Clinical and Epidemiological Analysis of Enterohemorrhagic (Shiga Toxin-Producing) Escherichia coli (EHEC) Infections: Case Study, Pathogenesis, Treatment, and Disease Incidence Trends

Table of Contents

Task 1: Clinical Aspects, Aetiology, Pathogenesis, Treatment and Control

The case summary has been retrieved from the following peer-reviewed article (Tanquilut et al., 2019): Tanquilut, C. D., Jung, C. W., Nelson, A. W., & Lau, S. K. (2019). Infection due to Shiga toxin-producing Enterohemorrhagic Escherichia coli presenting as ischemic colitis. IDCases, 18, e00629.

Case Study Summary

Patient Description:

The 32-year-old female patient arrived at the urgent care centre after 1 day of non-bloody diarrhoea and diffuse abdominal pain; she had no remarkable medical history. According to her, she had eaten a salad bought from a supermarket chain that had later been recalled for containing infectious microbes.

Patient History:

The patient denied having any personal or family history of colon cancer or inflammatory bowel disease. Her one outpatient medication was the hormonal vaginal ring. She denied using any NSAIDs. She stated that she used marijuana from time to time and e-cigarettes every day for six years. Yet she did not drink even heavily or take any antibiotics recently.

Physical Examination:

During her first check-up the patient presented with normal body temperature and standard white blood cell count measurements. However, the next day she reported having worsening abdominal pain and several episodes of bloody diarrhoea. Her tachycardia increased to 130 with an elevated WBC count of 20.3. Her blood pressure was 110/67 mmHg and her pulse was 105 bpm during the physical examination, indicating that she was afebrile. An examination of the abdomen showed generalised discomfort without guarding and hypoactive bowel sounds.

Laboratory Results:

- WBC Count: 18,000 cells/mcL (elevated).
- Haemoglobin: 13.5 g/dL.
- Sodium: 129 mEq/L (low).
- Bicarbonate: 19 mEq/L (low).
- Creatinine: 0.66 mg/dL (normal).

- Liver test: normal levels for alkaline phosphatase, aspartate aminotransferase (AST), and alanine aminotransferase (ALT), as well as a total bilirubin of 1.6 mg/dL.
- Stool Test: Positive for Shiga toxin gene via the BD Max enteric bacterial panel (EBP).
- CT Scan: Diffuse wall thickening of the colon, suggestive of colitis.

Diagnosis:

The patient was diagnosed with ischemic colitis likely triggered by Shiga toxin-producing *Escherichia coli* (EHEC) and if unmanaged can lead to haemolytic uremic syndrome (HUS)

Treatment Plan:

1. Initial Treatment: The patient was initially treated with ciprofloxacin and metronidazole.
2. Antibiotic Adjustment: Antimicrobials were later changed to ceftriaxone and piperacillin-tazobactam for managing the persistent fever.
3. Bowel Rest: The patient was kept nil by mouth and started on total parenteral nutrition.
4. Discontinuation of Antibiotics: On consultation with Infectious Disease, antibiotics were discontinued to avoid the risk

Outcome:

The patient improved with supportive care and was able to tolerate clear liquids by hospital day 5. She was discharged on day 7 without requiring surgical intervention.

Clinical Microbiology Aspects:

The eventual identification of the Shiga toxin gene in the stool employing the BD Max EBP validated the clinical diagnosis. Although the E. coli O157:H7 stool culture was negative, the presence of Shiga toxin indicated EHEC infection. The patient's clinical presentation and lab results were compatible with ischaemic colitis, an uncommon consequence of EHEC infection.

Aetiology

Enterohemorrhagic *Escherichia coli* (EHEC), particularly serotype O157:H7, is a Gram-negative bacterium that produces Shiga toxins (Stx1 and Stx2). The pathogenicity of EHEC is mainly dependent upon these toxins. The primary mode of transmission from the E. coli O157:H7 bacterium to humans is through contaminated food, contaminated water, and direct contact with ill persons (Martinez-Medina, 2021). This mainly included risking bacteria through contaminated ground beef, milk, and salad vegetables. Cattle, such as cows, goats, and sheep, are the main reservoirs of E. coli O157:H7. Contamination occurs as a result of their being used as food, dung as fertiliser, and by water supplies poisoned through runoff from animal farms.

