Enteric Bacteria Associated With Human Gastroenteritis: A Review

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ABSTRACT
Gastrointestinal infections are responsible for a high rate of morbidity in the world with higher incidence in the developing countries. A broad spectrum of microorganisms may be responsible for the infection and present in common the same clinical manifestations being the most common symptoms diarrhea, vomiting, fever, abdominal pain, malaise, anorexia and dehydration at different levels of severity. The family Enterobacteriaceae comprises a large group of Gram-negative non-spore forming bacteria typically 1-5 µm in length. Some members of the family such as Escherichia coli, Salmonella, Shigella and Campylobacter are associated gastroenteritis. Gastroenteritis is due excessive secretion of fluids in the proximal small intestine induced by the action of luminal toxins expressed by entero-pathogens, inflammatory of colonic mucosa or through penetration of the bacterium through the mucosa to the reticulo-endothelial system. The paper review the enteric bacteria associated with human gastroenteritis.

Keywords: Gastroenteritis, Campylobacter, Salmonella, Shigella, Escherichia coli

INTRODUCTION
Gastrointestinal infections are responsible for a high rate of morbidity in the world, although its highest incidence occurs in the developing countries, according to the World Health Organization (WHO) global health occur 1.700 million diarrheal diseases each year and kills 760,000 children under 5 each year for severe dehydration for this reason it is considered the second leading cause of death in the population at this age, even in developed countries, children under 3 years of age have on average 3 diarrhea episodes per year [1].

A broad spectrum of microorganisms may be responsible for the infection and present in common the same clinical manifestations being the most common symptoms diarrhea, vomiting, fever, abdominal pain, malaise, anorexia and dehydration at different levels of severity [2]. The medical diagnosis is usually relatively simple once a correct anamnesis and epidemiological history has been made, it is important to perform microbiological laboratory studies to determine the etiological agent responsible for the disease and initiate appropriate treatment [3]. Diarrhea is generally defined as three or more unformed stools evacuations per day and it is often associated with other enteric symptoms, diarrhea also may be considered to deposition of more than 250 grams of unformed stools per day. Based on the duration of diarrhea can be classified as chronic (greater than or equal to 30 days) acute diarrhea (less than 14 days), or persistent (14 to 29 days). The etiology of diarrhea, abdominal pain, and digestive disorders may be related to more than forty infectious pathogens which could be grouped in viruses, bacteria and parasites [4].

Viral gastroenteritis is a common cause of morbidity and mortality in humans around the world and is considered the most common infectious gastroenteritis, the most common causative agents are Rotavirus (RV), Norovirus (Nov), Sapovirus (SAV), Adenovirus (HAdV) and Astrovirus (Hast V). Some bacterial pathogens are able to develop persistent gastrointestinal symptoms and other complications; among the most frequently been identified: E. coli, Campylobacter, Salmonella and Shigella [5]. The primary mechanisms for bacterial gastroenteritis are:

- Excessive secretion of fluids in the proximal small intestine induced by the action of luminal toxins expressed by entero-pathogens or by minimally invasive bacteria.
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- Inflammatory or cytotoxic damage of the ileal or colonic mucosa which may produce blood and pus, or
- Penetration of the bacterium through the mucosa to the reticulo-endothelial system, as is the case with typhoid fever. Regardless of mechanism, most cases of bacterial gastroenteritis are self-limiting, and, with a few exceptions, neither empirical anti microbial therapy nor bacterial stool culture is indicated [2].

The family Enterobacteriaceae comprises a large group of Gram-negative non-sporing forming bacteria typically 1-5 µm in length. They are facultative anaerobes and with the exception of *Saccharinobacter fermenters* and some strains of *Yersinia* and *Erwinia*, they share the ability to reduce nitrate to nitrite. These bacteria are generally motile by peritrichous flagella except for *Shigella* and *Tatumella* and some other non-motile members of this family [6].

**TYPES OF GASTROENTERITIS**

Gastroenteritis is a syndrome characterized by gastrointestinal symptoms including nausea, vomiting, diarrhea and abdominal discomfort. There are three types of gastroenteritis;

**Secretary Gastroenteritis**

This is found mainly in small intestine. This type of gastroenteritis is associated with Diarrhea. Diarrhea involves abnormal fecal discharge characterized by frequent or fluid stool, usually resulting from diseases of the small intestines and involving increased fluid and electrolyte. The mechanism involved in this type of gastroenteritis includes production of enterotoxin by bacteria or bacterial invasion which caused a shift in water and electrolyte adsorption. This is caused by pathogens such as *Vibriochlorella*, *Escherichiacoli* (ETEC), *Chlos tridium*, *Bacillus cereus* and *Staphylo coccus aureus*.

