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Campylobacteriosis: A rising threat in foodborne illnesses

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ABSTRACT

Campylobacteriosis is a foodborne illness that is contracted by eating contaminated food, particularly animal products like meat from diseased animals or corpses tainted with harmful germs. The epidemiology of campylobacteriosis varies significantly between low-, middle-, and high-income countries. *Campylobacter* has a complicated and poorly known survival strategy for getting past host barriers and causing sickness in humans. The adaptability of *Campylobacter* to unfavorable environments and the host's immune system seems to be one of the most crucial elements of intestinal colonization. A *Campylobacter* infection may result in fever, nausea, vomiting, and mild to severe bloody diarrhea in humans. Effective and rapid diagnosis of *Campylobacter* species infections in animal hosts is essential for both individual treatment and disease management at the farm level. According to the most recent meta-analysis research, the main risk factor for campylobacteriosis is travel, which is followed by eating undercooked chicken, being exposed to the environment, and coming into close contact with livestock. *Campylobacter jejuni*, and occasionally *Campylobacter coli*, are the primary causes of *Campylobacter* gastroenteritis, the most significant *Campylobacter* infection in humans for public health. The best antibiotic medications for eradicating and decreasing *Campylobacter* in feces are erythromycin, clarithromycin, or azithromycin. The best strategy to reduce the number of human infections caused by *Campylobacter* is to restrict the amount of contamination of the poultry flock and its products, even if the majority of infections are contracted through handling or ingestion of chicken.

Keywords: *Campylobacter*, Campylobacteriosis, Food, Poultry, Public health.

Introduction

The zoonotic disease known as campylobacteriosis is brought on by bacteria belonging to the genus *Campylobacter*, which includes the species *Campylobacter jejuni*, *Campylobacter coli*,

Campylobacter lari, and *Campylobacter fetus* (Facciola *et al.*, 2017). This is a foodborne illness that is contracted by eating contaminated food, particularly animal products like milk and meat from diseased animals or corpses tainted with harmful germs (Chlebic and

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Ślizewska, 2018; Agumah *et al.*, 2024). The number of instances of campylobacteriosis has surpassed that of classical enteric bacteria. The information indicates that the prevalence of *Campylobacter* infections has risen recently (Behailu *et al.*, 2022). The incidence of this organism's isolation from gastrointestinal infections is roughly three to four times higher than that of *Salmonella* or *Escherichia coli* (Epps *et al.*, 2013; Yanestria *et al.*, 2019; Ansharieta *et al.*, 2021).

The digestive tracts of domestic animals, wild animals, and livestock serve as the organism's reservoir (Johnson *et al.*, 2017). Since the *Campylobacter* species that cause human gastroenteritis can grow at temperatures above 40°C, they are categorized as temperature tolerant (Yanestria *et al.*, 2024a). The two main variables that affect *Campylobacter* infection are transmission factors and body resistance. Human campylobacteriosis infections are mostly infrequent. The most common ways that these bacteria are spread are through the consumption of raw milk, drinking water, eating undercooked chicken and cattle meat, or coming into close contact with sick dogs or cats (Goddard *et al.*, 2022). The range of germs that can induce an illness in an individual is between 500 and 10,000 cells (Kreling *et al.*, 2020). Children are exposed to a lower infectious dosage than adults.

Foodborne *Campylobacter* infections are a human health problem that causes approximately 8.4% of global diarrhea cases (Igwaran and Okoh, 2019). One of the four primary causes of diarrheal illness worldwide is *Campylobacter*; diarrhea is the most prevalent foodborne illness, affecting 550 million people annually (Myintzaw *et al.*, 2023). Campylobacteriosis symptoms include vomiting, fever, and bloody or watery diarrhea. In general, people over 75 years old and younger children (under 4) are more likely to have *Campylobacter* infections (Guo *et al.*, 2023). Furthermore, patients with hemoglobinopathy, inflammatory bowel illness, and those with compromised immune systems are among the populations most at risk of contracting a *Campylobacter* infection (Igwaran and Okoh, 2019). Compared to low-income countries, high-income countries have a higher risk of *Campylobacter* infection. A multitude of environmental factors present a significant risk of *Campylobacter* transmission to people in low-income countries, and eating poultry meat and poultry products is the main cause of outbreaks (El-Saadony *et al.*, 2023). Worldwide incidences of campylobacteriosis are caused by 60%–80% of poultry meat and its by-products. Poultry meat from laying hens, turkeys, ostriches, ducks, and broilers is frequently consumed (Suzuki and Yamamoto, 2009). To lower product contamination and thus lower the incidence of human campylobacteriosis, intervention techniques to manage *Campylobacter* in hens must be prioritized as consumer demand for poultry meat and poultry products rises (Taha-Abdelaziz *et al.*, 2023).

Campylobacter, especially in poultry, can spread quickly by the fecal-oral pathway from one animal to the entire flock in less than a week (Rawson *et al.*, 2019). Once within the host body, these bacteria live in the intestines, which have the highest concentration of bacteria; the liver, deep muscles, spleen, thymus, and bursa of Fabricius have smaller concentrations of bacteria (Deng *et al.*, 2020). Bacterial colonization results in serosal fluid leakage, inflammation, toxin production, invasion of host cells, and active secretion, all of which lead to epithelial diseases (O Cróinín and Backert, 2012). In humans, campylobacteriosis typically takes two to five days to incubate. Similar to the toxins produced by *E. coli* and cholera, this bacterium also produces enterotoxins (Wysok *et al.*, 2022).

The yearly rise in instances of campylobacteriosis has raised concerns about the disease's occurrence around the world, with major socioeconomic and public health ramifications. This review article aims to provide a comprehensive explanation of campylobacteriosis, starting from etiology, history, epidemiology, pathogenesis, virulence factors, diagnosis, clinical symptoms, transmission, public health importance, treatment, antibiotic resistance, control, and vaccination. Understanding the overview of campylobacteriosis is essential to implementing effective control measures.

