

Review Article

Global Epidemiology and Management of Acute Diarrhea in Children from Developing Countries

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Abstract

Diarrheal disease remains one of the leading causes of death in children under the age of five years in developing countries. Extensive measures have been in effect in low- and middle-income countries (LMICs), worldwide, to provide clean water, good hygiene, and sanitary living conditions. However, many survivors continue to deal with persistent diarrhea and nutrient deficiencies, affecting their growth due to their low socioeconomic status. There are over 2.5 billion diarrheal illnesses cases annually, which account for an estimated 1,400 deaths daily, according to the World Health Organization (WHO). The lack of maternal education, insufficiency or early cessation of breastfeeding, poor handwashing technique, improper storage of food and water, and limited access to proper health facilities in developing countries has resulted in children facing severe dehydration and prolonged mucosal injury that ultimately results in their death. For the patients that can access healthcare, diagnosis is achieved by stool microscopy and culture. Furthermore, polymerase chain reaction (PCR), has been used to test for *Escherichia coli* and norovirus to detect toxin-encoding genes, while enzyme immunoassay is used to detect other pathogens, such as *Campylobacter*, rotavirus, adenovirus, astrovirus, *Entamoeba histolytica*, *Shigella*, *Giardia*, and *Cryptosporidium*. Additionally, subsequent septic bacterial infections that result from inadequate care and poor management of diarrheal illness have resulted in the use of oral rehydration and antibiotics with a minimal resolution of persistent diarrhea in some patients. Several interventions that are being implemented in LMICs to combat diarrhea-related mortality, include providing educational resources to caregivers and healthcare providers, training caregivers to be able to detect early signs of deterioration in children, as well as purifying water and sanitation. Additionally, the importance of highly nutritious foods and proper breastfeeding techniques for the first six months of life have been shown to provide children with stronger immune systems to enable them to combat infections.

INTRODUCTION

Acute diarrhea is the second leading cause of death in children under the age of five years, particularly in developing nations, even though the cause is easily preventable and treatable [1,2]. According to the World Health Organization (WHO), acute diarrhea is defined as the passage of three or more watery stools per day that lasts up to two weeks [2,3]. Each year there have been about 2.5 billion diarrheal cases reported in children under the age of five, out of which approximately 1,400 end up in death every day [4]. The most stereotypical cause of all diarrheal diseases around the world is bacteria [3]. *V. cholerae*, *C. botulinum*, *Shigella*, *C. jejuni*, *E. coli*, *Salmonella*, and *S. aureus* are the most common causes of diarrhea amongst children under the age of five [3]. Water sources that have been contaminated, bacterial infections, malnourishment, poor personal hygiene and poor living conditions all contribute towards acute diarrhea in children under the age of five years [2].

The mouth is the most common entry point for gastrointestinal

pathogens, particularly when children are in contact with fecal matter that has contaminated their food and/or water [3]. Once these pathogens get into the gastrointestinal tract, they trigger the over secretion of fluid in the lumen of the small intestine, leading to an electrolyte imbalance and diarrhea [3]. Majority of these children present with dehydration, dry mouth, irritability, lethargy, dark-colored urine, or no urine over three hours, fatigue, and dizziness [5]. In some cases, these children may also present with dysentery and fever, as reported by their parents [5]. It is therefore important to note that continuous and prolonged intestinal mucosal injury leads to ineffective repair of the gastrointestinal tract [6].

The diagnosis of acute diarrhea is done via a stool sample [5]. *Escherichia coli* is tested with a polymerase chain reaction (PCR), that detects the toxin-encoding genes: stx1, stx2, eae, bfpA, ipaH, aatA, and aaiC, as well as those encoding heat-labile enterotoxin and heat-stable enterotoxin [5]. Other pathogens, such as *Campylobacter*, rotavirus, adenovirus, astrovirus, *Entamoeba histolytica*, *Giardia*, and *Cryptosporidium* are detected using

enzyme immunoassay [5]. PCR is also used to test for norovirus [5].