**Inflammatory Gastroenteritis**

This is found mostly in colon and highly associated with dysentery. Dysentery is an inflammatory disorder of the gastrointestinal tract characterized with blood and pus in the faces and accompanied by symptoms of pain, fever and abdominal cramps, usually resulting from diseases of large intestine. Inflammatory gastroenteritis is caused by production of cytotoxins by bacteria or through bacterial invasion which cause mucosal damage that lead to inflammation. This is caused by bacteria such as *Shigella*, (STEC), *Salmonella* and *Campylo bacter*.

**Invasive Gastroenteritis**

This is found in distal small intestine which is commonly associated with enteric fever. Mechanism of infection is through bacterial penetration to the mucosa and invasion of radical endothelial system. This is caused by bacteria such as *Salmonella typhi/paratyphi* and *Yersinisenterocolitica*.

**ENTEROBACTERIACEAE**

The family Enterobacteriaceae comprises a large group of Gram-negative non-sporing forming bacteria typically 1-5 µm in length. They are facultative anaerobes and with the exception of *Saccharinobacter fermenters* and some strains of *Yersinia* and *Erwinia*, they share the ability to reduce nitrate to nitrite. These bacteria are generally motile by peritrichous flagella except for *Shigella* and *Tatumella* and some other non-motile members of this family. For example, *Salmonella* are typically motile, notable exceptions being the *Salmonellaseserotypes Pullorum* and *Gallinarum* [7]. A common feature of the Enterobacteriaceae, which helps to differentiate them from other closely related bacteria, is the lack of cytochrome Coxidase; although there are exceptions such as *Plesiom onasspp.*. Enterobacteria are catalase, positive with the exception of *Shigellady senteriae* and *Xenorhabdus* species. Entero bacteria eae ferment a variety of carbohydrates, but their ability to produce acid and gas from the fermentation of D-glucose is one characteristic that remains an important diagnostic property and is commonly used as a basis for their detection and enumeration. Some members of the Enterobacteriaceae (e.g., *Enterobacter* spp., *Escherichia coli*, *Citrobacter* spp. and *Klebsiella* spp.) can be recognized using methods that exploit their ability to ferment lactose rapidly (usually within 24-48 h) producing acid and gas [7]. Enteric bacteria are microbes that reside in the guts of animals and humans. However there are some among them that reside in intestinal tract of animal’s that can cause diseases and harsh reactions when human become infected with them [8]. They can cause a mild infection, such as food poisoning or severe community infection slike diarrhea. Such examples of enteric bacteria include *Salmonella*, *Escherichi acoli*, *Shigella*, *Klebsiella*, *Campylobacter*, *Enterobacter Yersinia*, *Vibrio* and *Citrobacter* [9]. The human gut is therefore the natural habitat for various bacteria species...
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and majority of them participate in metabolic activities that salvage energy and absorbable nutrients protecting the colonized host against invasion by alien microbes and important atrophic effects on intestinal epithelia and on immune structure and function [9].

An estimated 9.4 million food borne illness caused by a known pathogen occur annually in United State [10]. It has been reported that about 2 million diarrhea disease patients die per year throughout the world [11]. Considering the public importance of acute diarrhea disease, laboratory surveillance of acute diarrhea is utilized in many countries for safety and prevention efforts [12].

Escherichia coli

*Escherichia coli* (E. coli) are bacterium which belongs to family Enterobacteriaceae and are gram negative rod up to 3 um in length, ferment glucose and wide range of sugars. These lactase fermenters produce pink colonies on Mac Conkey agar. Hemolytic activity on blood agar is characteristics of certain strain of *E. coli*. It’s motile with peritrichous flagella and often fim briate [13, 14]. The O is the major serotype that was recognized as a cause of human illness. *E. coli* O 157; H is one of the more than 60 serotypes of verotoxin producing *E. coli* that cause that a variety of human illness such as mild diarrhea, hemorrhagic colitis and hemolytic-uremic syndrome (HUS) [15]. *Escherichia coli* were initially considered to only be a commensally residing in the gastrointestinal tract. However, several pathogenic variants (patho types) are now recognized and associated with diarrheal diseases. Although *E. coli* is easy to identify to species level, it is extremely difficult to recognize strains belonging to different pathos types of diarrheagenic *E. coli*, as these are defined by the expression of one or more group-septic virulence factors.

