

A review of the Prevalence of Enterohemorrhagic *E. coli* in Iraq

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ABSTRACT

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Background: Diarrhoeal illnesses were a serious public health issue and the main reason for increased newborn and young children morbidity and mortality in developing nations. In persons in Iraq and developing nations, Enterohaemorrhagic *E. coli* is a group of pathogenic *E. coli* that can cause diarrhea or hemorrhagic colitis. A significant contributor to pediatric acute renal failure, morbidity, and mortality in adults is hemolytic uremic syndrome (HUS), which can occasionally develop from Enterohaemorrhagic *E. coli*. This review focuses on the prevalence of Enterohaemorrhagic *E. coli* and its role in increasing mortality and morbidity in children and adults in Iraq and developing nations. **Conclusion:** Enterohaemorrhagic *E. coli* can cause diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome which are a significant contributor to pediatric acute renal failure, morbidity, and mortality in adults in persons in Iraq and developing nations.

Keywords: Enterobacteriaceae, *E. coli*, Enterohemorrhagic *E. coli*, Diarrhoea.

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1-INTRODUCTION

Although the family Enterobacteriaceae is seldom seen outside the gastrointestinal system, it is made up of a sizable diverse group of Gram-negative bacteria that are a major contributor to nosocomial illness. Because they can cause a wide variety of diseases in both humans and animals, they are widely disseminated around the planet and may be found in plants, soil, water, animals, and humans (1). These bacteria's antibiotic resistance has important clinical and economic repercussions because they are pathogens that cause severe infections, such as complicated urinary tract infections (cUTIs), community-acquired pneumonia (CAP), ventilator-associated pneumonia (VAP), complicated intra-abdominal infections (cIAIs), and hospital-acquired pneumonia (HAP) (2, 3).

Escherichia coli is a Gram-negative, rod-shaped bacterium belonging to the family Enterobacteriaceae. Most of them are commensal and live mostly in the lower intestine tracts of warm-blooded creatures, including humans. Commensal bacteria delivered vitamin K and B12 which were needed for post-translation modification of proteins employed in blood coagulation and metabolism and have been distinguished as a protective element against infection by pathogenic bacteria (4).

Bacteria are discharged through feces or wastewater effluent into the environment and for a long time, this bacterium's presence in ambient waterways is thought to be a sign of recent fecal contamination. Also, *E.coli* is responsible for UTI in humans, According to some earlier research, certain particular *E. coli* strains may survive for extended periods and may even be able to multiply in conditions outside of the intestines, although they seldom cause illnesses like sepsis and meningitis in children (5).

Worldwide, gastroenteritis in children has a high mortality and morbidity rate, but this is especially true in developing countries. There has been evidence of a significant frequency of bacteria enteritis (6). Prior to the identification of specific virulence components in pathogenic strains, *E. coli* was mostly categorized based on the serologic detection of O (lipopolysaccharide, LPS) and H (flagellar) antigens. (7). Based on 16SrRNA sequencing, this bacterium was classified according to the second edition of Bergey's Manual of Systematic Bacteriology as part of the large bacterial family Enterobacteriaceae (8). *E. coli* belongs to the Phylum: Proteobacteria, Class: Gammaproteobacteria, Order: Enterobacteriales, Family: Enterobacteriaceae.

***Escherichia coli* pathotypes:**

One of the most common illnesses worldwide particularly in emerging economies is diarrhoea and one of the most significant causal factors of bacterial diarrhoea is Diarrhoeagenic *E. coli* (DEC) which causes gastroenteritis. Enteroaggregative *E. coli* (EAEC), Enterohemorrhagic *E. coli* (EHEC), Enteroinvasive *E. coli* (EIEC), and diffusely-adherence *E. coli* (DAEC) are among the members of this category (9).

Enterohemorrhagic *E. coli* (EHEC):

A significant contributor to pediatric acute renal failure, morbidity, and deaths among adults is haemolytic uremic syndrome (HUS), which can occasionally develop from Enterohaemorrhagic *E. coli*. Enterohaemorrhagic *E. coli* is a group of pathogenic *E. coli* that can cause diarrhoea or haemorrhagic colitis in people (10). EHEC mostly colonizes the gut of cattle, where it can spread to neighboring farms and endure for months (11).

