**ABSTRACT**

Gastroenteritis is the inflammation of intestines and stomach which presents with vomiting, fever, abdominal pain and diarrhea. It could be persistent, acute, or chronic, and can also be classified as infectious or non-infectious. Despite improvement in management, the mortality can reach up to 17,000. In this study, our aim was to understand the various etiologies that cause gastroenteritis in adults, and also discuss methods of management. We conducted this review using a comprehensive search of MEDLINE, PubMed and EMBASE from January 1994 to March 2017. The following search terms were used: acute gastroenteritis, diarrheal disease, viral gastroenteritis, bacterial gastroenteritis, diagnoses of gastroenteritis. Each year, more than 350 million cases of acute gastroenteritis occur in the United States only. The largest portion of gastroenteritis cases is due to viral infections. Therefore, the empiric use of antibiotics is usually not recommended. However, in selected patients, empiric antibiotics therapy is indicated and is associated with significant improvement and decrease in mortality. The primary goal of management of gastroenteritis is treating dehydration.

**Keywords:** Gastroenteritis, Diarrheal diseases, Dehydration

**INTRODUCTION**

It is from the Greek language where the term ‘gastroenteritis’ was originally created, and it meant ‘stomach’ for ‘gastron’, and ‘small intestine’ for ‘enteron’, so the final meaning would be: ‘inflammation of the small intestines and the stomach’. The medical definition of gastroenteritis is diarrhea, or increased movement of the bowels regardless of the presence/absence of other symptoms like fever, vomiting, or abdominal pain. Movement of the bowel is considered increased when it occurs three or more times per day with loose or watery consistency. There are many used classifications when dealing with gastroenteritis, the most popular one being based on symptoms duration: acute, persistent, or chronic, being less than 14 days, between
14 and 30 days, and longer than 30 days, respectively. The term ‘recurrent gastroenteritis’ is generally used when the diarrhea recurs following at least a diarrhea-free week.¹

**METHODS**

We did a systematic search for gastroenteritis in adults using PubMed search engine (http://www.ncbi.nlm.nih.gov/). EMBASE, and Google Scholar search engine (https://scholar.google.com). All relevant studies were retrieved and discussed. We only included full articles. The following search terms were used: acute gastroenteritis, diarrheal disease, viral gastroenteritis, bacterial gastroenteritis, diagnoses of gastroenteritis

**Epidemiology**

In contrast to developing countries, acute gastroenteritis in the United States is usually considered to be a mild disease that is rarely associated with severe life-threatening complications. Reports published by the National Outbreak Reporting System estimate that over 350,000,000 acute gastroenteritis cases occur annually in the United States. In fact, both acute gastroenteritis and upper respiratory tract infections are considered to be among the most common causes of communicable diseases in the United State.²

The CDC has also reported, using the National Center for Health Statistics dataset, that all-cause mortality associated with acute gastroenteritis have been increasing since the year 1999, and in fact reached about 17,000 deaths annually. More than eighty percent of these deaths we found to be in the elderly population, and more than sixty percent of them were attributed to infections with Clostridium difficile. This leads to an important conclusion that older ages are associated with higher morbidity and mortality following an acute gastroenteritis attack. (https://www.cdc.gov/media/releases/2012/p0314_gastroenteritis.html)

**Etiology**

**Etiology of acute gastroenteritis**

Many organisms can usually cause an acute gastroenteritis attack. It is quite challenging to establish accurate incidence and prevalence of acute gastroenteritis because of under-reporting of attacks by many patients. Moreover, only 1.5% of stool samples get positive results for a bacterial cause.³

Norovirus and Rotavirus are the most common causes of viral gastroenteritis. Reports suggest that up to twenty-five million cases of acute viral gastroenteritis occur annually in the United States. This vast number of cases is responsible for about five million medical visits and over two hundred hospital admissions annually.⁴ When it attacks children, Rotavirus can lead to the development of a severe gastroenteritis that can be complicated with dehydration. The prior presence of malnourishment can make clinical picture worse and lead to significant morbidities and mortality. In fact, it has been estimated that over half a million deaths occur annually around the world due to rotavirus gastroenteritis. However, incidence of gastroenteritis from Rotavirus has been significantly decreasing in both the United States and Europe following the introduction of vaccination against the virus. This vaccination has been associated with more than 67% decrease in the incidence of rotavirus gastroenteritis.⁵