Pathogenesis

When EHEC penetrates the body, it attaches to the intestinal epithelium with adhesins, such as intimin that bind to the host receptor called TIR (translocated intimin receptor). In turn, this leads to the formation of attaching and effacing (A/E) lesions. EHEC strains release ribosome-inactivating Shiga-toxins (STX1 and STX2). STX 2 has been reportable to attribute to severe illness (Byrne et al., 2020). Shiga toxin comprises of two subunits: A and B.

A proteolytic degradation further separates subunit A into A1 and A2. In target organs such as the kidney, brain, and gut, subunit B binds to glycolipid receptors on cell surfaces. In humans, these receptors have been identified as Gb3, which are mostly expressed in kidney tubular cells, the brain, and the gut epithelium (Schwidder et al., 2019). The interaction of tumour necrosis factor-alpha enhances cytotoxicity in the kidney. Shiga toxin attaches to the cell surface and moves to the Golgi apparatus via endocytosis and ultimately reaches the cytosol where it inactive the ribosome leading to cell death (Amin et al., 2022).

This toxin disrupts membrane ion channels in the colon, causing loss of ions and water along with the clinical manifestation of diarrhoea. This toxin also functions as a cell transduction and immunological modulator, resulting in pro-inflammatory and pro-apoptotic effects. Shiga toxins penetrate the circulation and attack endothelial cells in the kidneys, brain, and other organs. Toxin-mediated injury in the kidneys causes thrombotic microangiopathy, which is characterised by platelet aggregation and haemolytic anaemia, thrombocytopenia, and acute kidney injury etc. (Cabrera-Sosa & Ochoa, 2020).

Clinical Symptoms and Laboratory Findings

- Early Symptoms: Watery diarrhoea, abdominal cramps, and vomiting.
- Progression: Bloody diarrhoea (haemorrhagic colitis) due to mucosal damage in the colon (Liu et al., 2022).
- Complications: HUS, characterized by the triad of haemolytic anaemia, thrombocytopenia, and acute kidney injury. Neurological complications, such as seizures or stroke, may also occur.

Laboratory findings include:

- Stool Culture: Isolation of EHEC O157:H7.
- Shiga Toxin Detection: PCR or immunoassay for Stx1 and Stx2.

- Blood Tests: Elevated creatinine, urea, and lactate dehydrogenase (LDH); low haemoglobin and platelet counts.
- Urinalysis: Hematuria and proteinuria

Treatment

Supportive Care:

Considering the prognosis, immediate supportive care including hydration, electrolyte balance, and renal support is vital. In certain cases, surgery is required.

Emerging Therapies:

- Monoclonal Antibodies that specifically bind to Shiga toxins to neutralize its effects (Dyatlov et al., 2022).
- For restoring the gut microbiota and reducing EHEC colonization, the use of probiotics is also on the rise.

Safety:

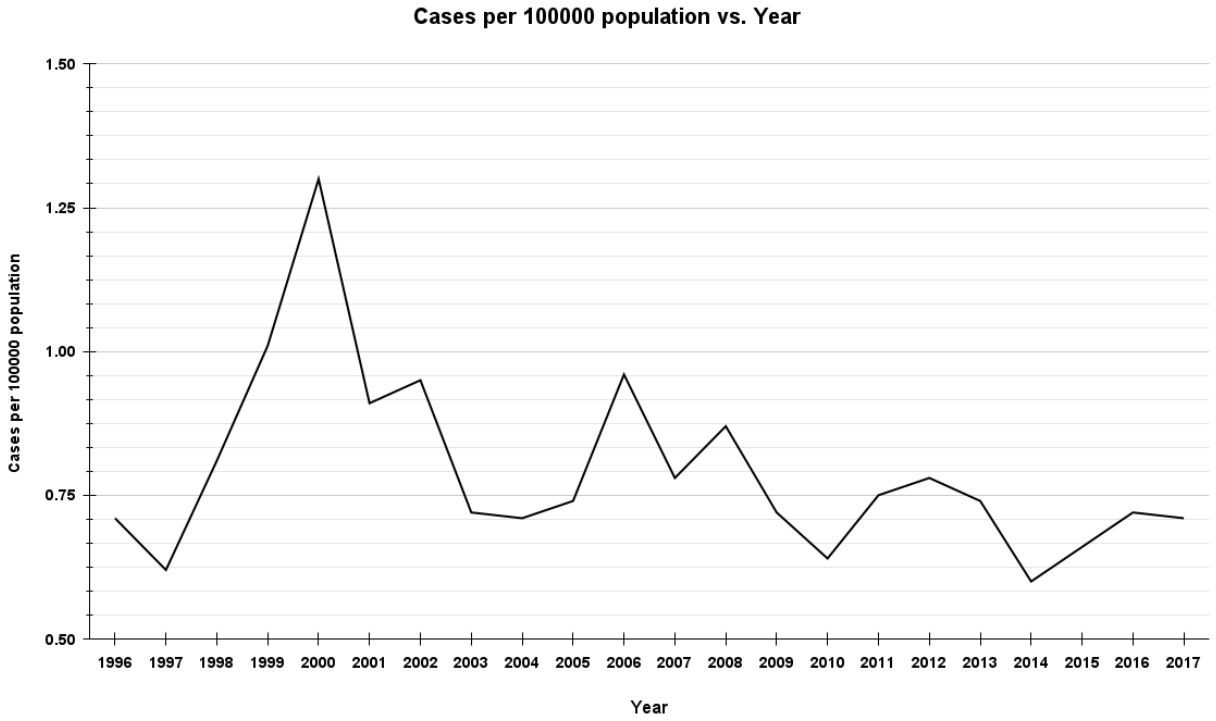
Eculizumab is shown by review studies for the treatment of HUS (Muff-Luett et al., 2021).

