



## INCIDENCE OF ACUTE DIARRHEAL DISEASE AMONG ADULT POPULATION IN MEWAR UNIVERSITY, CHITTORGARH, RAJASTHAN, INDIA.

**Nuhu Bobby Ezekiel, NuraYakubu, IntiMacdaleneAnto**

*MSc Public Health, Department of Paramedics, Mewar University, Rajasthan, India.*

### **ABSTRACT**

The study is conducted to identify the incidence of acute diarrheal disease among adult population residing within the Mewar University community. The study population is approximately 900 persons. Retrospective cohort study using patient record/register as instrument of data collection, between 1<sup>st</sup> July, 2021 to 10<sup>th</sup> June, 2022. Cases that met the case definition of acute diarrhea (equal to or above 3 episodes of watery/loose stool within 24 hours) were identified through vetting and computed across age categories and based on gender. The study revealed an incidence of 473 cases of acute diarrheal disease within the year, with male having the highest incidence of (34.8%). The incidence is also higher (323.3) within the ages (18 – 27) and cumulative of 525.6 per year. It was recommended to improve safe food handling, water source, conduct Rotavirus vaccination, substitute the worn out food equipment and organize sensitization on hygiene to prevent/limit future reoccurrence of the disease.

**KEY WORDS:** Incidence, acute diarrheal disease.

**METHOD:** A retrospective cohort study using secondary data from school health center( patient record).

**LIMITATION:** The study is limited to incidence of acute diarrheal disease among the people residing within the Mewar University community. Also, it only takes account of clinical diagnoses.

**STUDY POPULATION:** Involved 150 staff and their family members and 750 students, males and females (undergraduate and post graduate), approximately 900 people.



## **INTRODUCTION**

Acute diarrhea in adults is a common problem encountered by family physicians and one of the leading causes of death globally (GBD, 2016 & GBD, 2019). Most cases of diarrhea are associated with contaminated food and water sources, and more than 2 billion people globally have no access to basic sanitation (WHO, 2017). The most common etiology is viral gastroenteritis, a self-limiting disease. Increases in travel, co morbidities, and food borne illness lead to more bacteria-related cases of acute diarrhea. A history and physical examination evaluating for risk factors and signs of inflammatory diarrhea and/or severe dehydration can direct any needed testing and treatment. Most patients do not require laboratory confirmation, and routine stool cultures are not needed/recommended as it does not alter the management of the condition (Webber; Rogger, 2009). Treatment focuses on preventing and treating dehydration. Diagnostic investigation should be reserved for patients with severe dehydration or illness, persistent fever, bloody stool, or immunosuppression, and for cases of suspected nosocomial infection (hospital-acquired/health care related) or outbreak. Oral rehydration therapy with early refeeding is the preferred treatment for dehydration. Antimotility agents should be avoided in patients with bloody diarrhea, but loperamide/simethicone may improve symptoms in patients with watery diarrhea. Probiotic use may shorten the duration of illness. When used appropriately, antibiotics are effective in the treatment of shigellosis, campylobacteriosis, *Clostridium difficile*, traveler's diarrhea, and protozoan infections. Prevention of acute diarrhea is promoted through adequate hand washing, safe food preparation, access to clean water, and vaccinations.

## **LITERATURE REVIEW**

Acute diarrhea is defined as stool with increased water content, volume, or frequency that lasts less than 14 days (Guerrant RL, Van Gilder T, Steiner TS, et al, 2001). A case of acute diarrhea was also defined as the presence of  $\geq 3$  passages of watery, loose, mucus, or bloody-stools within a 24-h period (WHO). Diarrheal illness accounts for 2.5 million deaths per year worldwide (Kosek M, Bern C, Guerrant RL, 2003). In the United States, an estimated 48 million food borne diarrheal illnesses occur annually, resulting in more than 128,000 hospitalizations and 3,000 deaths (Scallan E, Hoekstra RM, Angulo FJ, et al). In the developing world, infectious causes of



acute diarrhea are largely related to contaminated food and water supplies. In the developed world, technological progress and an increase in mass production of food have paradoxically contributed to the persistence of food borne illness, despite higher standards of food production. MohamAnandan,et al (2021) had reported a higher rate of acute diarrheal disease among under five (16.5%) and female constitute 6.8% among residents of Thir upper village, Tiruvallur district, Tamil Nadu, India, in 2016.