On contrast to rotavirus, Norovirus can cause acute gastroenteritis outbreaks in almost all age groups. These outbreaks can occur in places where there is a crowded, like nursing homes, prisons, cruise ships, schools, and other similar settings. Norovirus infection will cause severe attacks of vomiting that continue for up to 60 hours and regress spontaneously. This virus is usually transmitted through the fecal oral route.⁴

**Pathogenic viruses in the gastrointestinal tract**

Viruses had been discovered in the early 1900s and were identified as major pathology-causing organism. However, it was not until 1972 when the Norovirus was discovered as a gastroenteritis-causing virus. This discovery was made during a diarrhea outbreak in the state of California.⁷

Soon later, other viral organisms which cause acute gastroenteritis were identified, including the rotavirus that was first discovered within the epithelial cells of young children with gastroenteritis. Other viral agents included Astrovirus, enteric Adenovirus, and Sapivirus, which were discovered in cases of infantile diarrhea, children with acute diarrhea, and gastroenteritis outbreaks in children, respectively. All these mentioned viruses transmit through the fecal-oral route and from person to person. We will discuss this issue later in this review.⁸

Noroviruses are Caliciviridae viruses that cause gastroenteritis outbreaks in health care settings, military, cruise ships, and schools. Moreover, Norovirus has been associated with more than half of sporadic diarrhea cases reported in the literature. The pathological mechanisms of norovirus has been examined in vivo in several studies.⁸ However, it has been challenging since the discovery of norovirus to culture it. One recent study has described a culturing method of the virus in B cells. They found that in order to be able to culture Norovirus in vitro, several co-factors like enteric bacteria that express the histoblood antigen. Other members of the Caliciviridae virus family are the Sapoviruses. Scientists have been able to isolate five viral strains of the Sapovirus that are able to cause a disease in humans. These were found to be responsible for up to 12.7% of acute gastroenteritis worldwide. Outbreaks due to Sapovirus infection are
usually foodborne and can occur any time within the year.\textsuperscript{9}

The most common cause of acute viral gastroenteritis, especially in young children, is Rotavirus. Moreover, Rotavirus has also been known to cause gastroenteritis and infections among parents of infected children. Researchers performing in-vivo studies on rotavirus found that rotavirus, when infects a healthy adult, can cause diarrhea that leads to the shedding of the virus and a rise in the antibody titers.\textsuperscript{10}

Of all cases of sporadic diarrhea, it has been estimated that about ten percent could be attributed to an Astrovirus infection. Researchers have been able to isolate and identify astrovirus from people who were infected. Similar to rotavirus, when it infects healthy adults, astrovirus leads to diarrhea that sheds the virus. In addition, they were able to discover that Astrovirus has the ability of replication within the kidney cells of human embryos.\textsuperscript{11}

Adenoviruses are other important causes of diarrhea around the world, being responsible for up to 5.4\% of diarrhea cases in infants. Scientists have been able to isolate more than 55 subtypes of Adenovirus. However, only two types of these have been found to be linked with viral gastroenteritis, these two are Adenovirus subtype 40 and adenovirus subtype 41. Some scientists also argue that subtype 52 could also be linked with gastroenteritis. Others, on the other hand, believe that adenovirus subtype 52 is actually the same as subtype 41.\textsuperscript{12}

\textbf{Etiology of chronic gastroenteritis}

Gastroenteritis attacks that last for more than 30 days is known as chronic or persistent gastroenteritis. Generally, persistent gastroenteritis has etiologies that are different than acute gastroenteritis. These include drugs, parasites, protozoa, irritable bowel syndrome, inflammatory bowel diseases (including Crohn disease, ulcerative colitis, microscopic colitis, and collagenous colitis), celiac disease, eosinophilic gastroenteritis, colorectal malignancy, ischemic bowel, lactose intolerance, malabsorption, and intestinal obstruction.\textsuperscript{13}

Generally, hosts who are immunocompromised have a higher risk of developing severe persistent gastroenteritis. For example, patients with acquired immunodeficiency syndrome (AIDS) are known to have a relatively high incidence of cryptosporidium diarrhea. Cryptosporidium has also been known as an important cause of diarrhea outbreaks in swimming pools and contaminated supplies of water. Cryptosporidium can cause outbreaks because it produces resistant oocytes that can usually resist disinfectants.\textsuperscript{14}