Control Interventions

- A preventable contamination that can be prevented through hygiene is caused by EHEC, a type of foodborne illness (Singha et al., 2023). Other include cooking meat at least to a temperature of internal temperature ≥70°C, washing vegetables and fruits bought from the market properly as well as taking away unpasteurized dairy products.
- One must properly dispose of animal waste.
- Enhancing sanitary conditions throughout animal slaughter is vital.
- Teaching farm workers and food handlers the fundamentals of food hygiene can also lower the prevalence of EHEC infections.

Task 2: Disease Incidence Analysis

Shiga toxin producing E. coli (STEC) O157 is a great public health threat to the U.S. Since the Centres



for Disease Control and Prevention (CDC) have released data concerning the state of infection caused by STECO157 throughout 1966 to 2017 this analysis is discussed. The above given line graph reflects the occurrence of cases with the peak and dip of a disease per 100,000 populations given the timeline. According to the Agency, there had been 0.60 to 1.30 cases per 100,000 population associated with STECO157 in the U.S. The maximum was recorded as 1.30 cases per 100,000 in the year 2000, whereas a case occurred in 2014 per same 100,000."

The elevated rate from 0.71 to 1.30 during 1996 to 2000 may be attributed to better reporting systems of STEC. However, it soon declined to 0.91 in 2001. Then it fluctuated between 0.71 and 0.96 till 2007. This might be because of the initiation of the interventions at the farm level, such as improved animal hygiene and feed management. From 2007 to 2014 it gradually decreased. This is most likely because of the further improvement in the surveillance and detection methods, consumer education and food safety practices. Lastly, between 2014 to 2017 it has remained relatively stable between 0.60 to 0.87 cases per 100,000 thereby indicating the success of ongoing control measures.

The primary reservoir of STECO157 was cattle. So, the transmission of STECO157 to humans could have happened due to the consumption of STECO157-contaminated food especially undercooked ground beef, using unpasteurized dairy products, and eating vegetables and fruits raw without cleaning it. However, the beginning of the implementation of the Hazard Analysis and Critical Control

Points (HACCP) system in the meat industry that happened in 2002 might have resulted in a significant reduction in STECO157 cases (Hyde et al., 2016). HACCP is a control method which lower the risk of meat contamination from microbiological agents like STECO157 risks during the production. Besides that, increased educational campaigns for healthy and safe food handling, cooking practices, and hygiene might have also reduced the risk of infection from STEC0157.

Overall, Between the period of 1996 to 2017, the cases of STEC0157 have decreased significantly. However, some periodic increases in incidences like 2006, 2008, 2012, 2016 etc. from the previous year could be because of external climatic events. For example, the weather events like floods, and heavy rainfall in the agricultural areas could have caused the contamination of the water sources with cattle faeces. This might have caused such a small increase in incidences of STECO157. For example, (Osborn et al., 2024)reported that 13 children fell ill owning to play around or use such untreated, pressurized, municipal irrigation water. This shows that education of the people is vital to reduce the occurrence of such diseases.

References

Amin, M.A., Hashem, H.R., El-Mahallawy, H.S., Abdelrahman, A.A., Zaki, H.M. & Azab, M.M. (2022) Characterization of enterohemorrhagic Escherichia coli from diarrhoeic patients with particular reference to production of Shiga-like toxin. *Microbial Pathogenesis*, 166, p.105538. Available from: <https://www.sciencedirect.com/science/article/pii/S0882401022001516> [Accessed 14 March 2025].