Etiology

Organism description

Greek terms “campylos,” which means “curved,” and “baktron,” which means “rod,” are the sources of the word *Campylobacter*. Gram-negative bacteria belonging to the Campylobacteriaceae family are called *Campylobacter* species, and they do not produce spores (Wang *et al.*, 2023). There are six subspecies and seventeen species in the genus *Campylobacter*. More advancements in taxonomic standards could lead to a more precise classification of *Campylobacter* species. The two species that are most frequently linked to human illness are *C. jejuni* and *C. coli* (Pözlner *et al.*, 2018). More than 80% of human *Campylobacter*-related diseases are caused by *C. jejuni*, but up to 18.6% are caused by *C. coli* (Ammar *et al.*, 2020). Additionally, *C. fetus* has been connected to human foodborne diseases.

Morphology and characteristics of *Campylobacter* bacteria

Certain gram-negative bacteria called *Campylobacter* species do not produce spores. These organisms range in size from 0.2 to 0.8 µm in width and 0.5 to 5 µm in length. They have a spiral shape, are curved, or are occasionally observed as straight rods (Epps *et al.*, 2013). *Campylobacter* can be seen in short or occasionally large chains and can have shapes such as spiral, S, V, or comma (Mushi *et al.*, 2014). *Campylobacter* cells begin to age and then become coccoid in shape. Possessing one or more flagella at one end, the cells exhibit remarkable motility. A phase

contrast microscope can be used to observe the comma-shaped cells' quick, darting movement (Firdich *et al.*, 2019).

Growth and survival characteristics of *Campylobacter* bacteria

Species of *Campylobacter* are delicate organisms. This organism is susceptible to irradiation, disinfectants, freezing, drying, heating (pasteurization/cooking), and acidic conditions (preservation) (Kim *et al.*, 2021). Bacteria often do better at colder temperatures and struggle to thrive at room temperature (25°C). *Campylobacter jejuni* thrives in low-oxygen conditions, such as those with 5% O₂, 10% CO₂, and 85% N₂, and grows best at 37°C to 42°C (Kaakoush *et al.*, 2007). The gut has evolved bacteria to have a single polar flagellum and a corkscrew form. These characteristics promote motility (Liu *et al.*, 2018). It has been demonstrated that certain *Campylobacter* species can grow in viscous intestinal mucus under unfavorable circumstances, such as low nutrition availability, high temperature, freezing, or stationary phase (Ribardo *et al.*, 2024). The cells undergo a form of transition in this condition, going from a motile spiral to a coccoid. This coccoid form's nature and function are unknown. Due to its capacity to form a biofilm, *C. jejuni* can tolerate aerobic environments (Pokhrel *et al.*, 2022).

History

There is a vast and varied range of bacteria in the *Campylobacter* genus. Theodor Escherich identified the first reported case of *Campylobacter* in 1886 when he observed non-culturable, helical-shaped bacteria in colonic mucosal stains linked to diarrhea in infants who perished from an outbreak of the disease thought to be "*Cholera infantum*" (Sheppard and Maiden, 2015). In 1906, *Campylobacter* or bacteria resembling *Vibrio*, were first isolated from the uterus of a sheep that had been aborted (Tresse *et al.*, 2017). A similar pathogen, *Vibrio fetus*, was identified in 1912 from aborted bovine fetuses. After fifteen years, a different *Vibrio* pathogen called *Vibrio jejuni* was found in the feces of cows that had diarrhea (Epps *et al.*, 2013). *Vibrio coli* was discovered in 1944 in pigs that had diarrhea.

For more than 40 years, it has been believed that *Campylobacter* causes animal illness, especially in 1938 when *Campylobacter* spp. was reported to be involved in foodborne illness outbreaks (Sokett and Rodgers, 2001). Due to the ingestion of tainted milk, a *Vibrio jejuni*-like virus was found in the blood of 13 outbreak victims. This outbreak resulted in acute diarrheal sickness in 357 prisoners at an Illinois state institution in the United States (Poly *et al.*, 2019). To distinguish this bacterium from *Vibrio* spp., it was moved to the newly formed genus *Campylobacter* in 1963 because of its unique traits, which included low DNA base composition (low G+C concentration), microaerophilic development, and nonfermentative metabolism (O'Loughlin *et al.*, 2015). The Greek word

"kampyo's" is the source of the genus name, which signifies bent or curled (Sheppard and Maiden, 2015). The American bacteriologist Elisabeth King provided the first accurate description of the genus *Campylobacter*. King was determined to isolate these bacteria from feces and thought that the prevalence of *Campylobacter* was higher than the few cases that had been reported (Moore and Matsuda, 2002). Butzler was able to isolate *Campylobacter* from the feces of human patients who were experiencing diarrhea and elevated body temperatures in the early 1970s, thanks to the development of a unique filtration technique for the identification of this bacteria in veterinary medicine (Butzler, 2004). However, adding certain antimicrobial drugs, such as trimethoprim, polymyxin B, and vancomycin to the basic medium allowed for significant advancements in *Campylobacter* isolation (Bonnet *et al.*, 2019).

Four distinct species of *Campylobacter* were identified by Veron and Chatelain in their 1973 comprehensive study on the taxonomy of microaerophilic vibrio-like organisms: *C. coli*, *C. sputorum*, *C. fetal*, and *C. jejuni* (Costa and Iraola, 2019). *C. jejuni* was not widely acknowledged as one of the most common causes of foodborne bacterial enteritis in people until the 1980s, around a century after it was initially discovered.

