



## Acute Gastroenteritis in Children, Overview, Etiology, and Management; Literature Review

Meshary Abdullah Alhammad<sup>1\*</sup>, Sami Sulaiman Alanazi<sup>1</sup>, Zainab Hassan Almadan<sup>2</sup>, Ghaliyah Amin Thiga<sup>3</sup>, Ali Yahya Alabbas<sup>4</sup>, Zainab Abdulmajid Almubarak<sup>5</sup>, Maiar Najeeb Hijazi<sup>3</sup>, Shuruq Abdullah Albalawi<sup>6</sup>, Dina Ghurmullah Alzahrani<sup>6</sup>, Majdah Ahmed Almaghrabi<sup>3</sup>, Duaa Tariq Abdulhadi Almasri<sup>7</sup>

<sup>1</sup> Faculty of Medicine, Almajma'ah University, Riyadh, KSA

<sup>2</sup> Faculty of Medicine, Imam Abdulrahman bin Faisal University, Dammam, KSA

<sup>3</sup> Faculty of Medicine, Umm Al Qura University, Makkah, KSA

<sup>4</sup> Department of Family Medicine, Ministry of National Guard - Health Affairs, Najran, KSA

<sup>5</sup> Faculty of Medicine, King Faisal University, Al Ahsa, KSA

<sup>6</sup> Faculty of Medicine, Alfarabi Medical College, Riyadh, KSA.

<sup>7</sup> General Practitioner, Maternity and Children Hospital, Makkah, KSA

### ABSTRACT

**Background:** Acute gastroenteritis is a new diarrhea illness commonly self-limiting disease in children and sometimes associated with significant mortality and morbidity among children in developing countries. The most common cause is a viral illness, but other causes must be excluded in certain circumstances. Clinical features can be mild, as watery diarrhea to severe diarrheal illness complicated by dehydration, pre-renal azotemia, and eventually death. **Objective:** the aim of this literature review to address the common cause of gastroenteritis in children, the impact on the health system globally, and the management approach to avoid such complications. **Methodology:** We searched in the PubMed database looking for relevant articles to the topic. We used Mesh terms: Gastroenteritis in children, diarrhea in children, viral gastroenteritis in children. **Conclusion:** Children with gastroenteritis illness must be assessed adequately for the degree of dehydration and possible consequences. The cornerstone of therapy is rehydration, either orally or intravenously, depending on the associated symptoms, such as nausea or vomiting, and the dehydration degree.

**Keywords:** Diarrhea in Children, Pediatric diarrhea, Infectious diarrhea, gastroenteritis, infectious enteritis, Rotavirus.

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**Corresponding author:** Meshary Abdullah Alhammad

**E-mail** ✉ [dr.mesh970@gmail.com](mailto:dr.mesh970@gmail.com)

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### INTRODUCTION

Acute gastroenteritis (AGE) is a new diarrheal onset with or without vomiting that causes significant morbidity and mortality in children [1-5]. Generally, it is a self-limiting condition, but still, it is the most frequent cause of hospitalization and associated with a significant disease burden [1]. Furthermore, AGE is the commonest cause of death among infants and children in

developing countries and is commonly caused by infection, particularly viral [1, 6]. Based on the World Health Organization (WHO), diarrhea is defined by passing three or more loose or liquid stools per day or more frequently than the usual pattern for the individual [1]. Acute gastroenteritis in children is causing a public health issue [1]. Worldwide, around 10.6 million children are dying annually before reaching five years of age, and 20% of deaths are caused by

gastroenteritis alone [1]. Diarrhea usually lasts less than seven days; if it lasts more than 14 days, it is named protracted diarrhea [6]. In the neonatal period, a change of stool consistency compared to the usual pattern for the individual child is a better indicator of acute diarrheal illness more than stool frequency [6].