Generally, the main reasons for the infection with EHEC were O157:H7 but later the infections caused by EHEC strains were linked to other serogroups than O157 like O26, O111, O103, and O145. Among the major causes of bloody diarrhoea, which may resolve on its own or worsen into Haemolytic Uraemic Syndrome (HUS), is *E. coli* O157 (12). According to significant features of STEC serotype and outbreak, the STEC is classified into two essential groups, O157 and non-O157. There are several strains non-O157 Shiga toxin responsible for life-threatening like haemorrhagic colitis and haemolytic uremic syndrome but not all strains of Shiga toxin-producing *E. coli* cause HC or HUS (13).

E. coli O157:H7 in the US rose to national prominence in 1994, as opposed to non-O157 STEC infections, which were not reported until 2000. Screening for non-O157 remained difficult to identify in the laboratory because of its similarity to commensal *E. coli* behaviour (14). Shiga-toxin-producing *E. coli*, or typical EHEC strains, are substantially dangerous diarrhoea-causing *E. coli* strains to date as they contain Shiga-like toxins that are identical to those that were made by *Shigella dysenteriae* (15). Shiga toxin-producing *E. coli* (STEC) O157:H7 is responsible for almost 96,000 instances of diarrhoeal illness and 3,200 infection attribute hospitals in the USA are on the rise each year (16). The first instance of STEC infection was connected to haemolytic syndrome (HUS), and it was also acknowledged in China as a cause of bloody diarrhoea due to contamination of raw hamburgers. Shiga toxin (Stx)-producing *E. coli* (STEC) present new community health issues owing to the incidence of even more common or serious illnesses and risk factor shifts brought on by pathogens, population, and alterations in the environment (17).

Toxins

Shiga toxins, or Stx1 and Stx2, which are tightly related to the Shiga toxin of *Shigella dysenteriae*, are the primary pathogenic characteristic of EHEC. A more dangerous toxin, Stx2, inhibits the production of protein gastrointestinal epithelial cells, which causes cell demise (18). Similar mucosal destruction infections are observed in the colon with *Clostridium difficile*. After entering the bloodstream through the gut, the toxin further harms vascular endothelial cells in several organs, including the colon and kidneys, which aggravates haemorrhagic colitis (19).

To identify the "auxiliary" variables that allow a STEC strain to produce illness in humans, more information is required to characterize the pathophysiology of EHEC infection, which is not fully comprehended (20). The outcomes of the local research carried out in 2022 (10), showed that stx1 (9.3%) was more commonly found among EHEC isolates than stx2. Type III secretion system (T3SS) in the colon was the best-characterized mechanism mediating bacterial protein transport into target eukaryotic cells (21). Dynamic surface filaments known as bacterial type 4 pili support bacterial adhesion, motility, and macromolecular transport. Their expression in EHEC promotes adherence to intestinal epithelia and pro-inflammatory signalling owing to the great conservation of their genes among enterobacteria (22).

In addition to the above, the EHEC carries considerable virulence determinants such as intimin. It is important to learn more about the bacterial determinants that are overexpressed in vivo during infection and may be responsible for the potential for human disease caused by STEC strains (17).

Resistance to antibiotics

Treatment of *E. coli* infections has become increasingly difficult due to resistance's emergence to the majority of primary antimicrobial medicines. The resistance of the Enterobacteriaceae family to Cephalosporins has grown over time as a result of the proliferation of Extended-spectrum-Lactamases (ESBL) (23). In 862 clinical isolates

tested between 2004 and 2012, some investigations determined susceptibility to 18 antimicrobial drugs. Of these isolates, 94% exhibited drug resistance to at least one medication, with 83% displaying resistance to at least three distinct antimicrobial drug types (24, 25).

The building of different resistance to common antibiotics may result from the moving of resistance genes between species. The pathogenic and ecological characteristics of bacterial species have been significantly altered by these transfers, and a high prevalence of EHEC isolates that are resistant to regularly used antibiotics has been observed such as Cephalothin, Ampicillin, Amoxicillin, Chloramphenicol, Tetracycline, Cotrimoxazole, and Nalidixic acid according to certain study findings (25, 26).

For EHEC infections, there is no current treatment. The cytotoxicity caused by Shiga toxin is even worse by the use of standard antibiotics. According to an epidemiological study by the Centre for Disease Control and Prevention (CDC), people who had antibiotic treatment for EHEC enteritis had a greater chance of getting HUS. Additional research confirms that antibiotics should not be used to treat EHEC infections; children receiving antibiotic treatment for haemorrhagic colitis brought on by EHEC had an increased risk of acquiring HUS. By promoting the expression as well as replication of the *stx* genes, which are encoded within a chromosomally integrated lambdoid prophage genome, antibiotics encourage the generation of the Shiga toxin. Shiga toxin is released and disseminated into the environment by *stx* induction's promotion of phage-mediated destruction of the EHEC cell membrane (27).