### **WORLDWIDE INCIDENCE**

In contrast to the available data for younger children, incidence of diarrheal disease in older children and adults has not been calculated for many countries. In a systematic review of 23 prospective studies of diarrheal disease in individuals older than five years, estimated diarrhea morbidity rates ranged from 30 episodes per 100 person-years among adults in southeast Asia to 88 episodes per 100 person-years in the eastern Mediterranean region; rates had not changed substantially over 30 years (Walker CL, Black RE,2010). Incidence in Africa was not evaluated in any of the studies included in the review. Diarrheal illness occurs at a baseline frequency in resource-limited countries, superimposed with epidemic cases of diarrhea, either dysentery or watery diarrhea. Epidemics are generally due to *Shigelladysenteriae* serotype 1 (Sd1) and *Vibrio cholerae*. Major outbreaks due to Sd1 have occurred in Africa, South Asia, and Central America. In 1994, an explosive outbreak among Rwandan refugees in Zaire caused approximately 20,000 deaths during the first month alone (Public health impact of Rwandan refugee crisis, 1995). Epidemics due to *V. cholerae* have occurred throughout Africa, Asia, the Middle East, South and Central America, and the Caribbean (Harris JB, LaRocque RC, Qadri F, et al, 2012). A cholera epidemic in Yemen has been ongoing since 2017 and is the largest in epidemiologically recorded history (Federspiel F, Ali M, 2018).

### **RISK FACTORS/MODE OF TRANSMISSION**

Transmission may occur from drinking contaminated water or when people share personal objects (Webber, Rogger, 2009). Water quality typically worsens during the rainy season and outbreaks are more common at this time (Webber, Rogger, 2009). In areas with four seasons, infections are more common in the winter (Dolin, Raphael; Mandell, et al, 2010). Transmission



rates are also related to poor hygiene, especially among children in crowded households (Eckardt AJ, Baumgart DC, 2011) and in those with poor nutritional status. Adults who have developed immunities might still carry certain organisms without exhibiting symptoms (Dolin, Raphael; Mandell, et al, 2010) thus, can become natural reservoirs of certain diseases. Human immunodeficiency virus (HIV) infection is prevalent in many of the resource-limited areas where acute diarrheal diseases occur, and diarrhea-related morbidity and mortality may be increased in these individuals. Several enteric bacteria, such as *Campylobacter*, *Salmonella*, *Shigella*, enteroaggregative *E. coli*, and *Vibrio* species, occur with increased frequency and/or severity in individuals with HIV/acquired immunodeficiency syndrome (AIDS). Coinfection with multiple pathogens may also occur. Nontyphoidal salmonellosis is a particular concern in HIV-infected individuals, who have a higher risk for recurrent or extra intestinal infection.

**CLASSIFICATION OF DIARRHEA**

Diarrhea is defined as the passage of loose or watery stools, typically at least three times in a 24-hour period (Guerrant RL, Van Gilder T, Steiner TS, et al, 2001). Acute diarrhea is defined as diarrhea of ≤14 days in duration, in contrast to persistent (>14 days and ≤30 days) or chronic (>30 days) diarrhea. Invasive diarrhea, or dysentery, is defined as diarrhea with visible blood, in contrast to watery diarrhea. Dysentery is commonly associated with fever and abdominal pain.

