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Preventing E. coli O157:H7 Infection in Pregnancy

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Abstract

E. coli O:157 causes 73,000 illness in the United States annually. It is estimated that up to 10% of patients with EHEC infections may develop HUS, with a case-fatality rate ranging from 3% to 5%. Overall, HUS is the most common cause of acute renal failure leading to chronic renal sequelae in approximately 50% of survivors. A common theme to these EHEC outbreaks is their association with food such as fruit and vegetables including both fresh and frozen apart from ground beef. As pregnancy has been demonstrated to be a relatively immunocompromised state, bacterial and viral diseases in pregnancy often have much more serious sequelae than in non-pregnant individuals. In this review we will investigate the important and unique sources of E. coli infection and its potential impact to pregnant individuals.

Introduction

E coli is a Gram negative rod shaped bacteria residing in the human digestive tract and is usually considered a part of normal flora. E coli 0157:H7 is a pathogenic strain of E coli that was identified as a cause of serious gastrointestinal and systemic illness. As pregnancy has been demonstrated to be a relatively immunocompromised state, bacterial and viral diseases in pregnancy often have much more serious sequelae than in non-pregnant individuals. In this review we will investigate the important and unique sources of E. coli infection and its potential impact to pregnant individuals.

Background

German pediatrician and bacteriologist, Theodor Escherich discovered the bacterium in 1885, hence its name Eschericia coli, and it is classified as part of the Enterobacteriaceae family of gamma-proteobacteria. E coli O157:H7 is also called Enterohemorrhagic E coli (EHEC) and was first identified as a cause of human infection in 1982 [1]. EHEC strains are capable of producing shiga toxin and can cause bloody diarrhea leading to severe dehydration. Human symptoms demonstrate a wide range from asymptomatic shedding, non-bloody diarrhea, hemorrhagic colitis and possible HUS (Hemolytic Uremic Syndrome) potentially leading to death. It is estimated that up to 10% of patients with EHEC infections may develop HUS, with a case-fatality rate ranging from 3% to 5%. Overall, HUS is the most common cause of acute renal failure leading to chronic renal sequelae in approximately 50% of survivors [2-4].

Pathophysiology

The pathogenesis of EHEC is due to introduction of bacteria into the gastrointestinal tract, resulting in colonization and release of virulence factors. From 63% to 85% of cases are results of exposure to the pathogen through food. The major virulence factors such as shiga toxins are associated with human disease. Shiga toxins activate enterocyte cyclic GMP and lead to stimulation of sodium chloride channels and inhibition of its absorption. The end result is secretion of free water into the intestinal lumen which manifests clinically as watery diarrhea as well as elaboration of one or more Shiga toxins that are responsible for the vascular damage (hemorrhagic colitis) and for the systemic effects of infection, such as hemolytic- uremic syndrome. The infection dose of E coli 0157:H7 for humans is only 10- 100 organisms, which is very low as compared many other gastrointestinal pathogens.

Pregnancy is believed to be a relatively immunocompromised state and pregnant women are more prone to complications from bacterial and viral infections. Some Infections are of even greater concern during pregnancy,as they have the ability to infect both the mother and the fetus . The major organisms of concern are Listeria, Toxoplasma, Influenza, Listeria, Parvovirus B19 and Group B streptococcus.

E. coli O:157 causes 73,000 illness in the United States annually. Reviewing E.coli O157 outbreaks reported to Centre for Disease Control and Preventionb (CDC) to better understand the epidemiology of E. coli O157. E. coli O157 outbreaks (>2 cases of E. coli O157 infection with a common epidemiologic exposure) reported to CDC from 1982 to 2002 were reviewed. In the period from 1982 to 2002, 49 states reported 350 outbreaks representing 8,598 cases, 1,493(17%) hospitalizations, 354 (4%) hemolutic uremic syndrome cases and 40(0.5%) deaths. Transmission route for 183(52%) was food borne, 74 (21%) unknown, 50(14%) person-to-person, 31(9%) waterborne, 11(3%) animal contact, and 1(0.3%) laboratory-related. The food vehicle for 75 (41%) food borne outbreaks was ground beef, and for 38 (21%) outbreaks was due to fresh produce [5].

In the summer of 2011 Germany experienced one of the largest outbreaks of a food- borne infection caused by enterohaemorrhagic Escherichia Coli (EHEC) with the serotypes O 104:H4. A largest number of cases with bloody diarrhea and hemolytic uraemic syndrome occurred. In the outbreak from May to September 2011, a Shiga toxin producing E. coli strain, serotype O104;H4, was identified as the cause of an outbreak of bloody diarrhea and hemolytic-uremic syndrome in Germany and 15 other countries, largely in travelers returning from northern Germany. The cause of was due to enteroaggregative E. coli O104:H4 strain that had acquired a

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bacteriophage- encoded Shiga toxin, creating a hybrid of E. coli strain [6-8]. Approximately 3,000 EHEC cases were observed with a median age of 46 yrs, 58 percent of those patients were female and 18 deaths were observed among the EHEC patients (0.6 percent). An additional 355 EHEC patients who developed HUS were identified. The largest majority of these patients were adults, the average age was about 42 yrs, 68 percent of the HUS cases were female, and 35 deaths were observed among the HUS patients (4.1 percent). The total death toll was 53 patients [9]. Based on these cohort studies, it was proved that sprouts were the vehicle of infection. Similar outbreaks in Japan in 1996 have occurred due to consumption of Radish sprouts.