STEC is the most frequently recognized DEC strain. To reduce the burden of the infant to adult diarrheal diseases, it is important to avoid the indiscriminate use of antibiotics and rely instead on accurate pathogen identification when using specific antibiotics to treat diarrhoea (28).

Symptoms and transmission

The *E. coli* O157:H7 infections can vary in severity from non-symptoms to fatal. A potentially lethal condition like haemolytic uremic syndrome (HUS) seldom occurs in people. Chronic renal pathology occasionally lingers in the survivor's *E. coli* O157:H7 can be contracted by people through a variety of routes, including contaminated water and food as well as close contact with infected people and animals (29). Typically, outbreaks are caused by the consumption of infected foods such as fresh fruit, dairy items, and ground meat. Since cattle are used as food, their dung is used as fertilizer, and runoff from cattle ranches contaminates water sources, it is believed that cattle are the major source of *E. coli* O157:H7 pollution. The incidence of *E. coli* O157:H7 faecal shedding has been shown to vary among cow populations, varying from 0 to 80%, but a periodic pattern has furthermore been identified, with rising frequency over the summer. The summertime increase in temperature may be the reason for encouraging bacterial survival and growth (30).

Epidemiology

The STEC infections had a dynamic appearance with changeable over time with geographical position and season (31). Epidemiological studies reported a high rate of infectious STEC in humans leading to a broad and strong challenge to public health services in several countries with high morbidity and mortality worldwide (32).

The CDC states, that the Outbreak of infection by EHEC worldwide was more widespread in Australia, Europe, and Latin America, and more than 90% of infections in the United States of America U.S.A. led to bloody diarrhoea caused by non-O157 STEC. Despite the large health guidelines, the outbreaks of illness in the U.S.A. are still mostly brought on by tainted food, particularly beef. (33).

In the early 2017 publication released by the Foodborne Diseases Active Surveillance Network (FoodNet), the 10 US locales, STEC was included as being among the nine diseases often spreading through food. Compared to the incidence from 2014 to 2016 it was 28% higher in 2017, there were 47 cases of HUS, which was not significantly different from the incidence from 2013 to 2015. HUS was listed as the second-most widespread cause of acute infection of the kidney (AKI) in kids in Norway, with a 0.5 cases per 100,000 kids per a year as incidence estimate (30).

In Iraq, The first report of *E. coli* O157 among Iraqi children was reported in 2003 (34), they recorded that among 200 samples from children with bloody diarrhoea, 39.5% of them were caused by bacterial infection and 11.5% as *E. coli* O157. The findings of a study conducted in 2022 (10) revealed a significant EHEC prevalence in children with diarrhoea, which could be the case caused by a variety of factors. The use of tainted food and water as well as the drinking of raw and unpasteurized milk, all of which have been linked to significant EHEC outbreaks and

may act as a vehicle for the spread of germs, are among the most significant causes.

The local study done by (35) in 2019 recorded that among (50) stool human samples, 39 EHEC isolates (78%) from human infection were identified. Also, in 2020 research recorded that from 250 clinical samples, 210 (84%) samples were identified as *E. coli*. 74 isolates were identified as pathogenic *E. coli*, and the types of pathogenic *E. coli* in the examined diarrhoeal samples were (16 isolates) of Enterohemorrhagic *E. coli* (EHEC). They conclude that most pathogenic *E. coli* isolates (EHEC and EPEC) were found in diarrhoeal sample of children's stools less than 2 years of age than other ages (36). In the local study in the AL-Karamma Teaching Hospital, stool samples were taken from 161 individuals with sporadic bouts of diarrhoea, whose ages ranged from 1 month to 75 years. The seriousness of the diarrhoea brought on by Shiga toxins generated by *E. coli* (STEC) from a human disease only in Iraq's Wassit area was evaluated using stool samples. As a result of the lack of conventional O157 detection techniques in any of their hospitals, they come to the conclusion that the frequency of *E. coli* O157 in humans remains still not diagnosed. Additionally, they demonstrated how STECs that cannot be found using traditional techniques may be found utilizing molecular approaches in detection (37).

A local investigation found that a total of 349 (87.2%) of the samples yielded positive outcomes for *E. coli* growth. Of these, 5/50 (10%) Enterohemorrhagic *E. coli* EHEC were found, and all *E. coli* pathotypes were more prevalent in samples from male children who were artificially fed and were between the ages of 2 and 3 years. They conclude that children's diarrhoea is caused by diarrhoeagenic *E. coli* pathotypes in their town (38).