Public health importance

Campylobacter jejuni, and occasionally *C. coli*, are the primary causes of *Campylobacter* gastroenteritis, the most significant *Campylobacter* infection in humans for public health (Igwaran and Okoh, 2019). It is estimated that 80% of human *Campylobacter* infections are caused by chickens, which are the primary reservoir of *Campylobacter* spp. infections (Epps *et al.*, 2013). Campylobacteriosis is thought to be carried asymptotically by chickens. Most chicken flocks can become colonized by *Campylobacter* spp. (Yanestria *et al.*, 2023). According to basic research conducted by the European Union, *Campylobacter* was found in 75.8% of broiler carcasses, 71.2% of a batch of broiler chickens' cecal content contained *Campylobacter*, and 61.3% of chicken skin samples from retail settings had *Campylobacter* prevalence, with 18.6% of those samples having counts of more than 1000 CFU/g (Hue *et al.*, 2010).

Despite the low severity of campylobacteriosis (0.03%), there are more instances of *Campylobacter* infection in humans (Facciola *et al.*, 2017). Remarkably, among foodborne microbes, *Campylobacter* infections are the most prevalent cause of death in humans. Patients with compromised immune systems, such as those with cancer, liver disease, and acquired immunodeficiency syndrome (AIDS), are susceptible to death from *Campylobacter* infections (Louwen *et al.*, 2012). In most cases, campylobacteriosis is sporadic and self-limiting. The symptoms of *Campylobacter*-induced gastroenteritis include fever, headache, vomiting,

cramping or pain in the abdomen, watery or often bloody diarrhea, and weight loss (Hsu *et al.*, 2023).

A *Campylobacter* infection can result in post-infectious immune disorders like Guillain Barré syndrome (GBS), a neurological disorder characterized by flaccid paralysis and advanced weakness in the extremities. It can also cause reactive arthritis (RA), or inflammation of the joints, and paralysis of the respiratory muscles (Finsterer, 2022). Not only that, but this bacterial infection also results in Miller-Fisher syndrome (MFS), which manifests as visual abnormalities (ophthalmoplegia) and coulometer weakness (areflexia and ataxia) (Ang *et al.*, 2001). Campylobacteriosis is hyperendemic in underdeveloped nations, and infections with *Campylobacter* are symptomatic, virtually exclusively occurring in young children and babies (Coker *et al.*, 2002). In adults or older children, the signs of this infection are uncommon since subsequent infections may be asymptomatic.

It is interesting to note that developed and developing nations have very different campylobacteriosis epidemiologies. Due to the lack of national systems for the surveillance of *Campylobacter* infections, it is challenging to assess the prevalence of *Campylobacter* infections in underdeveloped nations, since *Campylobacter* is not the most common cause of bacterial foodborne diseases (Platts-Mills and Kosek, 2014). Research articles on *Campylobacter* isolation from various specimens are the primary source of information regarding the prevalence of *Campylobacter* infections in underdeveloped nations (Chala *et al.*, 2021).

Epidemiology

The epidemiology of campylobacteriosis varies significantly between low-, middle-, and high-income countries. These variations are most likely due to variations in food habits, nutritional status, environmental cleanliness, climatic conditions, immune system status (especially among elderly people and children) diagnostic methods, and the availability of natural reservoirs (Sanchez *et al.*, 2020). *Campylobacter* infections are hyperendemic in children under the age of two, with up to two cases per child in low- and middle-income countries (Kiarie *et al.*, 2023). Most cases in children and adults are asymptomatic. *Campylobacter* infections without symptoms are uncommon in high-income nations, but the average lifetime frequency of infections is less than one (Pascoe *et al.*, 2020). Children are typically more likely to have *Campylobacter* infections, which suggests that early exposure may result in the formation of protective immunity but later asymptomatic shedding (Samie *et al.*, 2022).

The exact nature of the global incidence rate of *Campylobacter* outbreaks is largely unclear, and reports of their incidence differ between nations. The underreporting of *Campylobacter* infection cases, variations in reporting systems, challenges in diagnosis,

and variations in surveillance in the event of an outbreak are among the factors contributing to the inaccurate incidence of campylobacteriosis outbreaks. Outbreaks of campylobacteriosis typically result from multiple humans contracting food- or water-borne diseases, and the majority of these outbreaks are caused by animals (Llarena and Kivistö, 2020). Despite the fact that many people rely on rivers and streams as their main supply of drinking water, environmental sources like these are typically the source of campylobacteriosis outbreaks in low-income nations (Whiley *et al.*, 2013). Apart from their role in the spread of human diseases in low-income nations, water sources have also been linked to epidemics of campylobacteriosis in high-income nations including Finland (Suominen *et al.*, 2024), Canada (Guy *et al.*, 2018), Norway (Hyllestad *et al.*, 2020), Denmark (Boysen *et al.*, 2014), and New Zealand (Gilpin *et al.*, 2020).

There have also been reports of *Campylobacter* infections and outbreaks in both high- and low-income nations that are caused by milk. Milk consumption is associated with outbreaks of campylobacteriosis in a number of countries, including the United States (Jaakkonen *et al.*, 2020), Sweden (Artursson *et al.*, 2018), Italy (Bianchini *et al.*, 2014), China (Li *et al.*, 2020), Japan (Ohno *et al.*, 2023), India (Modi *et al.*, 2015), and the Netherlands (Heuvelink *et al.*, 2009). Apart from that, other countries that have recorded campylobacteriosis outbreaks due to the consumption of poultry meat are Canada (Hodges *et al.*, 2019), Australia (Keerthirathne *et al.*, 2022), British Columbia (Hakeem and Lu, 2021), Belgium (Gellynck *et al.*, 2008), Denmark (Kuhn *et al.*, 2018), England (Royden *et al.*, 2021), Germany (Stingl *et al.*, 2012), Poland (Szosland-Fałtyn *et al.*, 2018), New Zealand (Sears *et al.*, 2011), Norway (Llarena *et al.*, 2022), Madagascar (Randremanana *et al.*, 2014), Kenya (Mbai *et al.*, 2022), Indonesia (Yanestria *et al.*, 2024b), Malawi (Mason *et al.*, 2013), Iceland (Stern *et al.*, 2003), Estonia (Tedersoo *et al.*, 2022), Guatemala (Benoit *et al.*, 2014), and Peru (Harvey *et al.*, 2003).