Clinical manifestations include watery stools, occasionally mixed with blood, after a 1-7 days incubation period [6]. Vomiting and fever may follow or precede diarrhea or can be absent completely [6]. Infrequent complications include intussusception, toxic, or hypovolemic shock with pre-renal azotemia as a feature of severe dehydration [6]. Convulsion has been reported in some cases, and it usually resulted from multi factors [7]. Electrolyte disturbances and dehydration due to the severe loss of electrolytes and water resulted from stool loos or vomiting may provoke neurological symptoms [7]. Also, high-grade fever (>39 C) that associate diarrhea illness may induce convulsions, especially in infants and toddlers who have an immature central nervous system, makes them highly susceptible to neurological symptoms [7]. Vomiting usually stops within a few hours after proper rehydration, and diarrhea usually stops within two days to one week [6].

#### **Epidemiology and Disease Burden:**

The severity of the diarrhea illness is directly related to the causative agent [8]. AGE caused by rotavirus is responsible for severe diarrheal illness, which usually required hospitalization [8]. Globally, up to 40% of children with diarrhea aged below five years are hospitalized with rotavirus [8]. In Europe, rotavirus is responsible for > 50% of gastroenteritis hospitalizations and around one-third of seeking emergency department [8]. Not surprisingly, the economic burden of AGE is essential, not only the cost of therapy but also the indirect cost caused by absence from work by parents or caregivers of sick children [8]. In the USA, Canada, and Europe, social costs related to rotavirus infection in children < 5 years have been considered > 50% of the total cost of care [8]. Given the disease's burden, the development of the rotavirus vaccine became a priority [8]. Immunization for rotavirus is recommended in the States and Europe [8].

Universally, 3-5 billion AGE cases and almost 2 million deaths occur each year in less than five

years old children [9]. Annually in the United States, AGE considers nearly 10% (220.000) admission to hospital, more than 1.5 million outpatient visits, and around 300 deaths in children under five years, which costs about \$1bn [9]. In Australia, within the same group of age, around 100,000 hospital admissions, 22,000 emergency department visits, and 115,000 general practice referrals occur annually for rotavirus alone, with an estimated cost of \$A30m [9]. Children with inadequate nutrition are at higher risk of complications [9].

## **DISCUSSION**

### **Etiology**

Worldwide, a viral infection is the most common cause of AGE; moreover, rotavirus and norovirus being the most common in young children [9, 10]. Viral infections destroy small bowel enterocytes and lead to low-grade fever and watery diarrhea without blood [9]. Rotavirus causing seasonal infection in temperate climates, peaking in late winter but occurs during the tropics year [9]. Also, it causes severe dehydration, the main reason for mortality in children <5 years of age globally [10]. Most children will be infected by the age of 2 to 3 years, and many got infected more than once [10]. Almost 80% of Rotavirus infections are caused by five serotypes (G1-G4 and G9) [10]. Consequently, two rotavirus vaccines have been recently introduced and showed a high degree of immunity and protective efficacy: a naturally attenuated pentavalent human-bovine (WC3) reassortant rotavirus vaccine containing G1-G4 and P and an attenuated G1P monovalent human rotavirus vaccine [10]. A recent multi-center case-control study discovered rotavirus, *Cryptosporidium*, enterotoxigenic *Escherichia coli*, and *Shigella* spp. are associated with significant moderate to severe diarrhea in children [11].

While viral infection invades only the small intestine destroying the mature epithelium, bacterial and parasite infection exert their pathogenic impact in both bowel segments [12]. Pathologically, infectious diarrhea is categorized into three main groups: secretory, osmotic-secretory, and exudative-secretory [12]. Viruses cause Osmotic-secretory diarrhea, and secretory is caused by *Vibrio cholera* and toxinogenic strains of *E-coli*, and exudative-secretory by entero-

invasive bacteria (*Salmonella*, *Shigella*, *Campylobacter*) and *Entamoeba histolytica* [12]. Consequently, osmotic and osmotic-secretory diarrhea are manifested by liquid stools, and exudative-secretory by aqueous-mucilaginous and often bloody diarrhea [12].

Enteropathogenic *E. coli*, *Giardia lamblia*, and *Cryptosporidium* adhere to the proximal small intestine's mucosal surface, hence disturbing its function, primarily causing a malabsorptive diarrheal illness [12]. The immune-mediated response of acute infective diarrhea may lead to certain complications, which are listed in **Table 1** [12]. Ingestion of food containing enterotoxins of *Staphylococcus aureus*, *Clostridium perfringens*, and *Bacillus cereus*, causing secretory diarrhea [12]. Unlike infections, no bacterial colonization of the bowel in alimentary intoxications; besides, *Staphylococcus aureus* excretes a thermostable, while *Clostridium perfringens* and *Bacillus cereus* excrete thermolabile enterotoxins [12]. However, certain causes of acute diarrheal illness must be excluded found in **Table 2** [13].

