A BURDEN OF GASTROENTERITIS ASSOCIATED WITH COMORBIDITIES AN EFFECTIVE MANAGEMENT STRATEGY

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ABSTRACT: Acute gastroenteritis prevalent amongst children and newborns is considered a serious infection globally. The Acute diarrhea as a result of gastroenteritis as per logistics suggest that there were more than 1.5 million outpatient visits along with 200,000 hospitalizations and 300 fatalities per year in children in U.S. Diarrhea is the leading cause of deaths amongst children with 30% relapse rate. The viral gastroenteritis caused by the Rotavirus is one the significant strain contributing the gastroenteritis. The suggestive therapies include Oral rehydration therapy (ORT) respective to age modulating the diet and ORS solutions. The gastroenteritis condition cannot be neglected but can be considered as significant public health issue especially in the elder patients with fatality ratio compared to children. The diagnosis of gastroenteritis includes signs, symptoms and stool cultures. The comorbidities in the patients when treated with variety of drugs is resulting damage of stomach lining and worsening the conditions of gastroenteritis. The comorbidities include the cardiovascular diseases, kidney related diseases and other infections playing major role for the chronic condition. There is need of clinical intervention for improvement of treatment, prevent reoccurrence and suggest the antibiotic rational use in the patients with comorbidities. The present review has represented the global data of infection causing agents, contributing factors of comorbidities leading to gastroenteritis, diagnosis and alternative treatment. The need of change in diet and rationale use of antibiotics is best measure to prevent the relapse of disease leading to less hospitalizations. The support from the alternative systems of medicine was suggested to improve the patient condition and also to prevent the reoccurrence.

INTRODUCTION: Acute gastroenteritis infection is considered as one of the most serious illnesses leading to deaths in children globally causing severe vomiting. The gastroenteritis has led to 1.4 to 2.5 million deaths per year during 2021. The condition of gastroenteritis is condition caused with or without symptoms of nausea, vomiting and diarrhea.

The most significant infection is viral gastroenteritis caused by Rotavirus which includes symptoms of nausea, vomiting, anorexia, weight loss and dehydration. The inflammation of the stomach, small intestine/ large intestine leads to abdominal pain, muscle cramps, vomiting, nausea and diarrhea.

The condition normally lasts from 1 to 2 weeks if unchecked may even become persistent from 14-30 days [1, 2]. The side effects include fever, dehydration and headache which lasts to couple of weeks [3-5]. The common causes of the gastroenteritis include virus, bacteria and parasites [6]. The Viruses are cause the infectious type of gastroenteritis along with bacteria, parasites and fungus can also cause

illness [8, 9]. The Rotavirus causes the serious illness in children. The other viral strains like Campylobacter and Norovirus are common in adults [11-12]. The reports suggest that there were 3-5 billion cases of acute gastroenteritis every year with rough estimates of 2.25 million deaths especially in children below five worldwide around 525 000 children every year. Recently the WHO reports suggested that diarrhea is second most leading cause of death in children and can be preventable or treated with proper nutrition and management. There are around 1.7 billion deaths a year worldwide. The malnourished Children develop low immunity and HIV infected people are at risk of life-threatening diseases like diarrhea, and people living with HIV are most at risk of life-threatening. The Bacterial sources of gastroenteritis are often caused by *Escherichia coli, Shigella* (which causes bacterial dysentery), *Clostridium difficile,* or *Salmonella.* The viral infections are caused by rotavirus and norovirus. The Rotavirus is highly contagious and survives on dry surfaces till10 days and on human skin up to 4 hours. Due to its low infectious dose, it is present in 10^{11} particles/gram present on skin and stools before and after infection up to 2 weeks. The rotavirus can be even spread to the adults who work on the infected children. Effectiveness of second-generation Rotavaccines is used to combat the disease with fewer side effects.