**CLINICAL MANIFESTATIONS CAUSED BY SPECIFIC PATHOGENS**

Pathogen	Fever	Abdominal pain	Nausea, vomiting, or both	Fecal evidence of inflammation	Bloody stool	Heme-positive stools
<b>Bacterial</b>						
<i>Campylobacter</i>	Common	Common	Occurs	Common	Occurs	Variable
<i>Clostridium difficile</i>	Occurs	Occurs	Not common	Common	Occurs	Occurs
<i>Salmonella</i>	Common	Common	Occurs	Common	Occurs	Variable
Shiga toxin-producing <i>Escherichia coli</i>	Not common	Common	Occurs	Not common	Common	Common
<i>Shigella</i>	Common	Common	Common	Common	Occurs	Variable
<i>Vibrio</i>	Variable	Variable	Variable	Variable	Variable	Variable
<i>Yersinia</i>	Common	Common	Occurs	Occurs	Occurs	Occurs
<b>Parasitic</b>						
<i>Cryptosporidium</i>	Variable	Variable	Occurs	None to mild	Not common	Not common
<i>Cyclospora</i>	Variable	Variable	Occurs	Not common	Not common	Not common
<i>Entamoeba histolytica</i>	Occurs	Occurs	Variable	Variable	Variable	Common
<i>Giardia</i>	Not common	Common	Occurs	Not common	Not common	Not common
<b>Viral</b>						
Norovirus	Variable	Common	Common	Not common	Not common	Not common

Information from references 1 and 14.

## CLINICAL ASSESSMENT AND DIAGNOSIS

The initial evaluation of adults with acute diarrhea should include a careful history and physical exam in order to assess the type of diarrhea and the severity of hypovolemia. Based on the appearance of the stool, diarrhea can be classified as watery or bloody.

The physical exam should focus on characterizing the degree of volume depletion:

**Early hypovolemia:** signs and symptoms may be absent. **Moderate hypovolemia:** thirst, restless or irritable behavior, decreased skin turgor, and sunken eyes. **Severe hypovolemia:** diminished consciousness, lack of urine output, cool moist extremities, rapid and feeble pulse, low or undetectable blood pressure, peripheral cyanosis. Gastroenteritis is typically diagnosed clinically, based on a person's signs and symptoms ((*Eckardt AJ, Baumgart DC, 2011*). Determining the exact cause is usually not needed as it does not alter the management of the condition (Webber, Roger, 2009). However, stool cultures should be performed in those with blood in the stool, those who might have been exposed to food poisoning, and those who have recently traveled to the developing world. It may also be appropriate in children younger than 5, old people, and those with poor immune function. Diagnostic testing may also be done for surveillance. As hypoglycemia occurs in approximately 10% of infants and young children, measuring serum glucose in this population is recommended. Electrolytes and kidney function should also be checked when there is a concern about severe dehydration.

## DIFFERENTIAL DIAGNOSIS

Acute diarrhea in adults in resource-limited settings is most frequently caused by an infectious agent. In addition to the pathogens above, diarrhea may also occur in the context of other systemic infections, such as influenza, HIV infection, dengue fever, and malaria. Non-infectious etiologies of diarrhea are often missed and should be considered in patients with repeated episodes of self-limiting or acute diarrhea or chronic diarrhea. Such causes include inflammatory bowel disease and malabsorptive syndromes.

## TREATMENT

**REHYDRATION THERAPY:** The first step to treating acute diarrhea is rehydration, preferably oral rehydration (Guerrant RL, Van Gilder T, Steiner TS, et al, 2001). The



accumulated fluid deficit (calculated roughly as the difference between the patient's normal weight and his or her weight at presentation with diarrheal illness) must first be addressed. Next, the focus should turn to the replacement of ongoing losses and the continuation of maintenance fluids. An oral rehydration solution (ORS) must contain a mixture of salt and glucose in combination with water to best use the intestine's sodium-glucose coupled cellular transport mechanism. In 2002, the World Health Organization endorsed an ORS with reduced osmolarity (250 mOsm per L or less compared with the prior standard of 311 mOsm per L). The reduced osmolarity ORS decreases stool outputs, episodes of emesis, and the need for intravenous rehydration (Hahn S, Kim Y, Garner P, 2001) without increasing hyponatremia, compared with the standard ORS (Alam NH, Yunus M, Faruque AS, et al, 2006). A reduced osmolarity ORS can be roughly duplicated by mixing 1/2 teaspoon of salt, 6 teaspoons of sugar, and 1 liter of water. If oral rehydration is not feasible, intravenous rehydration may be necessary.