**Table 1.** The immune-mediated response of acute infective diarrhea

Organism	Complications
<i>Yersinia</i> , <i>Campylobacter</i> , <i>Salmonella</i>	Erythema nodosum
<i>Campylobacter</i>	Guillain-Barre syndrome
<i>E. coli</i> O157:H7, <i>Campylobacter</i> , <i>Yersinia</i>	Hemolytic-uremic syndrome
<i>Campylobacter</i> , <i>Yersinia</i>	Hemolytic anemia
<i>Campylobacter</i>	IgA nephropathy
<i>Shigella</i> , <i>Salmonella</i> , <i>Campylobacter</i> , <i>Yersinia</i>	Reiter syndrome
<i>Shigella</i> , <i>Campylobacter</i> , <i>Yersinia</i>	Glomerulonephritis
<i>Salmonella</i> , <i>Shigella</i> , <i>Yersinia</i> , <i>Campylobacter</i> , <i>Cryptosporidium</i>	Reactive arthritis

**Table 2.** Differential diagnosis to Infectious Gastroenteritis

<ul style="list-style-type: none"> <li>• <b>Postenteritis syndrome (cow's milk protein intolerance or irritable bowel syndrome variant).</b></li> <li>• <b>Ongoing gastrointestinal infection (Chronic infection)</b> <ul style="list-style-type: none"> <li>• Excessive juice/fructose intake</li> <li>• Coeliac disease</li> </ul> </li> <li>• <b>Constipation with overflow diarrhea</b></li> <li>• <b>Factitious or fabricated illness</b></li> </ul>
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Sapoviruses (SaVs), a member of the *Calicivirida* family, is a causative gastroenteritis agent, mainly in children in both sporadic and outbreaks worldwide [14]. SaVs are considered the second most common causative virus behind *Norovirus* in children having acute diarrhea after achieving the rotavirus vaccine [14]. SaVs-associated outbreaks have resulted in semi-closed institutions such as schools, kindergartens, hospitals, and nursing homes for the elderly, and spread through the fecal-oral route, the main route of transmission [14]. SaVs transmit through exposure to SaVs-positive aerosols from feces, vomitus, or the ingestion of SaVs-contaminated food and water [14]. In one epidemiological study, SaVs has been linked to an outbreak of gastrointestinal infection in 482 primary school students during spring activities from February 24 to March 11, 2019, in Shenzhen city, China [14].

### Traveler's diarrhea

Traveler's diarrhea is often defined by the passing of three or more unformed stools/24 hours, associated with or without nausea, vomiting, abdominal cramps, or fever that occurs during or within 14 days of returning from travel to a resource-limited location [15]. Some experts defined the traveler's diarrhea as a two or more fold increase in stool frequency following overseas travel [15]. Almost 10% to 41% of traveler children are affected by diarrheal illness, and they are found to have a higher rate compared to adults [15]. Some data from multi-centers showed that ill children who return from international travel were less frequently have received pretravel medical advice than adults and more commonly required inpatient care [15]. During 2004-2009, almost 13% of the 64,039 enteric infections studied by the Center for Disease Control and Prevention were travel-related; also, 24.2% were children [15]. The primary causative organism in the whole sample *Campylobacter* (42%), non-typhoidal *Salmonella* (32%), and *Shigella* (13%) spp, resulting in 5 deaths [15]. The incidence and severity of traveler's diarrhea are based on the age, where infants and toddlers have the greatest incidence rates, highest severity, and a higher likelihood of requiring inpatient care [15].