The norovirus is extremely contagious (<10 particles) and survives up to 4 weeks in a dried state. The viral infections cause fever, head ache, vomiting and fatigue. The bacterial infections may be persisting several weeks and may sometimes lead to severe abdominal pain. The prime cause of bacterial infection includes *Campylobacter jejuni*. The *Clostridium difficile* is a toxigenic strain stands as lead cause of diarrhea in the elderly and without symptoms in the children. The parasitic infections are caused by *Giardia lamblia* mostly but also by other strains like *Entamoeba histolytica, Cryptosporidium* species. The transmission mainly occurs by the unhygienic conditions, sputum transmission *etc*. The prevention of the infection and control of disease is a major factor that controls the disease and progression to worse condition. The need of update on the types, prevention and effective control strategies as a compiled work in this review would create awareness.

MATERIALS AND METHODS: The Medline, Embase, PubMed, Scopus, SciDirect and other well-known scientific databases were searched for the literature findings. The Medline (1980 to till date), Embase (1985 to tilldate), Scopus (2001 to till date). The literature findings suggested string evidence of severity and need of prevention and control strategies.
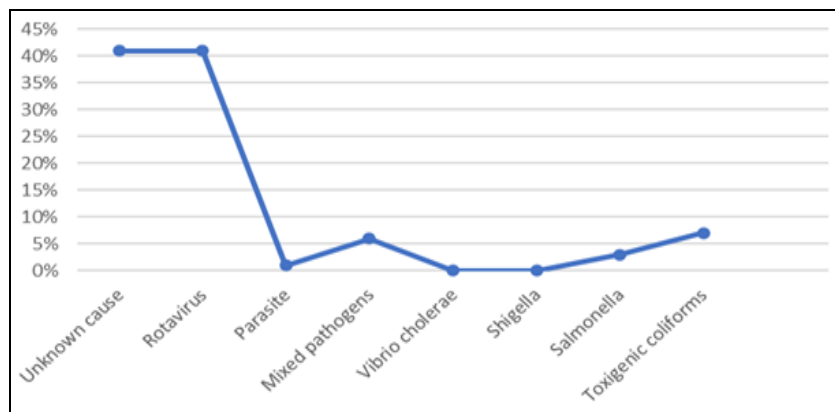

FIG. 1: CAUSATIVE ORGANISMS ALONG WITH THE INCIDENCE

Causatives of Acute Gastroenteritis: Acute gastroenteritis is caused by many infectious agents as listed in **Table 1** ang **Fig. 1** along with the incidence rate. The viral gastroenteritis is the most common form followed by bacteria and parasitic infection.

S. no.	Type of infectious agent(Incidence percentage)		
	Viral (50%-70%)	**Bacterial (15%-20%)**	**Parasitic (10%-15%)**
1	Norovirus	Shigella	Giardia
2	Rotavirus	Salmonella	Amebiasis

3	Enteric adenovirus type 40&41	Campylobacter	Cryptosporidium
4	Astrovirus	E coli	Isospory
5	Coronavirus	Vibrio	Cyclospora
6	Some picornaviruses	Yersinia	Microsporidium

The condition of gastroenteritis is also progressive or the occurrence was also seen due to comorbidities. The most contributing factors **Fig. 2** for gastroenteritis was observed more with the cardiovascular diseases like hypertension, arrythmias, CHF, CCF, Angina pectoris. Followed by nephron dysfunction leading to kidney failures, this may include creatinuria, GFR disturbances, tubular dysfunction, sparing electrolytes abnormalities. The liver problems have minute effect; this may include liver cirrhosis, bilirubinuria, liver toxicity etc.
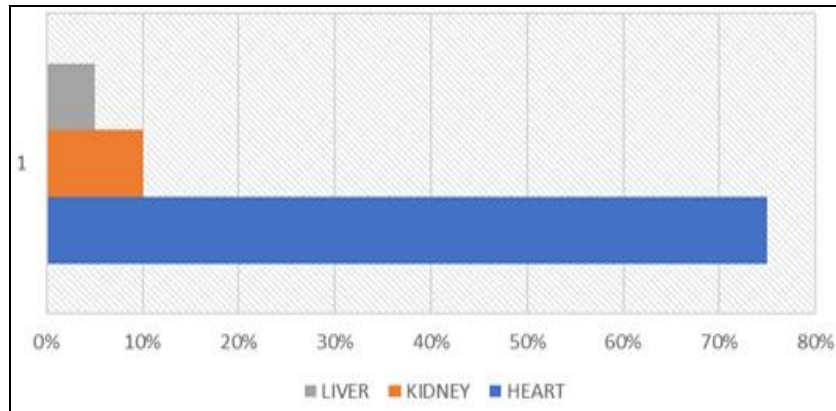