The six major diarrheagenic patho types described to date are enteropathogenic* E. coli*, Shiga toxin-producing *E. coli* (STEC), entero invasive *E. coli* (EIEC), enterotoxigenic *E. Coli*, entering aggregative *E. coli* and adherent invasive *E. coli* [16]. Of these, only STEC is routinely denied by most clinical and public health laboratories, and it will be the focus of the discussion here. STEC is definedby the presence of a Shiga toxin 1 (Stx1) and/or Shiga toxin 2(Stx2) genes. Historically, these isolates were called enterohemorrhagic *E. Coli* (EHEC) or verocytotoxin-producing *E. coli* (VTEC). STEC includes both O157 and non-O157 serotypes of *E. coli*. Ruminants, such as cattle, are the major reservoir for STEC. Poor sanitation, fecal runoff into rivers and streams, and inadequate control measures in the meat and food processing industries have all led to the recovery of STEC from virtually any consumable product. Infection with STEC occurs following consumption of these contaminated products. Infections occur predominantly in the summer months but can be observed year round [17]. The chief symptoms included bloody diarrhea, abdominal pain, nausea, and vomiting [18]. Importantly, not all STEC infections are associated with bloody diarrhea [19,20], and so laboratory algorithms that only test bloody specimens for STEC are no longer considered standard of care. The most common and serious complication of STEC infection is the development of HUS, which typically presents 5 to 13 days after the onset of diarrhea [21].

HUS is life-threatening and consists of the triad of renal failure, microangiopathic hemolytic anemia, and thrombocytopenia. The mortality rate connected with HUS is 3% to 5% [22]. It has been estimated that 61% of all HUS cases are related to STEC infection [22]. HUS has been observed more frequently in O157 (11% of cases) versus non-O157 (1% of cases) STEC infections [23]. Approximately 15% of children10years of age develop HUS following STEC infection. However, in the recent outbreak of O104 STEC in Germany, 22% of children developed HUS [24, 25, and 26]. It should be noted that this outbreak was caused by an atypical STEC strain that harboredentero aggregative *E. coli* virulence factors in addition to the Shigatoxins. HUS occurs much less frequently among adults and is associated predominantly with advanced age (75 years) [27]. Increased rates of HUS have been more frequently associated withStx2-expressing STEC strains. Exposure to antibiotics also increases the risk of HUS in children [26]. However, recent data demonstrated that treatment with ciprofloxacin reduced the risk of HUS in patients infected with the 2011 German O104 STEC strain [28]. These data are supported by a recent meta-analysis of studies between 1980 and 2011 [29]. Despite this, the decision to treat a patient with STEC infection with antimicrobials remains contro versial. In addition, use of ant motility agents has been associated with longer duration of bloody diarrhea, as well as progression to HUS [30].

The incubation period is 72-120 hours. The clinical sign initially may be diarrhea with
abdominal cramps, which may turn into grossly bloody diarrhea in a few days. There is however, no fever. The symptoms of *E. coli* septicemia are mainly referable to bacteremia, end toxemia and the effect of bacteria localization in a variety of tissue spaces throughout the body [31].

**Salmonella species**

*Salmonella*, a member of the family Enterobacteriaceae, is a facultative anaerobic gram negative, non-spore forming rods that are indistinguishable from the *Escherichia coli* under the microscope or ordinary nutrient media. They are widely distributed in the nature with humans and animals being their primary reservoirs. *Salmonella* food poisonings results from ingestion of food containing appropriate strains of this genus in significant numbers. Some significant changes have occurred in the taxonomy of *Salmonella* [32]. The genus *Salmonella* are considered to have two species named *Salmonella* enteric and *Salmonella* bongori. Sero typing differentiates the strains and they are referred as to by, for example *S. enterica* serotype *typhimurium* or as *S. typhimurium* [33]. For epidemiological purposes, the *Salmonella* can be placed into three groups; the first are those that infect humans only. This includes, *S. typhi*, *S. paratyphi* A, S. Paratyphi C. this group includes the agents of typhoid and paratyphoid fevers, which are the most severe of disease caused by *Salmonella*. The epidemiology of the *Salmonella* is complex, which often make animals control of the disease is difficult. Animals are the reservoir of food born disease of *Salmonella* [34, 35].The majority of *Salmonella* cases occurs as the result of ingesting contaminated food or water. *Salmonella*can also be acquired by contact with domestic animals and their food products, farm animals or animals in petting zoo, and exotic pets like turtles, hedgehogs, and iguanas [36]. *Salmonella* can also be transmitted from person to person via the oral-fecal route.