Humans are susceptible to campylobacteriosis due to a wide range of risk factors. According to the most recent meta-analysis research, the main risk factor for campylobacteriosis is travel, which is followed by eating undercooked chicken, being exposed to the environment, and coming into close contact with livestock (Facciola *et al.*, 2017).

Reports from the United Kingdom indicate that the occurrence of campylobacteriosis is linked to a seasonal increase in fly populations throughout the summer because of high temperatures and rainy weather that promote fly development (Nichols, 2005). This leads to the flies coming into touch with animal and human feces, which supports the theory that environmental factors cause the seasonal epidemics that are common in the summer (Penakalapati *et al.*, 2017). It was also discovered that both conventional

and organic environmental factors were linked to campylobacteriosis. According to a different Danish study, human campylobacteriosis incidence rose in tandem with environmental temperatures, with the biggest rise in incidence occurring between 13°C and 20°C (Patrick *et al.*, 2004).

Pathogenesis

Research on the pathogenesis of *Campylobacter* is curiously typically conducted on *C. jejuni*. *Campylobacter* has a complicated and poorly known survival strategy for getting past host barriers and producing sickness in humans. It is thought that 350–10,000 cells are necessary for a *Campylobacter* infection, and the infectious dose frequently corresponds with the severity of the disease (Janssen *et al.*, 2008). Immunocompromised individuals, the elderly, and children are the most common groups to contract *Campylobacter* infections (El-Tras *et al.*, 2015). *Campylobacter* must cross the stomach's gastric acid barrier and the upper small intestine's bile duct's extremely alkaline secretions after consuming tainted food or drink (Facciola *et al.*, 2017). Pathogenic microorganisms like *Campylobacter* can survive and proliferate when the stomach acid barrier is disrupted. Thus, individuals who take proton pump inhibitors and antacids, or who have lowered stomach acidity, may be more susceptible to campylobacteriosis (Janssen *et al.*, 2008).

Once *Campylobacter* enters the lower digestive tract, it targets the distal ileum and colon epithelial cells, causing severe inflammation and cell destruction; however, in chickens, the cecum is a crucial location for *Campylobacter* colonization (Pang *et al.*, 2023). *C. jejuni* is the source of invasive inflammatory illness in affluent nations. However, *Campylobacter* is the cause of non-inflammatory watery diarrhea in underdeveloped nations (Coker *et al.*, 2002). Chemotaxis and motility are thought to be necessary for *Campylobacter* host colonization, adhesion, and invasion (Elmi *et al.*, 2021). These bacteria require iron uptake, bile salt and gastric acid resistance, and oxidative stress tolerance for growth and survival (Kreling *et al.*, 2020). Toxins produced by bacteria mediate tissue damage and inflammatory reactions (Callahan *et al.*, 2021).

Numerous parameters related to survival and virulence are thought to have a major role in the pathophysiology and induction of gastroenteritis caused by *Campylobacter* spp. It is thought that the clinical and epidemiological aspects of the illness have an impact on the molecular mechanisms of *Campylobacter* infection.

Virulence factors

The expression of virulence has been linked to a number of genes. Virulence genes implicated in colonization and adhesion include *racR*, *flaA* (flagellin A gene), *dnaJ*, and *cadF* (adhesin gene) (Hermans *et al.*, 2011). The genes that cause invasion are virulence plasmid genes (*ciaB*, *virB11*), and (invasion-associated gene A (*iamA*)) (Kovács *et al.*, 2020). Virulence genes

implicated in the synthesis of lipopolysaccharides are β -1,3-galactosyltransferases-encoding genes (*cgtB* and *wlaN*) (Guirado *et al.*, 2020). Vital pathogenic virulence genes for the expression of cytotoxin synthesis are *cdtC*, *cdtB*, and *cdtA*, or cytolethal bloating toxins C, B, and A (Talukder *et al.*, 2008). The adaptability of *Campylobacter* to unfavorable environments and the host's immune system seems to be one of the most crucial elements of intestinal colonization. Under the influence of chemoattractants, organisms enter the intestinal environment through fecal-oral transfer and populate the intestinal tract (Parker *et al.*, 2020). Additionally, the proximal digestive system contains a number of antimicrobial proteins, including beta-defensin gallinacin-6 (van Dijk *et al.*, 2007). There has been a great deal of research done on the virulence traits of *Campylobacter*, as these traits affect how pathogenic the species is. The ability of the *Campylobacter* genus, particularly its pathogenic species like *C. jejuni*, to live and tolerate physiological stressors contributes to its pathogenicity. These bacteria have a variety of virulence factors.

Chemotaxis

Campylobacter uses a process known as chemotaxis, which facilitates directed movement toward or away from chemical stimuli (effectors/chemo ligands, which can be either repellent or attractant) in the environment, to adapt to different environments (Kreling *et al.*, 2020). Transducer-like protein (Tlps), which has a methyl acceptor domain, and core signal transduction protein make up the chemotaxis system (Clark *et al.*, 2019). Ligands binding to Tlps send signals to cytoplasmic chemotaxis proteins, which in turn trigger a signal transduction cascade leading to directed movement of the flagella (Zautner *et al.*, 2012). *Campylobacter* can more easily participate in substrate-specific chemotaxis when transducer-like proteins are present. This is crucial for the pathogen's capacity to adapt, grow its pathobiology, and invade the gastrointestinal tract (Chandrashekar *et al.*, 2017).