**FEEDING:** Early resumption of feeding decreases intestinal permeability caused by infections, reduces illness duration, and improves nutritional outcomes (Gadewar S, Fasano A, 2005). This is particularly important in developing countries where underlying preexisting malnutrition is often a factor. Although the BRAT diet (bananas, rice, applesauce, and toast) and the avoidance of dairy are commonly recommended, supporting data for these interventions are limited. Instructing patients to refrain from eating solid food for 24 hours also does not appear useful (De Bruyn G, 2008). Also, the continuous provision of nutritious food is important for all patients with diarrhea. Small meals can be provided frequently, as soon as the patient is able to tolerate.

**ANTIDIARRHEAL MEDICATIONS:** The antimotility agent loperamide (Imodium) may reduce the duration of diarrhea by as much as one day and increase the likelihood of clinical cure at 24 and 48 hours when given with antibiotics for traveler's diarrhea (Riddle MS, Arnold S, Tribble DR, 2008). A loperamide/simethicone combination has demonstrated faster and more complete relief of acute nonspecific diarrhea and gas-related discomfort compared with either medication alone (Hanauer SB, DuPont HL, Cooper KM, Laudadio C, 2007). Loperamide may cause dangerous prolongation of illness in patients with some forms of bloody or inflammatory diarrhea and, therefore, should be restricted to patients with nonbloody stool. The antisecretory



drug bismuth subsalicylate (Pepto-Bismol) is a safe alternative in patients with fever and inflammatory diarrhea. There is inadequate evidence to recommend the use of the absorbents kaolin/pectin, activated charcoal, or attapulgit (no longer available in the United States). The antisecretory drug racecadotril, widely used in Europe but unavailable in the United States, appears to be more tolerable than and as effective as loperamide (Matheson AJ, Noble S, 2000).

**ANTIBIOTIC THERAPY:** Because acute diarrhea is most often self-limited and caused by viruses, routine antibiotic use is not recommended for most adults with nonsevere, watery diarrhea. Additionally, the overuse of antibiotics can lead to resistance (e.g., *Campylobacter*), harmful eradication of normal flora, prolongation of illness (e.g., super infection with *C. difficile*), prolongation of carrier state (e.g., delayed excretion of *Salmonella*), induction of Shiga toxins (e.g., from Shiga toxin-producing *E. coli*), and increased cost. However, when used appropriately, antibiotics are effective for shigellosis, campylobacteriosis, *C. difficile*, traveler's diarrhea, and protozoan infections. Antibiotic treatment of traveler's diarrhea (usually a quinolone) is associated with decreased severity of illness and a two-or three-day reduction in duration of illness (De Bruyn G, Hahn S, Borwick A, 2000). If the patient's clinical presentation suggests the possibility of Shiga toxin-producing *E. coli* (e.g., bloody diarrhea, history of eating seed sprouts or rare ground beef, proximity to an outbreak), antibiotic use should be avoided because it may increase the risk of hemolytic uremic syndrome. Conservative management without antibiotic treatment is less successful for diarrhea lasting more than 10 to 14 days, and testing and treatment for protozoan infections should be considered (Guerrant RL, Van Gilder T, Steiner TS, et al, 2001). Antibiotics may be considered in patients who are older than 65 years, immunocompromised, severely ill, or septic.

**PROBIOTICS:** are thought to work by stimulating the immune system and competing for binding sites on intestinal epithelial cells. Their use in children with acute diarrhea is associated with reduced severity and duration of illness (an average of about one less day of illness) (Allen SJ, Martinez EG, Gregorio GV, Dans LF, 2008). Although many species are generally categorized as probiotics, even closely related strains may have different clinical effects. Effects



of strain-specific probiotics need to be verified in adult studies before a specific evidence-based recommendation can be made.