The primary habitat of *Salmonella* species is the intestinal tract of the animals such as farm animals, humans, birds, reptiles and insects. Although their primary habitat is intestinal tract, they may be found in other parts of the from time to time. As an intestinal form, the organisms are excreted in feces from which they may be transmitted by insects and other living creatures to large number of places [37]. *Salmonella* often enter the host by ingestion, and even with several system to mediate acid resistance, few survive the stomach and move into the small intestine. Normal flora protects against colonization of administration of oral antibiotics facilitates establishment of infection. Entry of *Salmonella* usually occurs without mucosal damage in systemic infections, but enteric infection is characterized by local damage without septicemia-*Salmonella* infection with M cells in payer’s patches is facilitated by fimbral adhesions. This is followed by ruffling of the target cell membrane which result in internalization of the bacteria in membrane bound vacuoles [38]. The ruffles facilitates uptake of the bacteria in membrane bound vacuoles or vesicles which often coalesce. The organisms replicate in these vesicles and are eventually released from the cells, which sustains only mild or transient damage. The complex invasion process is mediated by the product of a number of chromosomal genes, whereas growth within host a cell depends on the presence of virulence plasmids [39].

The incubation period of the *Salmonella* is 12-36 hours. The clinical sign includes diarrhea, which may be watery, greenish and foul smelling. This may be preceded by headache and chills. Other findings include prostration, muscle weakness and moderate fever. In most cases the symptoms resolve in 2-3 days without any complication [40]. The bacterium induces responses in the animal that is infecting, this is what typically causes symptoms, rather than any direct toxin product. Symptoms are usually gastrointestinal, including nausea, vomiting, abdominal cramps and bloody diarrhea with mucous, headache, fatigue and rose spots are also possible. These symptoms can be severe, especially in young children and elderly. Symptoms last generally up to a week, and can appear 12-72 hours after ingesting the bacterium. Reactive arthritis, sickle-cell anemia and osteomyelitis due to *Salmonella* infection is much more common that in the general population [41].

**Shigella**

*Shigella* is a species of enteric bacteria that causes disease in humans and other primates (*Shigella* is gram-negative rods that are non-motile and non-sporo forming. The bacteria’s are primarily a human disease, but has been found in some primates. *Shigella* are facultative anaerobes, similar to enteric such as *E. coli* [13, 41]. They can be acquired from ingestion of a
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variety of foods or water contaminated with human feces, sexually during oral-anal sex, or by laboratory workers. The four species of Shigella are Shigelladysenteriae, Shigella flexneri, Shigellaboydii, and Shigellasonnei. Transmission by person-to-person contact is common for Shigellasp. Because of a low infectious dose of 10 to 100 organisms [42]. Between 2009 and 2010, Shigella accounted for 508/8,523 (2%) of reported illnesses associated with food borne outbreaks [43]. The incidence of Shigella infections reported by Food Net in the United States in 2011 was 3.24 per 100,000 and ranged from 0.99 to 6.78 per 100,000, depending on the region [44]. Shigellosis and dysentery are diseases associated primarily with poor hygiene and lack of access to medical care. Approximately 150 million cases are reported annually in developing countries, in contrast to 1.5 million cases in industrialized nations. Of importance, one multicenter study found that half of patients with culture-negative, bloody stools were positive by PCR for Shigella, suggesting that the actual incidence of Shigellais grossly underestimated [45]. Shigellosis symptoms range from watery diarrhea to mucoid and/or bloody stools, which can be accompanied by fever, malaise, and abdominal pain. In one study of 1,114 culture confirmed patients followed for 14 days or longer, 29% (241) reported diarrhea persisting for 14 days [45]. Factors associated with persistence were age, fever, mucoid diarrhea, vomiting, and abdominal pain. Headache and nuchal rigidity are common, with 95% and 39% of patients reporting these symptoms, respectively. S. dysenteriae type 1 is responsible for classic dysentery, which is manifested by fever, abdominal cramping, and bloody stool. Sepsis occurs primarily in malnourished pediatric patients in developing countries and is most commonly caused by S. flexneri [46]. Long-term carriage (1 year) occurs but is rare [47]. Meningitis, pneumonia, and urinary tract infections (UTIs) are rare complications of shigellosis and are most commonly seen with S. flexneri and S. sonnei [48]. Notably, 40% of UTIs are asymptomatic and 35% are culture negative [49]. Reactive arthritis has been reported in 1 to 3% of cases from outbreak data [42]. The onset of reactive arthritis occurs within 3 weeks of gastrointestinal symptoms, with the duration of symptoms ranging from a few days to a few months; only S. flexneri has been associated with reactive arthritis. HUS is the most serious complication of shigellosis. HUS occurs in 13% of cases of S. dysenteriae type 1 shigellosis and is attributable to the expression of Stx1 by this organism [50].