Flagellar motility

Campylobacter's motility is crucial to its survival in the digestive tract under a variety of circumstances. The mobility of flagella allows *Campylobacter* species to locate favorable environments within their hosts (Baldvinsson *et al.*, 2014). The human foodborne pathogen *C. jejuni* produces two structural flagellins, FlaA and FlaG, that are heavily glycosylated by nature (Radomska *et al.*, 2017).

Oxygen tension and oxidative stress defense

Campylobacter is able to withstand a number of adverse environmental conditions, such as pH fluctuations, oxygen restriction in the cecum, oxidative stress, elevated osmotic pressure, and the presence of digestive fluids, such as bile salts, from penetrating the digestive system (Kim *et al.*, 2021). Peroxide resistance regulators and *Campylobacter* oxidative

stress regulators control the expression of genes linked to oxidative stress resistance (Kim *et al.*, 2015).

Bile resistance

Bile salt resistance is another requirement for *C. jejuni* to successfully colonize (Lin *et al.*, 2003). Deoxycholate disrupts the lipid bilayer of the cell membrane and causes the unfolding and aggregation of proteins in the bacterial cytoplasm, killing detergent-like bile acids like cholate and bacteria (Talukdar *et al.*, 2022).

Adhesion

Numerous adhesins produced by *Campylobacter*, both separately and in combination, have the ability to affect or mediate the attachment of bacteria to various cell structures and hosts (Kreling *et al.*, 2020). The *Campylobacter* adhesion protein to fibronectin (CadF), a 37 kDa protein that binds to the fibronectin ligand present in epithelial cells and is expressed by the CadF gene, the adhesin that has been the subject of the greatest research (Konkel *et al.*, 2020).

Invasion

In addition to their ability to survive intracellularly, several species of *Campylobacter* are known to secrete invasion antigens (Cia), such as CiaB, CiaC, and CiaI (Lopes *et al.*, 2021). These virulence factors are essential for the bacteria's ability to infiltrate epithelial cells and populate the digestive system of their host (Callahan *et al.*, 2021).

Cytotoxic distending toxin

The cytotoxic distending toxin is a toxin that functions similarly to DNase to generate DNA damage that stops cell division and starts apoptosis (Méndez-Olvera *et al.*, 2016). Due to the toxin's parasitic nature, intestinal crypts are destroyed, which results in diarrhea.

Clinical symptoms

In humans

The clinical manifestations of human *C. jejuni* and *C. coli* enteritis are identical and cannot be distinguished from severe bacterial diarrhea brought on by other infections, such as *Salmonella* enteritis (Kemper and Hensel, 2023). A *Campylobacter* infection may result in fever, nausea, vomiting, and mild to severe bloody diarrhea (Tracz *et al.*, 2005).

Stomach ache may reoccur and linger for up to seven days. In addition to more severe and persistent abdominal discomfort and occasionally blood or mucus in the stool, campylobacteriosis sickness might start with abdominal cramps, myalgia, diarrhea, chills, fever, headache, and occasionally delirium (Huayanay *et al.*, 2020). Patients experience a lower percentage of extra-intestinal infections and chronic infectious problems. Less than 1% of patients with *C. jejuni* infection have been reported to have bacteremia (Gallo *et al.*, 2016). Meningitis and endocarditis are uncommon signs of infection with *C. jejuni* (Tsoni *et al.*, 2013). Rare cases of *C. jejuni* infections presenting as cystitis, acute cholecystitis, pancreatitis, and septic abortion have been reported (Vaughan-Shaw *et al.*, 2010).

Additionally, a number of autoimmune illnesses, including GBS and RA, have been related to campylobacteriosis (Malik *et al.*, 2022). It is expected that one occurrence of these two serious late-onset campylobacteriosis problems occurs for every 2000 infections (El-Saadony *et al.*, 2023). As postinfectious polyneuropathy, *Campylobacter* infection is acknowledged as the most often identified antecedent event in GBS (40%–60% of all cases) (Poropatich *et al.*, 2010). Acute inflammatory demyelinating polyradiculoneuropathy is the major lesion, resulting in flaccid paralysis. About 1% of people with *Campylobacter* enteritis develop RA (Ajene *et al.*, 2013).

In food and farm animals

Warm-blooded mammals and companion birds have *Campylobacter* spp. in their intestines as a component of their gut microbiota (Kreling *et al.*, 2020). Many animal species are susceptible to enteritis, abortion, and infertility due to *Campylobacter* species (Dai *et al.*, 2020). The role of *C. jejuni* as a major pathogen in livestock remains unclear. Enteritis is a common condition in dogs, cats, lambs, mink, calves, and certain types of laboratory animals caused by *C. jejuni* and occasionally *C. coli* (Facciola *et al.*, 2017). In young animals, the clinical indications could be more severe. Calves typically have thick, slimy diarrhea, sometimes with blood stains, and may or may not have a fever (Hansson *et al.*, 2021). The enzootic abortion caused by *C. fetus* and *C. jejuni* can result in late-term abortion, stillbirth, and poor lambs (Wolf-Jäckel *et al.*, 2020). In sheep, endometritis and occasionally even death can occur after infection (Sanad *et al.*, 2014). In the event of an outbreak in sheep, morbidity could reach 90%, although it typically falls between 5% and 50%. Sheep morbidity can lead to delayed lambing and decreased milk yield (van den Brom *et al.*, 2020). It is typical to recover with immunity against reinfection. Sheep may carry an infection for an extended period of time and continue to excrete bacteria (Ogden *et al.*, 2009).