A significant percent of diarrheal disease can be prevented by using clean drinking water, proper sanitation, and good personal hygiene [2]. Living in underdeveloped countries, along with a lack of maternal education has a positive correlation with diarrhea diseases in children [4]. Diarrhea can last up to several days, causing severe dehydration leading to inadequate amounts of salt and water in the body required for survival [2]. In the past, severe dehydration and fluid loss were the main causes of death in most of the children [2]. Now septic bacterial infections, especially in malnourished children or those with impaired immunity, are accounting for an increasing proportion of all diarrheal associated deaths [2]. Though the introduction of oral rehydration solutions (ORS), and antibiotics have reduced acute diarrhea fatalities, numerous children still develop persistent diarrhea and/or malnutrition, growth deficiencies, and decreased cognition [1]. Persistent diarrhea is defined as diarrhea lasting from one to fourteen days with increasing intensity [6]. 36% to 54% of diarrheal deaths in children under the age of five in developing nations have been linked to persistent diarrhea that started as acute diarrhea [6]. The objective of this paper is to review the epidemiology and management of acute diarrhea in children from developing nations.

METHODOLOGY

An electronic literature search was conducted using PubMed, Google Scholar, EBSCOhost, Mendeley, and MedLine Plus. The search was limited to peer-reviewed articles published between January 1, 2004, and September 22, 2020. Articles were chosen if they included keywords such as acute diarrhea, diarrheal disease, children in households, personal hygiene, sanitation, and water in developing nations. Articles were assessed and incorporated in the review based on their relevance to the topic.

EPIDEMIOLOGY OF ACUTE DIARRHEA IN CHILDREN FROM DEVELOPING NATIONS

Acute diarrhea is caused by many different types of parasitic, bacterial, and viral pathogens, which are commonly observed in the environment. Of these pathogens, bacterial infections are the most common causes of diarrheal illnesses in low-and middle-income countries (LMICs) [7]. To be specific, *Campylobacter*, enterotoxigenic *E.coli* (ETEC), *Cryptosporidium*, *Shigella*, adenovirus, and rotavirus were found to be the leading causes of moderate-to-severe acute gastroenteritis in children, followed by *Salmonella*, *Vibrio*, and other diarrheagenic *E. coli* (i.e. EHEC) [7,8]. Table 1 further elaborates on the most prevalent bacterial, viral, and protozoal organisms that cause diarrheal diseases in children [9]. This varied etiology of acute diarrhea brings challenges for health facilities to identify the culprit pathogen, making it difficult to properly manage, as well as prevent future episodes [7].

Over 2 billion cases of diarrhea occur annually, with a steady decline following the appropriate treatment of these cases in LMICs [10]. Unfavorable socioeconomic circumstances in LMICs such as improper sanitation, malnutrition, substandard maternal education, lack of or early cessation of breastfeeding, poor hand

Table 1: Prevalent bacterial, viral, and protozoal organisms causing diarrheal illness in children.

Pathogens		
Viruses	Bacteria	Protozoa
Rotavirus	Shigella	Cryptosporidium
Calicivirus	Salmonella	Cyclospora
Enteric adenovirus	Campylobacter	Entamoeba
Astrovirus	Yersinia	Giardia
	Escherichia coli	
	Vibrio	
	Clotridium difficile	
	Bacillus ceres	
	Staphylococcus aureus	

Note: Data recreated and reported by Dr. Karen L. Kotloff [9].

washing technique, and improper storage of food and water are several risk factors associated with an increased incidence of diarrhea [3,8]. To combat these risk factors and the decline in inappropriate treatment, a multipronged approach needs to be implemented. Some interventions that have shown promising results include purifying water and ensuring proper sanitation in families, training programs for mothers and health workers with behavioral interventions. Good childcare practices for caregivers and healthcare providers, educating caretakers to be able to recognize the signs and symptoms of diarrheal diseases early as well as signs of deterioration, and increased opportunity to seek professional help without delay will aid to reduce the incidence and prevalence of the disease [4,11]. Figure 1 shows the rate at which children under five years of age with diarrhea sought medical attention and/or advice in four selected LMICs: Bangladesh (29.5%), Kiribati (70.1%), Sierra Leone (85.3%), and Zimbabwe (35.2%) [12].