FIG. 2: CONTRIBUTING FACTORS FOR GASTROENTERITIS DUE TO COMORBIDITIES

Diagnosis: Gastroenteritis's clinical diagnosis is based on the patient's signs and symptoms [15]. The etiology is underdetermined because of its low impact on the management of illness [16]. The stool cultures will be collected from the patients with food poisoning and who expel the blood in the stools [17]. The most prominent diagnosis of the gastroenteritis includes diarrhea, vomiting, nausea, abdominal ache and headache. This type of diagnosis **Fig. 3** can even be a surveillance [20]. About 10% of elderly patients and children report hypoglycemia. The severe infection can be recognized by dehydration and renal dysfunction [21].

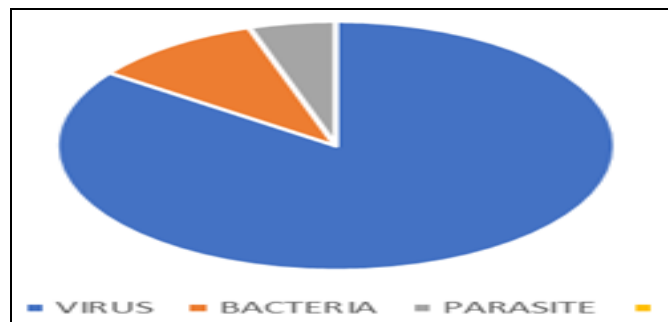**Types of Gastroenteritis:**

FIG. 3: IMPACT OF DIFFERENT INFECTIOUS AGENTS AND THEIR INCIDENCE

Viral Gastroenteritis: The Viral type of gastroenteritis occurs by noroviruses, adenoviruses, rotaviruses and astroviruses [21, 23]. The most prevalent species of gastroenteritis is caused by the Rotavirus which is seen in children [22-24] and is widely prevalent in developed and underdeveloped countries with poor hygiene. The viruses are cause for 50-70% of the occurrences of infectious diarrhea in children. The acquired immunity prevents this type in adults. The norovirus affects about 18% of all cases. The U.S reports a high number of infectious diarrhea cases, with norovirus accounting for 85% of viral gastroenteritis outbreak [27-29].

The most common localized epidemics occurs in adults being places of poor hygiene status [29-31] The prevalence continues even after diarrhea stops [33]. The norovirus affects around 10% of infections in youngsters [33-35].

Bacterial Gastroenteritis: The bacterial infection is mostly caused by the *Campylobacter jejuni* [34]. The Bacteria affects 15% of children. The other bacterial species include *Salmonella, Shigella, E. coli* and *Campylobacter* [35]. The contamination of food with germs and left for several hours any cause multiplication of the bacteria, thus thereby increasing the risk of infection for who consumes the food that has been contaminated with germs and left at room temperature for several hours multiplies the bacteria, increasing the risk of infection in those who consume it [36]. The raw meat, under-processed meat, seafood, eggs, raw sprouts, soft cheese, unpasteurized milk, fruit and vegetable juices are linked to the disease [37]. The widest cause of gastroenteritis in the world is cholera, with contamination of water and food [38].

TABLE 1: ONSET, DURATION AND SYMPTOMS AS CAUSED BY SPECIFIC BACTERIA

Bacteria	Onset	Duration	Signs
Salmonella	6-48h	1-7d	N, V, F, P, ± blood
Campylobacter	1-10d	5-14d	F, H, P, N, V ± blood
Vibrio	6h-4d	SL(upto 3d)	N, V, D
Shigella	1-6d	SL(2-3d)	F, P, D, ± blood
ETEC	1-3d	2-3d	D
C perfringens	8-16h	<24h	P, D
EHEC	1-9d	1 week	N, P, D + blood
C difficile	4-5d	Variable	F, N, P, D ± blood

Abbreviations: D stands for diarrhea; F stands for fever; H stands for headache; N stands for nausea; P is for abdominal pain; SL stands for self-limiting; V stands for vomiting.