Diagnosis

Effective and rapid diagnosis of *Campylobacter* species infections in animal hosts is essential for both individual treatment and disease management at the farm level. Furthermore, prompt detection aids in the appropriate surveillance and monitoring of *Campylobacter* infections, which may be dangerous for human health due to zoonotic transmission.

Isolation and identification

A common procedure in *Campylobacter* species identification, which employs a range of commercially available media, is to enrich the sample in a suitable broth, like Bolton broth, and then isolate it by plating it on a particular medium, like modified cefoperazone deoxycholate charcoal medium (Bojanić *et al.*, 2019). In research laboratories, a range of biochemical assays is typically conducted after bacterial separation, such as urease expression, oxidase and catalase production, nitrate and nitrite reduction, H₂S synthesis, and

hydrolysis of indoxyl acetate and hippurate (Sadek *et al.*, 2023).

Immunological tests

Campylobacter diagnosis can be achieved by a variety of enzyme immunoassay techniques, including flow cytometry, quantitative immunofluorescence, and enzyme-linked immunosorbent assays (ELISA). However, ELISA is the most effective method since it targets many particular antigens on the microorganism's surface (Ricke *et al.*, 2019). It is possible to generate monoclonal and polyclonal antibodies to recognize particular pathogen epitopes. Moreover, antibodies can be altered, which frequently calls for the conjugation of several detection systems, like horseradish peroxidase, to boost the specificity and sensitivity of identifying various target epitopes (Hochel *et al.*, 2007). It is significant to remember that immune-based detection methods can produce false-positive results even while they are somewhat sensitive to *Campylobacter* species. This has been noted when comparing conventional molecular and microbiological techniques with commercial equipment.

Molecular diagnosis

DNA or RNA sequences that are unique and extremely particular are found using technologies based on nucleic acids (Effendi *et al.*, 2018; Wibisono *et al.*, 2021). After that, these sequences can be separated, amplified, and shown on gel for molecular typing, identification, and quantitative analysis. DNA sequencing and polymerase chain reaction (PCR) provide quick, easy, and accurate identification of *Campylobacter* species while exposing their epidemiological traits (Yanestria *et al.*, 2023). This approach also makes it possible for researchers to produce data that can be shared via web-based databases and utilized in phylogenetic analyses. This technology is known by two names, quantitative PCR (qPCR) and real-time PCR (Sails *et al.*, 2003).

Differential diagnosis

The clinical manifestations of avian campylobacteriosis resemble those of other enteric infections, including rota virus, *Salmonella*, *Shigella*, *E. coli* 0157:H7, *Yersinia*, *Clostridium difficile*, and *Entamoeba histolytica* (Sadek *et al.*, 2023).

Poultry

One of the primary ways that humans contract campylobacteriosis is through poultry, particularly from broiler chickens (Yanestria *et al.*, 2024a). Furthermore, the chicken industry serves as a significant reservoir for additional *Campylobacter* species, including *C. jejuni*, *C. lari*, and *C. upsaliensis* (Skarp *et al.*, 2016). Worldwide, the prevalence of campylobacteriosis and other *Campylobacter* infections is increased by both indigenous and imported broiler chickens (Carron *et al.*, 2018). Additionally, *Campylobacter* can enter broiler chicken houses through vectors like flies, insects, or rodents, or it can travel through vehicles in the form of dust or aerosols. It can also be disseminated through excrement and be found everywhere in the

environment, including surface water (Bahrndorff *et al.*, 2013).

Domestic animals

In addition to a broad range of food products derived from animal groups, such as poultry, household animals (particularly cats and dogs) are the most common source of infection (Acke, 2018) and livestock are significant transmission vectors. *Campylobacter* bacteria can also be found in ruminant animals including cows, sheep, and goats (Hoque *et al.*, 2021; Sanad *et al.*, 2014; Cortés *et al.*, 2006). Rather than in the rumen, *Campylobacter* bacteria are primarily located in the gut (duodenum, jejunum, and small and large intestine) (Chlebicz and Ślizewska, 2018). Therefore, there is a substantial danger of *Campylobacter* species transmission and spread when consuming meat from domestic animals or coming into touch with pets and companion animals.

Wildlife

Campylobacter species (particularly, *C. jejuni* and *C. coli*) are mostly commensals in birds, and they frequently invade the intestines in huge numbers (Hald *et al.*, 2016). Wild animals can function as reservoirs in addition to acting as transmission vectors, such as wild birds (Olvera-Ramírez *et al.*, 2023). It has been possible to isolate *C. jejuni* from wild birds, including pigeons, seagulls, geese, crows, ducks, and herons (Marotta *et al.*, 2020). It is interesting to note that migrating birds have the ability to travel great distances and may provide novel genotypes of the *Campylobacter* species to various animals, including sheep, cattle, and broilers (Shad and Shad, 2019). Furthermore, wild birds congregate in metropolitan parks and recreation areas, particularly pigeons and crows. As a result, individuals with poor or neglected hygiene practices as well as children are more vulnerable to acquiring *Campylobacter* infections.

Water

According to a number of earlier studies, drinking water poses the greatest risk to the spread of campylobacteriosis (Ferrari *et al.*, 2019; Whiley *et al.*, 2013). The ability of *Campylobacter* to form a biofilm in the water pipes of broiler chicken houses contributes to the species' increased growth and survival and is a key risk factor for colonization in chicken flocks (Pokhrel *et al.*, 2022). Recent research conducted in Ireland found that on seven out of twenty farms, there were serious issues with getting rid of *Campylobacter* species colonies in water pipes following disinfection (Battersby *et al.*, 2017). More people than any other documented enteric disease are at risk of contracting campylobacteriosis when they drink water from private wells as opposed to municipal surface water systems (Galanis *et al.*, 2014). Another factor in the spread of *Campylobacter* is contaminated pet waste and wild bird droppings that pollute outdoor water sources (Pitkänen, 2013).