Diarrhea has a detrimental impact on the health of a child and can lead to deterioration of their growth and cognitive development. One major factor that can contribute to such a decline in a child's health is poor nutrition. There is a well-

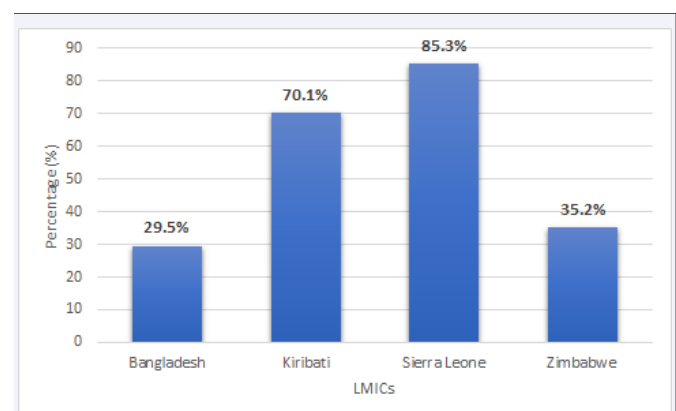


Figure 1 Percentage of children under five years of age with diarrhea from four LMICs who sought care from a medical provider or healthcare facility in 2019.

Note: Data recreated and reported by UNICEF, 2019 [12].

established relationship between the severity of diarrhea and nutritional deficiency [10]. Also, there is an inverse correlation between the duration and severity of diarrhea with macro and micronutrient deficiencies in children affected. Diarrhea on its own causes malabsorption of nutrients leading to a life-threatening cycle of undernutrition. Moreover, malnourishment leads to an inadequate immune response in affected children, which can predispose the children to dehydration, fever, vomiting, chronic illness, and developmental retardation [10]. Irregular immune responses are one major reason why 61% of childhood mortality from diarrhea is ascribed to malnutrition [10]. Thus, access to food that is high in nutritional value and is prepared and stored hygienically is crucial to the well-being of children. Another important factor that can lessen the disease burden of diarrhea is proper breastfeeding for the first six months of life [10]. Breast milk has several immunological properties that can protect a child during the early stages of life from infections, especially from pathogens that cause diarrhea. Therefore, nutritional support can serve as both a therapeutic and a preventative intervention against future diarrheal episodes [11,13]. Figure 2 identifies the percentage of children under five years of age with diarrhea in four selected LMICs that received ORS: Bangladesh (72.4%), Kiribati (61.3%), Sierra Leone (85.3%), and Zimbabwe (35.8%) [12].

DISCUSSION

This paper illustrates the predominance of diarrheal diseases in children under the age of five and its relation to unfavorable socioeconomic circumstances that abound in developing countries. The use of interventions such as purifying water and good sanitation and educating caretakers about early detection of diarrhea have proven to lower the prevalence of the disease. Figure 1 shows the percentages of caretakers that sought medical intervention from health professionals in four selected LMICs, which resulted in significantly lower rates of diarrhea compared to similar nations that did not receive medical intervention and had higher rates of diarrhea. The two nations that received higher rates of medical intervention, 85.3% of caretakers in Sierra Leone and 70.1% of caretakers in Kiribati, had lower cases of diarrhea in children [12]. However, in LMICs that received

lower rates of medical intervention, 35.2% in Zimbabwe and 29.5% in Bangladesh, had higher cases of diarrhea in children [12]. Also, the rates of ORS provided to children with diarrhea in LMICs and the incidence of diarrhea in these nations were compared. The three nations that received higher rates of ORS, 85.3% of patients in Sierra Leone, 61.3% of patients in Kiribati, and 72.4% of patients in Bangladesh had lower cases of diarrhea in children [12]. Furthermore, LMICs that received lower rates of ORS, 35.8% in Zimbabwe, demonstrated higher cases of diarrhea in children [12]. The data from our results demonstrated the importance of early intervention and supplementation of ORS by healthcare professionals, as well as proper education to caregivers of children with diarrhea.