Parasitic Gastroenteritis: Parasitic Gastroenteritis [41] is mostly caused by *Giardia lamblia* in developing countries. The other species, such as *Entameba histolytica, Cryptosporidium* species [40, 41] accounting for 10% of the infection in children. These agents account for roughly ten percent of all cases in children [42, 44].

Transmission: The transmission mainly occurs due to:

1. Poor hygienic conditions
2. Lack of nutrition in children
3. Low immunity
4. Contaminated persons
5. Infected vomit and faces.

The norovirus and rotavirus can be even transmitted through aerosolization. The mask should be worn while disposing the infected vomit and faces. Research has shown that hand washing with soap water for 20 seconds. Further drying with a disposable towel removes the norovirus from hands contaminated with infected stools [32, 34].

(A) *ROTAVIRUS*   (B) *CAMPYLOBACTER JEJUNI*   (C) *ENTAMOEBA HISTOLYTICA*
FIG. 4: VARIOUS INFECTIOUS AGENTS FOR GASTROENTERITIS

Clinical Manifestation: The clinical manifestations of the disease include nausea, vomiting, abdominal pain, and diarrhea, varying based on the infection and its type. The disease is

self-limiting and expected to be sorted within 3-4 days. When the hospital setting has low immunity, dehydration is of primary concern [41-46].

Vaccination: The World Health Organization in 2009 recommended the rotavirus vaccine be offered to all children due to its effectiveness and safety [26]. The commercial vaccines are stillin development. The vaccines were successful in Africa and Asian children [27-29]. There is need of national immunization programs to reduce the disease severity. When implemented in U.S for the children, the rotavirus vaccine has reduced the infection by 80 percent since 2000 [32-35]. The first dose of vaccine should be given to infants between 6 and 15 weeks of age [35-41].

Management of the Disease: The Management of acute gastroenteritis may include the following:

1. IV fluid and electrolyte replacement (Rehydration Therapy).

2. Anti-infective agents (Antibiotics).

3. Antiemetic agents (nausea and vomiting).

Treatment: The general Recommendations emphasize on the WHO guidelines of hydration or rehydration, nutritional dietary adjustments, reducing bowel movements and rational use of antibiotics. The oral rehydration can be used in case of diarrheal infections. To deliver glucose and electrolytes the Rehydration therapy using water containing salt, sodium bicarbonate and glucose is recommended by the World Health Organization.

Antibiotics: Antibiotics are most common treatment drugs administered orally with caution. Further the traveler's diarrhea and acute gastroenteritis with more than 10 stools per day along with the symptoms of dehydration lasting more than a week should be given careful attention according to IDSA 2001 treatment guidelines. Further there is lot of caution needed in immunocompromised patients. The symptoms of fever, bloody stools and headache may be treated with use of antibiotics as listed below

1. Ciprofloxacin (500 mg are given orally twice a day for 3–5 days).

2. Norfloxacin (400 mg twice a day for 3–5 days).

3. Levofloxacin (500 mg daily for 3–5 days).

4. If the patient is found with fluoroquinolone resistance oral administration of Azithromycin (500 mg daily for 3 days) is preferred.

This therapy can be suggested for immunocompetent patients. The general treatment using Antibiotic should be continued for 7 to 10 days in immunocompromised hosts.

Dietary Modifications and Need of Fluid Balance: The electrolyte replacement is considered to be ideal along with the clear fluids. The diarrhea condition can be balanced by few changes in the diet, including bananas, boiling rice, potato, noodles, oats, soups, coconut oil snacks *etc*. The BRAT diet consisting of Bananas, rice and the apple sauce along with toast is popularly recommended. The normal bowel function is restored by taking clear fluids and normal food with low fat diet. Suppose there is chance of development of secondary infection or lactose intolerance or malabsorption that may remain for several weeks. In that case, this can be treated with avoiding lactose containing foods for a period [36-45].

Rehydration and Replacement: The primary treatment for the acute gastroenteritis Rehydration is which can be followed both children and adults. The best suitable therapy is taking orally the rehydration fluids and the administration by I.V is suggestible when there is loss of consciousness inpatient or in cases of severe dehydration [46-49]. The replacement in the rehydration products includes complex carbohydrates like wheat/rice and may even include glucose. The soft drinks, fruit juices which are high in simple sugars are not suggested for the children under the age of five as it leads to diarrhea. There can be ORT preparations which when refused by the patient can be replaced simply by drinking water. The nasogastric route of delivery can be employed in the children [49-53].