**ZINC SUPPLEMENTATION:** Research in children suggests that zinc supplementation (20 mg per day for 10 days in children older than two months) may play a crucial role in treating and preventing acute diarrhea, particularly in developing countries. Studies demonstrate a decrease in the risk of dehydration, and in the duration and severity of the diarrheal episode by an estimated 20% to 40% (Bhutta ZA, Bird SM, Black RE, et al, 2007). Additional research is needed to evaluate potential benefits of zinc supplementation in the adult population.

## **PREVENTION**

Acute diarrheal diseases can be prevented with a variety of measures focused on preventing the spread of organisms from person to person and within the community (Casburn-Jones AC, Farthing MJ, 2004). These include: hand washing with soap, ensuring the availability of safe drinking water, appropriate disposal of human waste, breastfeeding of infants and young children, safe handling and processing of food and control of flies (particularly for Sd1). Two killed whole-cell oral cholera vaccines are internationally licensed and prequalified by the World Health Organization (WHO). A WHO global cholera vaccine stockpile of the lower cost bivalent vaccine was created in 2013 and has led to increasing use of killed oral cholera vaccines globally; the monovalent vaccine has been used primarily in travelers from resource-rich countries.

## **COMPLICATIONS**

Severe volume depletion is the most important complication of acute diarrheal illness in adults. However, several other systemic complications can occur, including bacteremia, hemolytic-uremic syndrome, Guillain-Barré syndrome, and reactive arthritis.





## FINDINGS

**Table 1: Socio-demographic distribution.**

The data collected in this category was intended to find out the distribution based on age and sex. The Frequency (f) for each category was found and percentages (%) calculated as shown in the tables below.

Age	Frequency (F)	Percentage (%)
< 18	24	2.6
18 – 27	291	32.3
28 – 37	58	6.4
38 – 47	36	4.0
48 – 57	02	0.3
58 – 67	03	0.4
68, and above	02	0.3
<b>Sex</b>		
Male	314	34.8
Female	159	17.6
<b>Total</b>	<b>473</b>	<b>100</b>

The table above shows that most of cases (32.3%) are between the ages of 18-27 years and most (34.8%) are males.



**Table 2: Incidence rate of acute diarrheal disease across age categories**

New cases (No of occurrence) and incidence rate (No. of probability of occurrence) are statistically calculated across age categories from 1<sup>st</sup> July, 2021 to 10th June, 2022.

Age	July	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	March	April	May	June	New cases	Incidence rate
< 18	-	-	1	1	5	2	3	2	5	5	-	-	24	26.7
18-27	13	15	25	30	33	19	25	20	39	50	57	22	291	323.3
28-37	2	6	3	2	4	-	1	2	6	10	17	5	58	64.4
38-47	2	1	2	1	1	2	-	-	2	3	13	9	36	40.0
48-57	-	1	-	-	-	-	-	-	-	-	-	1	02	2.2
58-67	1	-	-	-	-	-	-	-	1	1	-	-	03	3.3
68 & Above	-	-	-	1	1	-	-	-	-	-	-	-	02	2.2
<b>Total:</b>	18	23	31	35	44	23	29	24	53	69	87	37	<b>= 473</b>	<b>524.9</b>

**Grand total: 524.9**

The result shows a high incidence rate 524.9, mostly affecting 18-27 years of age.