There are various characteristics associated with maternal and household education that directly correlates with the management of diarrheal illness in children under five. In a study conducted by Pinzon-Rondon and colleagues, it was reported that the younger age of mothers compared to older mothers showed higher cases of diarrhea in children, which could be due to a lack of proper education about childcare and appropriate sanitation [4]. Additionally, mothers without higher education had increased rates of diarrhea in their children, with a 42% increased rate in mothers without formal education, a 45% increased rate in mothers without an elementary school education, and a 29% increased rate in mothers without a high school education [4]. Moreover, mothers who are employed and work while nursing their babies reported 14% higher chances of having children with diarrhea, which can be mostly due to the unavailability of mothers to detect when their children start developing signs and symptoms of diarrheal disease [4]. Lastly, mothers who had planned pregnancies presented with a 29% decrease in reporting of diarrheal illness in their children, as compared to mothers who had unplanned pregnancies; possibly due to their inability to receive proper health care [4].

The biggest factors leading to deaths in children under the age of five in developing countries is the lack of clean water supply, unsanitary living conditions, and poor personal hygiene, which have been associated with 88% of deaths resulting from diarrhea worldwide [4]. Out of these deaths, 84% occur in children under five years of age in developing countries [4]. The major detriment in the prevention and management of children with diarrheal illness in developing countries is insufficient resources and unstable infrastructure to effectively help treat these patients [4]. According to WHO, socioeconomic inequalities and poverty have continuously made it difficult to manage patients from developing countries despite providing the right education [9]. Most of the time management of diarrheal illnesses at home and outpatient facilities focus on rehydration and re-feeding of children under five years of age [9]. WHO recommends five methods for physicians to utilize to effectively prevent and treat diarrhea and its complications; these include the use of the rotavirus vaccine, ORS, zinc supplementation, proper personal hygiene with an emphasis on handwashing, and targeted antibiotic therapy for certain conditions [9].

The administration of the rotavirus vaccine to under-five children in developing countries have shown to substantially reduce the cases of rotavirus-associated diarrhea [9]. The

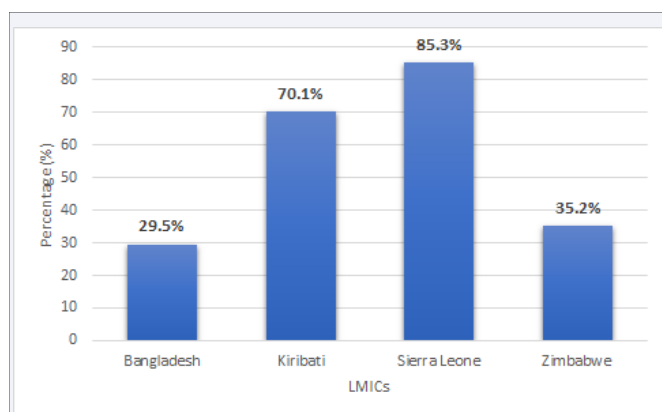


Figure 2 Percentage of children under five years of age with diarrhea from four LMICs who received ORS in 2019.

Note: Data recreated and reported by UNICEF, 2019 [12].

three live oral vaccines that have been licensed and are being administered in various countries are the three-dose pentavalent G1, G2, G3, G4, P[8], human-bovine vaccine (RotaTeq), the two-dose monovalent human G1P[8], vaccine (ROTARIX), and the three-dose monovalent human-bovine 116E G6P[11], vaccine (Rotavax) [9]. WHO currently recommends routine immunization of all infants with the rotavirus vaccine in high-and middle-income countries, as the rates of pediatric diarrheal illness, have dramatically declined, and further research on other vaccines are ongoing [9]. In high-and middle-income countries, the rotavirus vaccine has demonstrated direct protection from the virus, as well as herd immunity in unvaccinated children [9]. In LMICs, the rotavirus vaccination has not shown a significant effect, with a 51% to 64% decrease in rotavirus diarrhea, as compared to higher-income countries with an 85% to 98% decrease in rotavirus diarrhea [9]. The vaccine alliance, Gavi, has explained that the higher rates of diarrhea in children in LMICs are directly related to lack of resource availability, and have thus effectively introduced rotavirus vaccine in forty of the poorest countries worldwide [9].