Treatment with Antiemetics: The vomiting condition **Table 2** in the children proposes the use of Antiemetic drugs like ondansetron. Ondansetron has benefits that can reduce the need of IV Fluids, less hospitalizations and less vomiting after single dosage [52-55]. The use of metoclopramide is also found to be beneficial. The use of ondansetron **Table 2** was found to have a high incidence of

hospitalization in youngsters [56-59]. This can be minimized by giving the ondansetron orally. If clinical judgment allows, the intravenous preparation of ondansetron can be given orally [58]. The use dime hydrate can reduce vomiting giving a therapeutic advantage [59, 60].

TABLE 2: DRUG ADMINISTRATION FOR EMESIS IN GASTROENTERITIS

Name of drug	Dose	Administration
Ondansetron	16 mg orally	1 hr before the indication of anesthesia
Metoclopramide	10-15 mg	QID (30 mins before meal)
Dimenhydrinate	50-100mg (IM/IV)	Every 4 hrs as needed

Usage of Antimotility Agents: The general use of antimotility agents is restricted as it can worsen the condition of bloody diarrhea in patients and other complications [61]. The use of drugs like Loperamide, an opioid analogue **Table 3** to alleviate diarrhea symptoms [62-64] and also not suggestible for youngsters as it can cross through the immature blood–brain barrier and may induce toxicity. The use of bismuth subsalicylate in mild to moderate cases, as an insoluble compound of trivalent bismuth and salicylate is used with caution with respect to salicylate poisoning [64].

TABLE 3: DRUGS FOR IMPROVING MOTILITY IN GASTROENTERITIS

Drug	Dosage/ Administration
Loperamide	4mg/Oral
Bismuth Subsalicylate	524 Mg P/O/ Oral

Need of Clinical Intervention: The appropriate choice of treatment regimen in the gastroenteritis is a necessary task to prevent the condition from worsening. The contributing factors, including the complicated comorbidities associated with heart, liver and kidney in the patients, should be carefully monitored for the use of antibiotics in a rational way. Thus, the inclusion and exclusion of certain drugs that might lead to worsening condition are to be omitted. Care should be taken in designing the rehydration and replacement fluid management therapy; special caution is needed in children and youngsters. Need of dietary changes needs special attention. Further newer hospitalizations are havoc. Hence caution and necessary rationale for the use of drugs have to be carefully checked [61-64] and also the international guidelines of treatment *i.e* IDSA 2021 have to be followed.

CONCLUSION: Gastroenteritis is one of the leading causes of death for children in the united states. Infectious organisms like viruses, Bacteria and parasites cause different types of gastroenteritis. Viral gastroenteritis is a prevalent and severe form of infection amongst the variants. Acute gastroenteritis caused by the virus is serious and fatal if unchecked or no proper precaution is taken can adversely affect the health of the patient. The children, youngsters and elder patients are on the verge of this disease, which needs attention.

There are certain effects of the comorbidities acting as contributing factors to gastroenteritis. The review mainly focused on the management of the disease along with comorbidities, which suggests the use of restricted antibiotics, the need for dietary changes, and the use of rehydration/ replacement therapy that can help to improve the condition of the patient and thereby leading to less hospitalizations. Thus, the antibiotics like Ciprofloxacin, norfloxacin, levofloxacin, loperamide in suitable dosage form mostly preferring the oral route of administration is suggestible. As a point of note the IV route can be suitable for patients who lost their consciousness. Amidst this antibiotic therapy there is a definite need for rehydration therapy with electrolytes, suitable diet that prevents diarrhea. The replacement therapy as suggested in the treatment guidelines by the IDSA 2021 can be followed and strict management of the disease as per the WHO guidelines is prime requisite. Relapse of the infection and the prevention of the disease should be carefully monitored especially in patients with comorbidities. The future lies in the management of the disease with less use of antibiotics and the inclusion of a healthy diet with occasional rehydration therapies with rich vit C helps to combat the infection leading to no hospitalization.

CONFLICTS OF INTEREST: Nil

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