**Table 3: Incidence rate across the periods (monthly)**

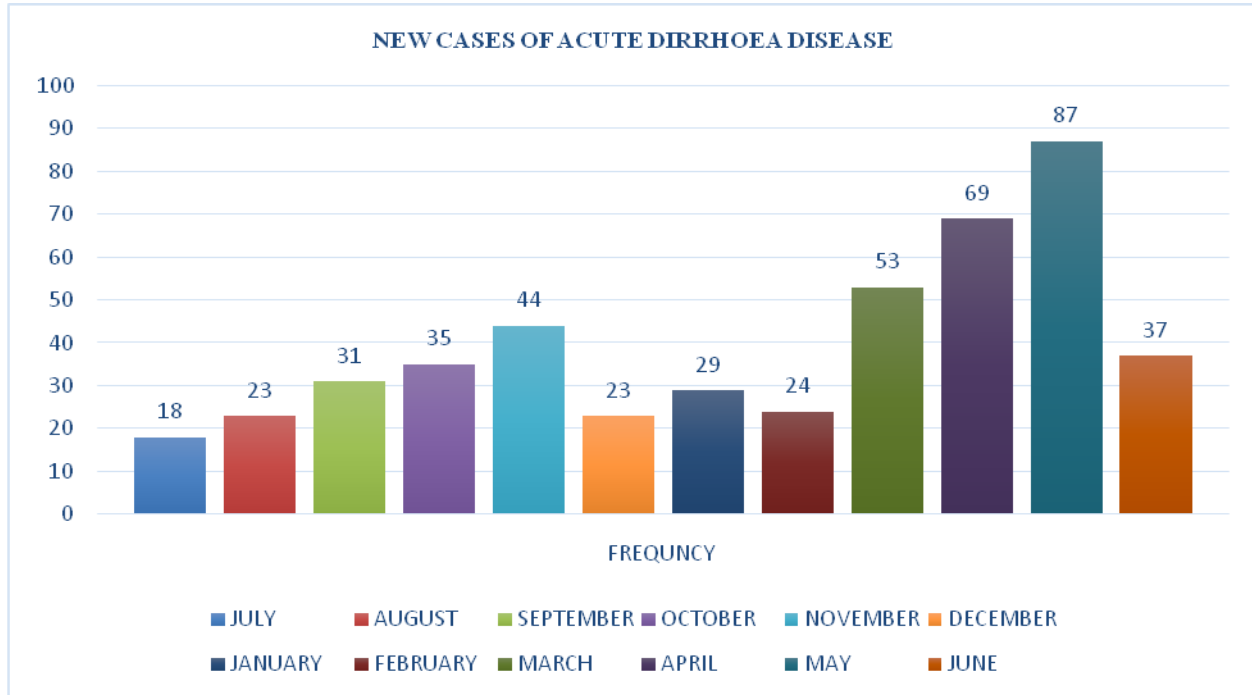
No of cases and incidence rate for one year was statistically calculated

July	Aug.	Sep.	Oct.	Nov.	Dec.	Jan.	Feb.	March	April	May	June	Total	
<b>New cases</b>	18	23	31	35	44	23	29	24	53	69	87	37	<b>473</b>
<b>Incidence rate</b>	20	25.5	34.4	38.8	48.8	25.5	32.2	26.6	58.8	76.6	96.6	41.1	<b>524.9</b>

The table above shows the increasing number of occurrence of new cases across the months with peak at May, 2022.



**Table 4: Distribution of cases within the period (1<sup>st</sup> July 2021 to 10<sup>th</sup> June, 2022)**



The result revealed an increasing incidence of cases with its peak at the month of May (87) 2022.

**DISCUSSION OF FINDINGS**

The findings revealed a high incidence of acute diarrheal disease among students and staff residing within the school community (approximately 900) in which the age of the under graduate students are between 18-25 years and these formed the majority with a high incidence of (32.3%) among the entire population. The high incidence of acute diarrheal disease (with a grand total of 524.9) is reflective of inadequate source of water supply, poor food, personal and environmental hygiene. Transmission may occur from drinking contaminated water or when people share personal objects (Webber, Rogger, 2009). Also, transmission rates are also related to poor hygiene, especially among children in crowded households (Eckardt AJ, Baumgart DC, 2011) and in those with poor nutritional status. Adults who have developed immunities might still carry certain organisms without exhibiting symptoms (Dolin, Raphael; Mandell, et al, 2010) thus, can become natural reservoirs of certain diseases. The total number of occurrence of new cases within (July 2021 to June 2022) was 473 and this revealed the incidence rate



(probability of occurrence) of 525.6 within the same period. The record affirmed high incidence of the cases among males (34.8%) and less in females (17.6%) counterpart. However, this contradict the findings of MohamAnandan,et al (2021) who reported a higher rate of acute diarrheal disease among female population which constitute 6.8% among residents of Thiruper village, Tiruvallur district, TamilNadu, India, in 2016 and this could be due to geographical difference. The school Health center adopt the use of ORS, Loperamide, Zincsulphate, metronidazole and Intravenous infusion in severe cases to counteract dehydration, the treatment yield a very good prognosis but even with this success, the number of cases found within a year is alarming and need to be addressed.