Another significant cause of persistent gastroenteritis is giardia, which is usually found in contaminated water sources, swimming pools, and da-care centers. Giardia usually lead to the development of attacks of pale, explosive foul-smelling diarrhea, along with flatulence and bloating.\textsuperscript{15}

\textbf{Pathophysiology}

Different mechanisms could be responsible for the diarrhea caused by intestinal bacteria. These mechanisms could include mucosal invasion, adherence, and the production of toxins. In order to establish management protocols of gastroenteritis, it is essential to well understand the pathophysiology of the disease. The small intestines have an important function of absorbing fluids. In cases of gastroenteritis, small intestines fail in this task due to the action of toxins on intestines.\textsuperscript{16}

One single most important factor in the determination of the severity of the pathology is the inoculum size. For example, when considering enterohemorrhagic \textit{Escherichia coli} (EHEC) and \textit{Shigella} as little as 10 organisms are able cause a disease. On the other hand, it requires one million organisms of \textit{Vibrio cholerae} to cause a disease. Therefore, we can conclude that the inoculum size differs depending on the bacteria.\textsuperscript{17}

Another significant virulence factor when considering gastroenteritis is adherence. Several bacteria require to adhere to the mucosa of the intestines, especially initially. In order to establish this adherence, they produce several adhesive factors and proteins that help establishing the required attachment to the intestinal walls. For example, vibrio cholera bacteria use a specific kind of surface adhesins to be able to adhere to the intestinal borders. Another example is enterotoxigenic \textit{E. coli} that leads to the development of watery diarrhea by producing the colonization factor antigen, which is an adherence protein. This step is crucial for the pathology of enterotoxigenic \textit{E. coli}. Dysentery can be caused in shigella and enteroinvasive \textit{E. coli} infections. This occurs as a result of invasion and destruction of the mucosa of the small intestines.\textsuperscript{18}

The last important virulence factor that plays an important role in the development of a gastroenteritis attack is the production of toxins, which include enterotoxins. Enterotoxins can lead to the development of watery diarrhea due to their direct secretory effects on the mucosa of the small intestines.\textsuperscript{19}

\textbf{Community-acquired diarrhea}

The most important causes of bacterial gastroenteritis in Europe have been reported to be enteroge aggressive \textit{E. coli} (EAEC), \textit{Campylobacter}, and enteropathogenic \textit{E. coli}. A study in 2012 has concluded that \textit{Campylobacter} was responsible for more cases of chronic gastroenteritis than Salmonella, with an incidence of 68 vs. 22 cases per 100,000. In addition, salmonella cases have been decreasing recently for many reasons including the application of new veterinary control protocols that target salmonella species. Another important cause of chronic
gastroenteritis is EAEC, which has been linked with gastroenteritis in developed countries.20

*Clostridium difficile* diarrhea has also been increasing lately, despite lacking known risk factors. A possible hypothesis for this is the possible transmission through the fecal-oral route. However, this hypothesis is still debatable and needs to be further established.21

Shiga toxin-producing *E. coli* (STEC) strains, *Yersinia* species, and non-cholera *Vibrio* species are also common causes of gastroenteritis, despite, however, being less common. An outbreak of STEC was reported in Germany in the year 2011 and resulted of more than four thousand infections and over a thousand cases of hemolytic uremic syndrome. The incidence of STEC in Europe was estimated in 2012 to be 1.5 per 100,000.22

**Traveler’s diarrhea**

Studies suggest that up to half of individuals who travel from a developed country to a developing country will suffer from a traveler’s diarrhea that depends on both the origin country and the destination country. In most cases, traveler’s diarrhea develops within three weeks of travelling following the ingestion of food or drinks. A previous systematic review and meta-analysis have concluded that the strict application of the ‘boil it, cook it, peel it, or forget it’ advice was not associated with any reduction in the incidence of traveler’s diarrhea. Despite having a relatively high incidence, traveler’s diarrhea is usually mild, and only requires hospitalization in less than one percent of cases.23

Most cases of traveler’s diarrhea could be attributed to bacterial causes, most commonly, EAEC, enteroinvasive *E. coli*, and Enterotoxigenic *E. coli*. Other less common causes include *Shigella, Salmonella, And Campylobacter*. It is relatively rare for parasitic organisms to be the cause of traveler’s diarrhea. However, one must suspect a parasitic cause of traveler’s diarrhea persists longer than usual.24