Campylobacter

They are small microorganisms as Gram-negative rods type and grow best in microaerobic conditions lead scourge in one of its poles which makes them actively motile with a corkscrew - like motion [51]. So far there has been 13 subspecies described but most are not pathogenic to humans, the most frequently reported C.jejuni, which requires an incubation period of 1 to 7 days, the dose required to present microorganism is 500 microorganisms disease, the degree of infection increases with higher doses but the degree of disease is not clearly dose related. The main symptoms are vomiting, abdominal pain, fever and diarrhea which may contain blood with mucus and fecal leukocytes; it is a common condition in developed countries [52]. Campylobacter inhabits the intestinal tracts of food animals, such as poultry, cattle, swine, and sheep, and domestic pets, including cats and dogs. The organism rarely causes disease in animals but is shed in the feces. Meat typically becomes contaminated with animal feces harboring Campylobacter spp. during slaughtering. Transmission of the organism is typically food borne, by ingestion of undercooked contaminated meat and meat products or contaminated dairy products. In addition, waterborne infections occur, via consumption of contaminated water and ice. Contact with infected animals, particularly cats and puppies, has also been shown to be a route of transmission. The typical incubation period for Campylobacter is 2 to 5 days, but it may be up to 10 days [53]. Most cases of Campylobacter enteritis are sporadic, but the incidence increases starting in March and throughout the summer months. Outbreaks associated with Campylobacter have been due to consumption of raw milk or well water contaminated with effluent from livestock operations [54]. Higher rates of Campylobacter enteritis are seen in those 4 years of age and 15 to 44 years of age [55]. Travelers to developing countries are also at increased risk of Campylobacter enteritis. Campylobacter jejuni and Campylobacter coli are the most common Campylobacter species associated with diarrheal illness. C. jejuniis responsible for 90% of cases [53]. The symptoms associated with this disease are usually flu-like: fever, nausea, abdominal cramping, vomiting, enteritis, diarrhea, and malaise. Symptoms begin within 2-5 days after
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ingestion of the bacteria, and the illness typically lasts 7-10 days. Recurrence of this disease can occur up to three months after pathogen ingestion [56]. Other complications can include meningitis, urinary tract infections and short-term reactive arthritis. Some individuals may develop Guillain-Barré (GB) syndrome, a nerve disorder that causes muscle weakness and paralysis of the limbs, about 2-4 weeks after infection [56].

CONCLUSION

Gastrointestinal infections are responsible for a high rate of morbidity in the world with higher incidence in the developing countries. The family Enterobacteriaceae comprises a large group of Gram-negative non-spore forming bacteria typically 1-5 µm in length. Some members of the family such as Escherichia coli, Salmonella, Shigella and Campylobacter are responsible for gastroenteritis. Gastroenteritis is due excessive secretion of fluids in the proximal small intestine induced by the action of luminal toxins expressed by entero-pathogens, inflammatory of colonic mucosa or through penetration of the bacterium through the mucosa to the reticulo-endothelial system. There is a need to implement strict hygienic measures in the manufacturing, handling, storage and selling of food in order to guarantee the quality of these foods so as to minimize or eliminate the risk of gastroenteritis.

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