Other sources

Person-to-person transmission, whether by fomites or faecal-oral routes, is uncommon but has great potential and a propensity to spread. There is a documented 3% person-to-person transmission of campylobacteriosis in the United Kingdom (Wensley et al., 2020). The ingestion of raw milk derived from dairy cows has also been linked to numerous cases of campylobacteriosis outbreaks (An et al., 2018). Several other *Campylobacter* species, such as *C. hyointestinalis*, *C. fetus*, and *C. ureolyticus*, can also be found in unpasteurized milk (Koziel et al., 2012; Koziel et al., 2014; Grouteau et al., 2023). A genomic study of the milk revealed a considerable level of fecal contamination. *Campylobacter* infections can also be dangerously transmitted by insects such as flies, roaming animals, and chicken products (Royden et al., 2016; Frosth et al., 2020).

Treatment

The best antibiotic medications for eradicating and decreasing *Campylobacter* in feces are erythromycin, clarithromycin, or azithromycin (Wieczorek and Osek, 2013). If therapy was initiated prior to the third day after the onset of symptoms, there was a noticeable improvement. Research on children with *C. jejuni*-caused diarrhea revealed that early erythromycin treatment led to a significant improvement in symptoms (Munoz et al., 2022). Clinical experience and controlled research demonstrate that patients with high fever, bloody stools, diarrhea, and more than eight evacuations per day respond better to antibiotic treatment (Eiland and Jenkins, 2008).

Despite the lack of animal clinical efficacy trials, it has been reported that dogs and cats can recover from this illness when given erythromycin, the recommended medication for humans, three times a day for seven days at a dose of 11.1 to 15.5 mg/kg (Gibreel and Taylor, 2006). There is currently discussion about *Campylobacter* resistance to widely used antimicrobials in both veterinary and human situations.

In the past 20 years, there has been a noticeable rise in the amount of antibiotic resistance in bacteria isolated from humans, particularly to fluoroquinolones (Luangtongkum et al., 2009). This high level of resistance is still present today in many parts of the world. The first-choice medications for treating adult campylobacteriosis are those in the fluoroquinolone class (Portes et al., 2023). Global reports relate the approval of the use of these antimicrobials in poultry production to *Campylobacter* sp. infections that are resistant to fluoroquinolones (Zhao et al., 2010).

Rastall (2004) looked into alternate sources to antibiotics for the treatment of campylobacteriosis and discovered that probiotics (*Lactobacillus acidophilus*) combined with prebiotics (fructooligosaccharides and lactosucrose) had a positive impact on the balance of intestinal microflora, improved immune status, and aided in the recovery from campylobacteriosis

infection. Following the usage of probiotics, pathogens are competitively excluded, resulting in this microflora balance.

Antibiotic resistance

In the US, 1% of *C. jejuni* strain isolates from infections in humans in 2010 had erythromycin resistance, compared to 43% for tetracycline and 22% for ciprofloxacin (Rodrigues et al., 2021). Almost the same data were reported in the same year about *C. jejuni* strain isolates from chicken flesh. In 2010, strains of *C. jejuni* recovered from chicken flesh in the European Union showed resistance to erythromycin in 2% of cases, tetracyclines in 21%, and fluoroquinolones in 52% of cases (Marotta et al., 2023). Antibiotic resistance in *C. coli* is higher than in *C. jejuni* in the US and Europe. The frequent use of veterinary antibiotics (enrofloxacin and danofloxacin) in the pharmacological treatment of chickens appears to be the root cause of the high level of resistance to fluoroquinolones (Cox and Popken, 2006). Consequently, the use of fluoroquinolones in chickens was outlawed in the US in 2005 (Price et al., 2007). Resistance to these antibiotics is uncommon in Australia, where the use of fluoroquinolones has not been allowed (Cheng et al., 2012). It is well recognized that travel, in both industrialized and developing nations, is often linked to fluoroquinolone-resistant illnesses. According to a recent study by Ghunaim et al. (2015), *C. jejuni*'s erythromycin resistance was comparatively low, accounting for just 8.6% of isolates, while ciprofloxacin resistance accounted for 63.2% of isolates. There have also been reports of high ciprofloxacin resistance in the United Arab Emirates, where 85.4% of isolates exhibited resistance (Sonnevend et al., 2006). Published ciprofloxacin resistance rates were 2% in Australia (Bell et al., 2022) and 40% lower in Poland (Jeżak and Kozajda, 2022). Azithromycin, a macrolide, is typically the next line of treatment when resistance to these medications is established, yet resistance to this class of antibiotics has also been documented (Dai et al., 2020). The use of antibiotics indiscriminately at different points in the chicken production chain can contribute to the establishment of resistant forms of campylobacteriosis since the disease is spread through food consumption (Epps et al., 2013). Therapeutic options are limited due to the emergence of strains that are resistant to various medicines, including the antibiotics of choice for humans.

Control

The best strategy to reduce the number of human infections caused by *Campylobacter* is to restrict the amount of contamination of the poultry flock and its products, even if the majority of infections are contracted through the handling or consumption of chicken (Newell et al., 2011). A common way to stop *Campylobacter* infection outbreaks is to steer clear of unpasteurized milk (Facciola et al., 2017; Tyasningsih et al., 2022). It is important to stress that those who

are pregnant, have young children, are elderly, have weakened immune systems, are visiting low- or middle-income countries, or are campers should not drink unclean water (Asuming-Bediako *et al.*, 2019).