**Diagnosis**

It is not uncommon for patients with a gastroenteritis attack to show abnormal vital signs; fever, tachycardia, and pain can all be present. The clinical picture of dehydration could also present depending on the severity of the disease. This clinical picture includes the following signs and symptoms: dry membranes, less turgor of skin, absent pulsations of the jugular vein, and altered mental status. These signs and symptoms can, however, have low specificity due to being vague and non-specific, but they still contribute to the treatment and management of the disease.25

**Investigations**

The first most important step in examining and evaluating a patient with suspected gastroenteritis is a thorough medical history with an accurate complete physical exam. This history must include food history and must also look for the presence of any alarming signs and symptoms. In most cases of acute gastroenteritis, the determination of the causing organism is not important and will not affect the management plan, which is most likely supportive. However, when there is severe dehydration, the case is different, and it is essential to look for the presence of any derangement in electrolytes levels.26

Routine investigations like a complete blood count are not usually able to determine the etiology of the disease, but they can still suggest the risk of developing a severe complicated disease. For example, a complete blood count that shows an increase in the number of leukocytes can suggest the presence of bacteremia, or *C. difficile* and pseudomembranous colitis. On the other hand, a complete blood count that shows decreased platelets can suggest the presence of hemolytic-uremic syndrome.27

Any patient with gastroenteritis complicated with high fever must have blood culture. Other symptoms that indicate testing for bacteria include signs and symptoms of dehydration, the presence of severe pain, or the need for hospital admission. In addition, some host-related factors can also require stool culture including pregnancy, old age, the presence of other co-morbidities, and decreased immunity.28

The routinely administrated stool culture can mainly detect the presence of *Campylobacter, Salmonella*, and *Shigella*. If the physician suspects the presence of another pathogen like *Yersinia, Listeria, or Vibrio*, this will need further specific analyses. Moreover, when there is bloody diarrhea, investigations to detect leukocytes and Shiga toxin in stool must be ordered. Testing for parasitic and protozoal agents should be indicated when the diarrhea persists longer than usual.29

**Treatment**

**General recommendations**

Rehydration is the single most important intervention in the management of gastroenteritis. Other measures include diet improvements and bowel rest. Regarding rehydration therapy, the first and best choice in mild-to-moderate cases is oral rehydrating therapy. It is especially effective in cases of small intestines diarrhea.25

**Control of symptoms**

The use of antiemetics and antimotility could be beneficial for symptomatic treatment. Antiemetic agents can be used to decrease vomiting and nausea caused by gastroenteritis. Both promethazine hydrochloride and prochlorperazine are indicated for this, with recent evidence suggesting that prochlorperazine could have higher efficacy and less sleepiness. On the other hand, the use of antimotility agents is generally indicated to
decrease the output of stool. These drugs include loperamide, narcotics, and diphenoxylate with atropine. Of these mentioned drugs, the most commonly used one is Loperamide, due to the best safety profile along with the highest efficacy. However, it is still considered safer to avoid the use of loperamide and other antimotility drugs in patients who have bloody diarrhea. In addition, antimotility drugs must not be used in children suspected to have *E. coli* O157:H7 infection. Moreover, previous studies have suggested that patients with *C. difficile* who take loperamide are at a higher risk of developing toxic megacolon.29

**Antibiotics**

Antibiotics should not be routinely used in the management of gastroenteritis and should be cautiously used if they are indicated. Recent guidelines suggest that empiric antibiotics treatment should be indicated in the following cases: severe traveler’s diarrhea, the presence of more than eight bowel movements daily, severe dehydration, symptoms persisting for more than a week, and the presence of an immunocompromised state.29

**Dietary modifications**

The ideal treatment in most cases is liquids with sufficient replacement of electrolytes. Patients who suffer from watery diarrhea are recommended to take potato, noodles, boiled rice, crackers, soup, and bananas. Moreover, they are advised to avoid the intake of foods that contain a high fat index.30

**CONCLUSION**

Gastroenteritis is a common disease that is considered one of the most common causes of infectious diseases around the world. It can cause several signs and symptoms including vomiting, nausea, abdominal pain, and, most importantly, diarrhea. Gastroenteritis can be acute, chronic, or recurrent. Each year, more than 350 million cases of acute gastroenteritis occur in the United States only. The largest portions of gastroenteritis cases are due to viral infections. Therefore, the empiric use of antibiotics is usually not recommended. However, in selected patients, empiric antibiotics therapy is indicated and is associated with significant improvement and decrease in mortality. The primary goal of management of gastroenteritis is treating dehydration.

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