ORS, as stated by WHO and United Nations International Children's Emergency Fund (UNICEF), has shown to effectively decrease the morbidity and mortality resulting from diarrheal illnesses in children, as demonstrated in Figure 2 [12,14]. The low osmolarity ORS composition consists of 13.5 grams of anhydrous glucose, 2.6 grams of sodium chloride, 2.9 grams of trisodium chloride, and 1.5 grams of potassium chloride dissolved in 1 liter of water [15]. This specific composition has shown to decrease the stool output, lower episodes of emesis, and the need for interventional therapy [15]. The reports of diarrhea cases have declined in high-and middle-income countries that have utilized ORS; however, LMICs have not effectively used ORS in their therapeutic modalities due to lower rates of patients presenting to healthcare facilities in the early stages of diarrheal disease [14]. The involvement of private and public sectors, as well as providing appropriate supply and demand to patients by effectively upscaling ORS in developing nations, can potentially lead to a decrease in mortality [14]. Moreover, the use of zinc replacement has been shown to decrease the duration of diarrhea and reduce the complications associated with diarrhea [9]. WHO recommends that all children with diarrhea receive 10 mg for those less than six months of age and 20 mg in older children, for a duration of 10 to 14 days [9].

It is highly recommended that children that present with persistent diarrhea, severe dehydration, and malnutrition be hospitalized and managed with the inpatient guidelines outlined by WHO [3]. Also, the use of various antibiotics has shown to be effective in only certain infections, as continuous use of antibiotics in some children can increase their chance of developing serious conditions [3]. This is evident with the use of antibiotics for Shiga toxin-producing *E. coli* (STEC) infection, which can predispose the child to the risk of hemolytic uremic syndrome. Furthermore, nontyphoidal *Salmonella* (NTS) can increase the chances of deterioration of the infection [3,9]. For the most part, diarrheal illnesses are managed with local guidelines of re-feeding and rehydration. Patients that present with dysentery from an unknown cause and are in unstable condition, are recommended to receive Ciprofloxacin 15 mg/kg twice a day

for three days, or Ceftriaxone 50 mg to 80 mg intravenously if severe [9]. Additionally, patients that present severely ill with cholera can receive Erythromycin estolate 12.5 mg/kg four times a day for three days, or Ciprofloxacin 15 mg twice a day for three days [9]. The use of antibiotics, other than these guidelines, is not recommended as they can lead to further complications.

Lastly, mothers and caregivers that do not adhere to strict hand washing techniques have shown an increase in children presenting with diarrhea [3]. Feeding bottles and other utensils used by children can be easily contaminated with fecal bacteria and can ultimately lead to contaminated breast milk [3]. Inadequate disposal of waste and using unsanitary toilet facilities can predispose children to diarrhea [3]. Older children in developing countries can also get diarrhea through contaminated water sources, improper packaging of food and water, as well as fecal contamination of food and improper handwashing techniques [3]. Most of the population in developing countries consume water from a potable water source that is used by the entire community, which can predispose children to diarrheal illnesses [3]. Studies from developed and developing countries have shown a decrease of 42% to 47% of cases of diarrhea in children with caregivers who wash their hands with soap and water before handling food sources and feeding their children [3]. With a combined approach of proper education for caregivers, adequate sanitary living conditions, and prompt management of diarrheal illnesses, the rates of mortality due to diarrhea in children can drastically decline in developing countries as seen in the developed nations worldwide.

CONCLUSION

Diarrhea, although preventable and treatable, is still a concerning threat to global public health, especially in LMICs with children under the age of five. This is mainly due to socioeconomic and demographic constraints from inadequate access to healthcare and lack of affordability. To reduce mortality rates, preventative measures such as clean drinking water, proper sanitation, and good personal hygiene must be implemented. If diagnosed, treatment should be conducted quickly and efficiently. To save the life of a child, most underdeveloped countries will require resources, such as funding and support to achieve this goal. It is therefore recommended that a multidisciplinary approach along with parents' competency, knowledge, and ability to recognize risk factors be met with improved behavioral interventions. In other words, the spectrum of basic social, behavioral, and applied investigations related to diarrheal cases need to be acknowledged to be effective in its prevention.

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