There was a large EHEC outbreak in Japan in April and May 2011. A case-control study showed that raw beef dishes consumed at a chain of barbecue restaurants were the vehicles for these infections. A total of 941 individuals ate at the restaurant chain from 19 April to 4 May 2011, and 181 presented as outbreak-related cases, including 34 HUS cases. Only 55 of the 181 infections were confirmed by laboratory isolation to be from the EHEC O111 and/or O157 serogroups. Of the 34 HUS cases, 21 developed acute encephalopathy and 5 died. Here, we report studies characterizing the *E. coli* O111 and O157 strains isolated from the cases in this outbreak

Sources of Outbreak

A common theme to these EHEC outbreaks is their association with food such as fruit and vegetables including both fresh and frozen apart from ground beef. Fruit such as strawberries, blueberries and vegetables that are grown at ground level or in open area near cattle and deer are of greatest concern. Also water source contaminated by these animals used for irrigation may reach fruit and vegetables during cultivation. In a study done in Belgium, microbiological analysis of strawberries positive for the presence of Salmonella species and Shiga toxin producing E coli at primary production and processing sites traced the elevated pathogen isolation from water samples used for irrigation [10].

While most contaminated fruit originate at ground level, fruit commonly found elevated in trees such as apples often fall on the ground and may get contaminated with E coli at ground level prior to collection. While most human cases of EHEC have been linked to direct or indirect contact with cattle leading to major recall of beef, some EHEC cases have been associated with sheep, goats (unpasteurized goat milk), pigs (dry fermented pork salami), deer (venison), horses, rabbits and birds [11].

In 2013 in Oregon there were 15 patients identified as infected with E coli in one outbreak after consumption of strawberries from a locally grown farm. Six cases were hospitalized, including 4 with hemolytic-uremic syndrome (HUS). Two patients with HUS died. The illness was determined to have originated from strawberry consumption from roadside stands or farmers' markets. A single farm was identified as the source of the contaminated strawberries. Ten of 111 (9%) environmental samples from the strawberry farm were positive for E. coli O157:H7. All samples which tested positive for E. coli O157:H7 contained evidence of deer feces. This investigation identified fresh strawberries as a novel vehicle for E. coli O157:H7 infection, implicating deer feces as the source of contamination and highlights problems concerning produce contamination by wildlife and the consequences of existing regulatory exemptions for locally grown produce [12].

In animal studies investigating the effect of E coli shiga toxin in pregnancy, pregnant mice were injected with shiga toxin. After injecting the mice, infection resulted in premature delivery, intrauterine hemorrhage and placental infarction leading to death of the fetus [13]. In another study, with inoculation of Shiga toxin in human amniotic cells lead to apoptosis of the cells [14]. There are two case reports of EHEC infection in pregnancy [15]. Although the patient in question delivered a normal baby at term, it has not been established whether EHEC infection affects pregnancy. There is a case report of 31 year pregnant women with history of recurrent UTI who was admitted to the Hennepin County Medical Centre in Minneapolis, MN for abdominal pain and spontaneous incomplete abortion (22 weeks) (Reorted by Dr. Anil Kaul). E. coli O:157 in urine samples was responsible for causing spontaneous incomplete abortion at 22weeks.

Diagnosis

The symptoms of E. coli O157:H7 include bloody diarrhea, diarrhea leading to dehydration, prolonged diarrhea, weight loss, neurological involvement (such as paresthesias, motor weakness, fever, cranial nerve palasies) and severe abdominal pain. Definitive diagnosis is made by rapid stool assay for shiga toxin presence and using stool cultures

Newer diagnostic technique for EHEC infection focus on direct detection of Shiga toxins in stool, or the use of DNA probes for detecting the toxin genes in fecal isolates. Enzyme- linked immunosorbent assays detect both Shiga toxin 1 and Shiga toxin 2 in stool [16,17]. In addition, these assays do not identify the serotype of the strain, which is important for tracing the source of infection in outbreaks. For these reasons, the CDC recommends both strain isolation using cultures and direct detection of Shiga toxins in stool.

Using culture techniques screening for E. coli O157:H7 in stool may be performed with sorbitol MacConkey (SMAC) agar, as the organism ferments sorbitol slowly. Sorbitol-negative (translucent) colonies can be confirmed as E. coli biochemically and then tested for reaction with antisera to the O157 antigen. Strains presumptively identified as E. coli O157:H7 should be sent to a reference laboratory for confirmation.