### Medical Assessment

In assessing a child with AGE, it is essential to determine the onset, frequency, quantity, and features of the vomiting and diarrhea, recent meal intake or fluid, and recognize associated symptoms, including abdominal pain or fever [16]. Also, assess the amount of fluid loss is useful to evaluate urine output and deteriorate in mental illness [16]. Extraintestinal symptoms associated with diarrhea and/or vomiting should be assessed adequately, such as otitis media, pneumonia, and urinary tract infection [16]. However, it is unlikely that diarrhea associated with these diseases will be severe [16]. Some conditions may increase the risk of severe dehydration and need proper assessment, including malnutrition, prematurity, immunodeficiency, and heart diseases [16]. Relevant epidemiological data are helpful as a first diagnostic approach, have recent contact with other sick individuals, determine of a potential source of infection (water or food), overseas travel (Traveler's diarrhea), and recent rotavirus vaccination in children below three years of age [16]. Importantly, physicians must explore the capabilities of parents or carers to provide adequate support at home, particularly the administration of oral hydration and the wellness to rapidly take the child to a medical center for re-assessment if needed [16].

The physical examination must be directed on specific parameters to assess the hydration status, complications, and to recognize extraintestinal disease [16]. Temperature, heart rate, respiratory rate, blood pressure, capillary refill time, abdominal skin fold, anterior fontanel level, mucosal hydration including eyes and mouth, and mental status should be evaluated [16]. Clinical dehydration must be considered if weight loss reaches 3-4% [16]. As the degree of dehydration increases, vital signs started to be compromised, especially after 10% fluid loss [16]. While it is difficult to distinguish between mild to moderate dehydration on physical examinations (3-9% weight loss), the patient must manage the same [16]. According to the CDC recommendations, dehydration can be categorized into three phases: no or minimal dehydration (with <3% weight loss), mild to moderate dehydration (3-9% weight loss), and severe dehydration (>9% weight loss) (Table 3) [16].

**Table 3.** Dehydration Stages and Estimated Weight Loss

Degree of Dehydration	Estimated Weight Loss
Mild	3%
Mild to Moderate	3-9%
Severe	>9%

### Diagnostic Work-up

Generally, AGE is a clinical diagnosis and does not require a specific diagnostic test [17]. However, certain circumstances in which microbiological tests may be necessary for diagnosis and treatment [17]. Microbiological workup may be necessary for children with underlying chronic conditions (e.g., malignant disorders, IBDs, etc.), in extremely severe conditions, or those with a prolonged course of symptoms [17]. During an outbreak in childcare, school, hospital, and nursing home, microbiological investigations are considered to identify the pathogen and establish its source [17]. Further, children with a history of overseas travel and bloody diarrhea may benefit from further investigations [17].

Hematological markers, such as C-reactive protein (CRP) and procalcitonin level, are not routinely tested to distinguish between viral and bacterial gastroenteritis, and it is unlikely to change treatment based on the result [17]. Hence, normal CRP does not entirely exclude bacterial infection, and the procalcitonin level seems to be more effective than CRP in distinguishing between viral and bacterial AGE [17]. Fecal markers are also not recommended to be routinely tested for viral vs. bacterial AGE differentiation [17]. Fecal calprotectin usually reflects intestinal inflammation and associated more with bacterial infection than viral or parasitic causes [17]. Fecal calprotectin and lactoferrin have been studied for inflammatory bowel diseases (IBD) diagnosis and monitoring [17]. Although they are good indicators for IBS, neither is specific for IBD [17]. The combination of high fecal calprotectin and CRP showed a 94% diagnostic accuracy for bacterial AGE [17].

### Management

#### Oral Rehydration Solution:

Dehydration treatment consists of three elements: rehydration, replacement of ongoing losses, and normal feeding continuation [18].

The mode of rehydration depends on the degree of dehydration, and the patient must be adequately assessed before therapy initiation [18]. In minimal or no dehydration, patient therapy must be directed at the replacement of ongoing losses; to explain, for each watery stool, a 10 cc/kg body weight of oral rehydration solution (ORS) must be provided, and for each episode of emesis, a 2 cc/kg body weight of ORS the patient must receive [18]. Alternatively, children weighing < 10kg must receive 60-120 cc of ORS for each diarrhea stool or an episode of emesis, where children weighing >10kg must receive 120-250 cc of ORS for each episode [18]. Breast-fed children should continue breastfeeding, whereas patients eating solid foods should continue their usual diet except for eliminating high-sugar beverages [18, 19]. Moreover, children should not receive any special or diluted formula [18].