The study conducted by Klaif *et al.*, (39) in 2018 documented the first prevalence report for the detection of *E. coli* O104:H4 isolated from meat items and vegetables, as well as from stool and urine of children under the age of 15 in Iraq. They presented evidence of the beginning of the spread of these bacteria in Iraq, which demonstrated the potential importance of this group of *E. coli* as a foodborne pathogen and the possible significance of meat products as a major reservoir for O104. They advise consumers to recognize the significance of handling meat products with care, cleaning their hands before preparing them, and cooking them thoroughly so that the inside temperature is toxic to vegetative germs.

Previous studies have shown that Enterohemorrhagic *E. coli* is a pathogenic variety of *E. coli* which can give individuals diarrhoea or haemorrhagic colitis. Rarely, this illness can evolve into haemolytic uremic syndrome, which is a major factor in both morbidity and death in adults in Iraq and developing countries as well as acute renal failure in children.

Treatment and Prevention

Patients with EHEC diarrhoea receive supportive care. Replace any lost electrolytes and depleted water. Due to recent advancements in dialysis and intensive care, the fatality rate has dropped, mostly in young children. For children, peritoneal dialysis is the best option. Bilateral nephrectomy, particularly in cases with treatment-resistant malignant hypertension as the kidneys are the main organs affected by illness, can prevent the progression of microvascular lesions and preserve lives (40). It is possible to do plasma exchanges, platelet transfusions, and red blood cell transfusions. EHEC vaccines are being researched, but the FDA has not yet given its approval (30).

In conclusion, Enterohaemorrhagic *E. coli* can cause diarrhoea, haemorrhagic colitis, and haemolytic uremic syndrome which are a significant contributor to pediatric acute renal failure, morbidity, and mortality in adults in persons in Iraq and developing nations. The effective hygiene standards and the management of food contamination by biological and chemical dangers must be the cornerstones of the prevention of foodborne infections and the most efficient way to do this is by putting food safety assurance programs to use.

2-DISCUSSION

Due to the last 30 years of surveillance, EHEC has consistently been one of the biggest dangers to foodborne pathogens globally. EHEC mostly colonizes the gastrointestinal (GI) tract of cattle, where it can spread to neighboring farms and endure for months. Generally, the main reasons for the infection with EHEC were O157:H7 but later the infections caused by EHEC strains have been linked to other serogroups than O157 like O26, O111, O103, and O145. Among the major causes of bloody diarrhea, which may resolve on its own or get complicated into (HUS), is *E. coli* O157.

3-CONCLUSION

Enterohaemorrhagic *E. coli* can cause diarrhea, hemorrhagic colitis, and hemolytic uremic syndrome which are a significant contributor to pediatric acute renal failure, morbidity, and mortality in adults in persons in Iraq and developing nations.

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انتشار بكتريا الاشريكية القولونية المعوية النزفية في العراق

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الخلاصة

الخلفية: مرض الاسهال مشكلة صحية خطيرة وسبب رئيسي لزيادة معدل الوفيات والامراض للاطفال وحديثي الولادة في البلدان النامية. بكتريا الاشريكية القولونية المعوية النزفية هي مجموعة من بكتريا الاشريكية القولونية الممرضة التي تسبب الاسهال والتهاب القولون النزفي في العراق والبلدان النامية. تعتبر متلازمة انحلال الدم اليوريمي من العوامل المساهمة في الإصابة بالفشل الكلوي الحاد لدى الأطفال، والوفيات عند البالغين ، والتي يمكن أن تتطور أحياناً من الإشريكية القولونية المعوية النزفية. **الهدف:** تركز هذه المقالة على انتشار بكتريا الاشريكية القولونية المعوية النزفية ودورها في زيادة معدلات حدوث المرض والوفيات في الاطفال والبالغين في العراق والدول النامية. **الاستنتاج:** يمكن للإشريكية القولونية المعوية النزفية أن تسبب الاسهال والتهاب القولون النزفي ومتلازمة انحلال الدم اليوريمية التي تساهم بشكل كبير في الإصابة بالفشل الكلوي الحاد لدى الأطفال والوفيات لدى البالغين في العراق والدول النامية.

الكلمات المفتاحية: العائلة المعوية، الاشريكية القولونية، الاشريكية القولونية المعوية النزفية، الاسهال.