Treatment

Treatment of E. coli O 157:H7 is supportive care and careful monitoring for the development of microangiopathic complications such as HUS. One important point is that treatment of E coli O157:H7 with antibiotics is not recommended at present because current antibiotics do not appear to be helpful, and inconclusive data have suggested that the incidence of complications, including hemolytic uremic syndrome, may be greater after antibiotic therapy [18,19]. HUS comprises acute renal failure and its consequential perturbation of fluid and electrolyte balance, hemolysis and disruption of the clotting cascade with thrombocytopenia with the risk of stroke. This syndrome, together with the further effects of toxin, and complement complex formation, must be managed and addressed urgently using a multi targeted approach. This involves the institution of general supportive measures, anti platelet and thrombolytic agents, thrombin inhibitors, selective use of antimicrobials, probiotics, toxin neutralizers (synthetic and natural binders, antibodies) and antibodies against key pathogenic pathway elements to interrupt pathological processes (for example, inhibition of terminal complement complex formation) [20]. Based on evidence that Shiga toxin activates complement and binds factor H and evidence for an active role of complement via the alternative pathway in diarrhea-associated hemolytic uremic syndrome [21,22], a few anecdotal reports of successful treatment of severe Stx-associated HUS with the monoclonal antibody eculizumab have been published [23]. Neurologically, the three patients improved dramatically within 24 hours after the first eculizumab infusion. Clinical improvement was associated with rapid normalization of markers of disease activity [24].

General measures of treatment includes

1) Intravenous fluids for correcting fluid and electrolyte imbalances.

2) Peritoneal dialysis or hemodialysis, plasma infusion and plasma exchange in case of acute renal failure.

3) Transfusion of packed red blood cells and platelet in case of hemolytic anemia and thrombocytopenia respectively.

4) Generally antibiotics are to be avoided because of shiga toxin release from dying/dead bacteria. Studies have indicated that antibiotic therapy could result in unexpected changes in the clinical

Table 1: General measures of treatment

	CDC's Preventive Measures include
1)	Hand washing for at least for 20 seconds with soap and running water making certain that the backs of hands, between fingers, and nails are scrubbed.
2)	Cutting away any damaged or bruised areas on fruits and vegetables before preparing or eating. Produce should be washed before it is peeled. A clean vegetable brush should be used to scrub firm produce, such as melon and cucumbers. Produce should be dried with a clean cloth or paper towel to further reduce bacteria that may be present. Discard away the outermost leaves of lettuce or cabbage.
3)	Washing surfaces and utensils after each use.
4)	Illness-causing bacteria can grow to pathogenic levels in many foods within two hours unless they are refrigerated. At elevated temperatures, the time can be shortened to one hour. Therefore produce that tends to spoil more quickly should be refrigerated within two hours.
5)	Washing hands after contact with animals or their environments (at farms, petting zoos, fairs).

	Specific recommendations for preparing food
1	Meat should be cooked thoroughly. Ground beef and meat that has been needle-tenderized should be cooked to a temperature of at least 160°F/70°C. A thermometer should be used as an indicator of adequate heating.
2	Cross contamination in food preparation areas can be prevented by thoroughly washing hands, counters, cutting boards and utensils after they touch raw meat.
3	Raw milk, unpasteurized dairy products, and unpasteurized juices (fresh apple cider) should be avoided.

picture of disease resulting in an increase of recurrence of HUS and fatal outcomes [17] (Table 1).

Prevention

The best strategy of course, is prevention. Sanitary measures include washing fruit with potable water thoroughly. With reference to frozen fruit, it has been shown that freezing does not result in death of E. coli O157:H7 [9]. Thus freezing must be preceded by cleaning the fruit and vegetables with water.

Summary

E. coli O157:H7 is a potentially devastating infection which can cause serious health problems in vulnerable persons such as pregnancy, if infected. It is found mainly in the feces of many mammals and thus appears widespread in the environment. It may be transmitted when fruit and vegetables grown or have fallen at ground level come in contact with infected fecal material. Prevention of infection and its serious consequences is easily accomplished by simple prevention strategies such as washing hands and cleaning fruits and vegetables thoroughly with running water. Because of the serious consequences that might result from a E. Coli O:157 infection in pregnancy, women should seriously consider avoiding all fresh farm berries and open produce garden vegetables while pregnant. This holds good for all the population of people.

Fruits picking activities from farms with children are a popular activity but may be a risk unnecessary for pregnant women. It is still imperative that even fruit bought in stores should be thoroughly washed. People getting fruit from road side stands or being directly picked from farms should wash their hands and the fruit and vegetables thoroughly before eating or touching their mouth. While organic and fresh produce are generally thought of as healthier products by the public, there is no evidence that the risk from pathogenic bacteria is less, therefore similar if not greater caution and vigilance should be encouraged.

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