## **CONCLUSION**

This study was conducted to identify the incidence of acute diarrheal disease among adult population in Mewar University Chittorgarh Rajasthan. Data was obtained from patient record of the University health center and high incidence of acute diarrheal disease cases among the population residing within the school community was recorded.

## **RECOMMENDATION**

Based on the findings above, the following recommendation should be put in place.

1. The school water source should be improve and inspected for any source of contamination.
2. Improve safe food handling in the school mess.
3. Ensure a periodic medical checks for people handling the food.
4. Worn out equipment such as cooking pots, serving plates and spoons should be discarded and replaced with new ones.
5. The University authority should implement Rotavirus vaccination to all the staff and students against diarrhea disease.
6. University authority should expand and equip the school health center to accommodate the severe cases.



7. University authority should organize a sensitization program on water and food hygiene on a periodic basis.

## REFERENCES

1. Alam NH, Yunus M, Faruque AS, et al (2006).Symptomatic hyponatremia during treatment of dehydrating diarrheal disease with reduced osmolarity oral rehydration solution. *JAMA*.296(5):567-573.
2. Allen SJ, Martinez EG, Gregorio GV, Dans LF (2010). Probiotics for treating acute infectious diarrhoea. *Cochrane Database Syst Rev*.(11):CD003048.
3. Bhutta ZA, Bird SM, Black RE, et al (2000).Therapeutic effects of oral zinc in acute and persistent diarrhea in children in developing countries: pooled analysis of randomized controlled trials. *Am J ClinNutr*.72(6):1516-1522.
4. Ciccarelli, S; Stolfi, I; Caramia, G (29 October 2013). "Management strategies in the treatment of neonatal and pediatric gastroenteritis". *Infection and Drug Resistance*. **6**: 133–61. doi:10.2147/IDR.S12718. PMC 3815002. PMID 24194646.
5. Casburn-Jones AC, Farthing MJ. Management of infectious diarrhoea. *Gut*. 2004;53(2):296-305.
6. Dolin, Raphael; Mandell, Gerald L.; Bennett, John E., eds. (2010). "Chapter 93". Mandell, Douglas, and Bennett's principles and practice of infectious diseases (7th ed.). *Philadelphia: Churchill Livingstone/Elsevier*. ISBN 978-0-443-06839-3.
7. De Bruyn G, Hahn S, Borwick A (2000). Antibiotic treatment for travellers' diarrhoea. *Cochrane Database Syst Rev*.(3):CD002242.
8. De Bruyn G. Acute Diarrhea in adults (2008). *Am FamPhysician*.78(4):503-504.
9. Duggan C, Nurko S (1997). "Feeding the gut": the scientific basis for continued enteral nutrition during acute diarrhea. *J Pediatr*.131(6):801-808.
10. DuPont HL. Diarrheal diseases in the developing world. *Infect Dis Clin North Am*. 1995;9(2):313-324.
11. Eckardt AJ, Baumgart DC (January 2011). "Viral gastroenteritis in adults". *Recent Patents on Anti-Infective Drug Discovery*. **6 (1)**: 54–63. doi:10.2174/157489111794407877. PMID 21210762.