Byrne, L., Adams, N. & Jenkins, C. (2020) Association between Shiga Toxin–Producing Escherichia coli O157:H7 stx Gene Subtype and Disease Severity, England, 2009–2019. *Emerging Infectious Diseases*, 26 (10), pp.2394–2400. Available from: <http://wwwnc.cdc.gov/eid/article/26/10/20-0319_article.htm>.

Cabrera-Sosa, L. & Ochoa, T.J. (2020) Escherichia coli Diarrhea. In: *Hunter's Tropical Medicine and Emerging Infectious Diseases*. Elsevier, pp.481–485. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B9780323555128000466>.

Dyatlov, I.A., Svetoch, E.A., Mironenko, A.A., Eruslanov, B. V., Firstova, V. V., Fursova, N.K., Kovalchuk, A.L., Lvov, V.L. & Aparin, P.G. (2022) Molecular Lipopolysaccharide Di-Vaccine Protects from Shiga-Toxin Producing Epidemic Strains of Escherichia coli O157:H7 and O104:H4. *Vaccines*, 10 (11), p.1854. Available from: <https://www.mdpi.com/2076-393X/10/11/1854>.

Hyde, R., Hoflund, A.B. & Pautz, M. (2016) One HACCP, Two Approaches. *Administration & Society*, 48 (8), pp.962–987. Available from: <https://journals.sagepub.com/doi/10.1177/0095399714548266>.

Liu, Y., Thaker, H., Wang, C., Xu, Z. & Dong, M. (2022) Diagnosis and Treatment for Shiga Toxin-Producing Escherichia coli Associated Hemolytic Uremic Syndrome. *Toxins*, 15 (1), p.10. Available from: <https://www.mdpi.com/2072-6651/15/1/10>.

Martinez-Medina, M. (2021) Special Issue: Pathogenic Escherichia coli: Infections and Therapies. *Antibiotics*, 10 (2), p.112. Available from: <https://www.mdpi.com/2079-6382/10/2/112>.

Muff-Luett, M., Sanderson, K.R., Engen, R.M., Zahr, R.S., Wenderfer, S.E., Tran, C.L., Sharma, S., Cai, Y., Ingraham, S., Winnicki, E., Weaver, D.J., Hunley, T.E., Kiessling, S.G., Seamon, M., Woroniecki, R., Miyashita, Y., Xiao, N., Omoloja, A.A., Kizilbash, S.J., Mansuri, A., Kallash, M., Yu, Y., Sherman, A.K., Srivastava, T. & Nester, C.M. (2021) Eculizumab exposure in children and young adults: indications, practice patterns, and outcomes—a Pediatric Nephrology Research Consortium study. *Pediatric Nephrology*, 36 (8), pp.2349–2360. Available from: <https://link.springer.com/10.1007/s00467-021-04965-5>.

Osborn, B., Hatfield, J., Lanier, W., Wagner, J., Oakeson, K., Casey, R., Bullough, J., Kache, P., Miko, S., Kunz, J., Pederson, G., Leeper, M., Strockbine, N., McKeel, H., Hofstetter, J., Roundtree, A.,

Kahler, A. & Mattioli, M. (2024) Shiga Toxin–Producing Escherichia coli O157:H7 Illness Outbreak Associated with Untreated, Pressurized, Municipal Irrigation Water — Utah, 2023. *MMWR. Morbidity and Mortality Weekly Report*, 73 (18), pp.411–416. Available from: <https://www.cdc.gov/mmwr/volumes/73/wr/mm7318a1.htm> [Accessed 14 March 2025].

Schwidder, M., Heinisch, L. & Schmidt, H. (2019) Genetics, Toxicity, and Distribution of Enterohemorrhagic Escherichia coli Hemolysin. *Toxins*, 11 (9), p.502. Available from: <https://www.mdpi.com/2072-6651/11/9/502>.

Singha, S., Thomas, R., Viswakarma, J.N. & Gupta, V.K. (2023) Foodborne illnesses of Escherichia coli O157origin and its control measures. *Journal of Food Science and Technology*, 60 (4), pp.1274–1283. Available from: <https://link.springer.com/10.1007/s13197-022-05381-9>.

Tanquilut, C.D., Jung, C.W., Nelson, A.W. & Lau, S.K. (2019) Infection due to Shiga toxin-producing enterohemorrhagic Escherichia coli (EHEC) presenting as ischemic colitis. *IDCases*, 18, p.e00629. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S2214250919301647>.