Implementing the guidelines mentioned earlier, many unnecessary referrals to hospital admissions can be avoided [19]. Patients with mild to moderate dehydration should receive 50-100 cc/kg of ORS over 304 hours, supplemented by fluids to restore continuous losses [18]. Initially, children must be taking a small amount (5-15cc) of ORS every 5 minutes and gradually increase ORS if tolerated [18]. Patients should also continue their breastfeed or solids except for high-sugar beverages [18, 19]. AGE children with mild to moderate dehydration are commonly encountered in the outpatient setting [20]. A trial of ORS may be ineffective if the patient is lethargic, has persistent vomiting, or refuses oral intake [20]. ORS may also be excessively time-consuming in a busy outpatient care facility, with a range of 10.7 to 16 hours required time for adequate hydration [20].

#### **Intravenous Rehydration Therapy:**

Intravenous rehydration is the standard gold treatment for severe dehydration or in cases of intolerance to oral rehydration therapy [21]. The volume and the rate of fluid administration are still questionable [21]. However, patients with severe dehydration should be initially resuscitated with Ringer's Lactate solution or normal saline via intravenous to achieve hemodynamic stability [18]. Oral rehydration therapy should be initiated as soon as possible after intravenous rehydration [18]. While no enough

data suggests an alternative approach of intravenous therapy, such as large-volume or rapid rehydration, future clinical trials may be required to solve some uncertainties [21]. In the absence of clear evidence, it is logical to follow the available recommendation of administering 20 ml/kg boluses [21].

#### **Oral vs. Intravenous Rehydration Therapy:**

A randomized clinical trial conducted to study the difference between ORT, and intravenous fluid (IVF) found that ORT was as effective as IVF in rehydrating moderately dehydrated AGE children [22]. Interestingly, some degrees indicated that ORT was superior to IVF and ORT patients have fewer hospitalization [22]. For example, ORT initiation was faster than IVF, especially in a busy emergency department often faced with overcrowding and long waits [22]. Also, ORT avoids the need for potentially painful and often difficult intravenous cannula placement [22]. After rehydration therapy, dehydration degree showed complete improvements with >90% of ORT receiving group compared to >82% of IVF group, having a 4-hours dehydration score that demonstrated resolution of their moderate dehydration [22]. Although different scores of successful rehydration were similar between groups, the IVF group showed better weight gain than the ORT group, and this difference was statistically significant [22]. The management of bacterial gastroenteritis is beyond the scope of this article.

#### **Antiemetic Therapy:**

Ondansetron, in particular, is used either orally or intravenously in young children with vomiting associated with AGE [21]. According to the Canadian Pediatric Society, oral ondansetron therapy, as a single dose, may be considered for 6 months to 12 years child with vomiting related to AGE and who have mild to moderate dehydration with intolerance to ORS [21]. The use of ondansetron is not recommended in patients for AGE patients with predominantly severe diarrhea, as ondansetron can worsen diarrhea as an adverse effect [21]. Ondansetron can cause electrolyte disturbances and be listed in the FDA black box alert published in September 2011 [21]. Therefore, electrocardiogram monitoring is recommended while the patient receives it, as it can result in QT interval prolongation, which can

lead to abnormal and potentially fatal heart rhythm, including Torsade de Pointes [21]. There is no evidence supporting the use of other antiemetics [21].

### CONCLUSION

Acute gastroenteritis is a common disorder among children with significant mortality and morbidity consequences. The most important consequence is dehydration, and the patient is assessed based on the degree of dehydration to establish adequate workup and treatment. While rotavirus is the most common causative organism of gastroenteritis in children, developing an effective vaccine is worthwhile to avoid potentially lethal dehydration and decrease the cost-effective burden on the health system globally. Also, various organisms can cause gastroenteritis, including bacterial or parasitic infection, with less incidence rate than viral infection. The diagnosis is based on clinical findings and the patient must be assessed adequately for dehydration status to establish the proper treatment approach. The mainstay of treatment is rehydration and monitoring, depending on the dehydration status.

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