. Chow C. Acute gastroenteritis: from guidelines to real life. *Clinical and Experimental Gastroenterology*. 2010;:97.
  16. Elliott E. Acute gastroenteritis in children. *BMJ*. 2007;334(7583):35-40.
  17. Tien F, Wu J, Jeng Y, Hsu H, Ni Y, Chang M et al. Clinical Features and Treatment Responses of Children With Eosinophilic Gastroenteritis. *Pediatrics & Neonatology*. 2011;52(5):272-278.
  18. Lin F, Huang Y, Huang Y, Huang L, Liu C, Chi H et al. Clinical and epidemiological features in hospitalized young children with acute gastroenteritis in Taiwan: A multicentered surveillance through 2014–2017.
  19. Nancy S. Graves, MD. Acute Gastroenteritis. 2021.
  20. Ternhag A, Asikainen T, Giesecke J, Ekdahl K. A Meta-Analysis on the Effects of Antibiotic Treatment on Duration of Symptoms Caused by Infection with *Campylobacter* Species.
  21. Hlashwayo D, Sigauque B, Noormahomed E, Afonso S, Mandomando I, Bila C. A systematic review and meta-analysis reveal that *Campylobacter* spp. and antibiotic resistance are widespread in humans in sub-Saharan Africa.