12. Federspiel F, Ali M (2018).The cholera outbreak in Yemen: lessons learned and way forward. *BMC Public Health* 2018.18:1338.
13. GBD (2016). Diarrheal Disease Collaborators. Estimates of the global, regional, and national morbidity, mortality, and etiologies of diarrhea in 195 countries: a systematic analysis for the Global Burden of Disease Study. *Lancet Infect Dis* 2018; 18:1211.
14. GBD (2019). Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study. *Lancet* 2020; 396:1204.
15. Gadewar S, Fasano A (2005).Current concepts in the evaluation, diagnosis and management of acute infectious diarrhea. *Curr Opin Pharmacol.*5(6):559-565.
16. Guerrant RL, Van Gilder T, Steiner TS, et al;(2001). Infectious Diseases Society of America; Practice guidelines for the management of infectious diarrhea. *Clin Infect Dis*;32(3):331-351.
17. Harris JB, LaRocque RC, Qadri F, et al (2012). Cholera. *Lancet.* 379:2466.
18. Hanauer SB, DuPont HL, Cooper KM, Laudadio C (2007). Randomized, double-blind, placebo-controlled clinical trial of loperamide plus simethicone versus loperamide alone and simethicone alone in the treatment of acute diarrhea with gas-related abdominal discomfort. *Curr Med Res Opin.*23(5):1033-1043.
19. Hedberg CW, MacDonald KL, Osterholm MT(1994). Changing epidemiology of food-borne disease: a Minnesota perspective. *Clin Infect Dis.*18(5):671-680.
20. Hahn S, Kim Y, Garner P (2001). Reduced osmolarity oral rehydration solution for treating dehydration due to diarrhoea in children: systematic review. *BMJ.*323(7304):81-85.
21. Hanauer SB, DuPont HL, Cooper KM, Laudadio C (2007). Randomized, double-blind, placebo-controlled clinical trial of loperamide plus simethicone versus loperamide alone and simethicone alone in the treatment of acute diarrhea with gas-related abdominal discomfort. *Curr Med Res Opin.*23(5):1033-1043.
22. Kosek M, Bern C, Guerrant RL (2003). The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. *Bull World Health Organ.*81(3):197-204.
23. Matheson AJ, Noble S (2000).Racecadotril. *Drugs.*59(4):829-835.
24. Public health impact of Rwandan refugee crisis: what happened in Goma, Zaire, in July, 1994? Goma Epidemiology Group. *Lancet* 1995; 345:339.



25. Riddle MS, Arnold S, Tribble DR (2008). Effect of adjunctive loperamide in combination with antibiotics on treatment outcomes in traveler's diarrhea: a systematic review and meta-analysis. *Clin Infect Dis.*47(8):1007-1014.
26. Scallan E, Hoekstra RM, Angulo FJ, et al (2011). Foodborne illness acquired in the United States. *Emerg Infect Dis.*17(1):7-15.
27. Scallan E, Griffin PM, Angulo FJ, Tauxe RV, Hoekstra RM (2011). Foodborne illness acquired in the United States—unspecified agents. *Emerg Infect Dis.*17(1):16-22.
28. Shen B, Khan K, Ikenberry SO, et al (2010). ASGE Standards of Practice Committee; The role of endoscopy in the management of patients with diarrhea. *GastrointestEndosc.*71(6):887-892.
29. Singh, Amandeep (July 2010). "Pediatric Emergency Medicine Practice Acute Gastroenteritis — An Update". *Pediatric Emergency Medicine Practice.* 7 (7).
30. Webber, Roger (2009). *Communicable disease epidemiology and control: a global perspective* (3rd ed.). Wallingford, Oxfordshire: Cabi. p. 79. ISBN 978-1-84593-504-7. Archived from the original on 2015-10-26.
31. Walker, CL; Rudan, I; Liu, L; Nair, H; Theodoratou, E; Bhutta, ZA; O'Brien, KL; Campbell, H; Black, RE (Apr 20, 2013). "Global burden of childhood pneumonia and diarrhoea". *Lancet.* **381** (9875): 1405–16. doi:10.1016/S0140-6736(13)60222-6. PMC 7159282. PMID 23582727.
32. World Health Organization (2017). *Progress on Drinking Water, Sanitation and Hygiene: Update and SDG Baselines.*
33. Walker CL, Black RE (2010). Diarrhoea morbidity and mortality in older children, adolescents, and adults. *Epidemiol Infect.* 138:1215.