Farm

Both domestic and wild animals, as well as the environment, frequently contract campylobacteriosis. As a result, it is critical to lessen the amount of contamination from these sources in chicken coops. It has been shown that using hygiene barriers at poultry house's entrances, limiting the access of livestock workers, offering hand washing stations, putting in place boot dips, and using specific house boots and overshoes, are all beneficial practices (Wagenaar *et al.*, 2006). One efficient way to stop the spread of contamination in slaughterhouses is to segregate *Campylobacter*-positive animals from negative animals and to kill *Campylobacter*-positive animals (Taha-Abdelaziz *et al.*, 2023). It has been demonstrated that more frequent emptying and cleaning of water troughs lowers the chance of *Campylobacter* colonization in animals (Ellis-Iversen *et al.*, 2009).

Food animals processing

Large concentrations of *Campylobacter* are found in the digestive tracts of chickens, and these bacteria have the ability to contaminate food products, the environment, and slaughterhouses (Kreling *et al.*, 2020). At this stage, the amount of *Campylobacter* organisms is decreased by treatment with organic acids, UV radiation, and chemical dipping tanks for corpses (Szott *et al.*, 2022). Reducing the amount of bacteria in the kitchen through heating, freezing, or radiation eliminates pathogens and lowers the degree of cross-contamination (Taha-Abdelaziz *et al.*, 2023).

Home

The prevention of *Campylobacter* species infection depends on proper food preparation and consumption practices. It is possible to guarantee that temperatures high enough to destroy *Campylobacter* species organisms are reached by using a meat thermometer and properly cooking the meat (de Jong *et al.*, 2012). After handling raw poultry or other meats, cutting boards and cutlery should be cleaned in hot, soapy water and used again to prepare other raw meals (Luber *et al.*, 2006). Hand washing and the separation of raw and ready-to-eat food must be put into practice. Individuals experiencing acute diarrheal illness ought to refrain from handling and preparing food until the condition has resolved (Hatchette and Farina, 2011). Eating raw meat, unpasteurized dairy products and exposure to animals such as pets suffering from diarrhea should be avoided (Facciola *et al.*, 2017). Prior to eating, everyone should wash their hands, especially if they are handling pets or other animals (Taha-Abdelaziz *et al.*, 2023).

Vaccination

The most effective control strategy is generally thought to be vaccination against *Campylobacter*. Numerous

field and experimental investigations on sheep and experimental research on guinea pigs have shown the efficacy of vaccination (Burrough *et al.*, 2010). However, there is limited cross-protection between strains or species, numerous strains of a species may be involved in the disease, and abortion can be induced by two or more separate species (*C. fetus*, *C. jejuni*, and *C. coli*) (Costa and Iraola, 2019). These factors make immunization complex. Therefore, even after using polyvalent vaccinations, vaccination may not offer full protection.

Conclusion

The primary cause of the infectious disease, campylobacteriosis, is the *Campylobacter* species. *Campylobacter* is an emerging global foodborne bacterial pathogen attributed to the cause of foodborne diseases and death, resulting in enormous social and economic losses. *Campylobacteriosis* is particularly prevalent in the paediatric and elderly population. This illness is zoonotic, which means that eating certain foods can spread it from animals to people.

Campylobacter has been isolated from farm animals and foods of animal origin. Worldwide, poultry and their by-products remain the major cause of foodborne illnesses, especially campylobacteriosis. The prevention of *Campylobacter* species infection depends on proper food preparation and consumption practices. The consumption of undercooked poultry products and the contamination of carcasses and other food products continue to be an important public health concern. More challenging is the increasing incidence, emergence, and spread of antibiotic-resistant *Campylobacter* species which has further complicated and limited treatment options. In order to curtail and avert this challenging public health problem, it is imperative to establish strong measures that are directed towards its eradication, especially good hygienic practices during food handling. Efforts to curtail *Campylobacter* contamination in the food industry also need to become a more determined priority. To comprehensively understand the disease burden of campylobacteriosis, more research studies with multiple intervention within the "one health" approach are needed to evaluate the under-reporting of diarrhoea incidents at national and intercontinental levels by enhancing and encouraging local capacities for continuous disease surveillance and monitoring. Also, more research that will devise alternative strategies or new therapeutics against campylobacteriosis will also greatly help in turning the tide against this emerging foodborne and zoonotic disease.

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Authors' contributions

ARK, IBM, and MKJK drafted the manuscript. SRA, MHE, FNAEPD, and SMY revised and edited the manuscript. OSMS, IF, AHF, and KHPR took part in preparing and critically checking this manuscript. AH, KAF, RR, and SA edited the references. All authors read and approved the final manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data availability

All references are open access, so data can be obtained from the online web.

References

- Acke, E. 2018. Campylobacteriosis in dogs and cats: a review. *N. Z. Vet. J.* 66(5), 221–228.
- Agumah, N.B., Effendi, M.H., Witaningrum, A.M., Tyasningsih, W., Ugbo, E.N., Nwagwu, C.S. and Ugbo, I.A. 2024. Antimicrobial resistance in *Campylobacter* species isolated from commercially sold steak (beef) and raw cow milk in Abakaliki, Nigeria. *Biodiversitas* 25(3), 950–956.
- Ajene, A.N., Walker, C.L.F. and Black, R.E. 2013. Enteric pathogens and reactive arthritis: a systematic review of *Campylobacter*, *Salmonella* and *Shigella*-associated reactive arthritis. *J. Health Popul. Nutr.* 31(3), 299–307.
- Ammar, A.M., El-Naenaeey, E.Y., El-Malt, R.M.S., El-Gedawy, A.A., Khalifa, E., Elnahriry, S.S. and Abd El-Hamid, M.I. 2020. Prevalence, antimicrobial susceptibility, virulence and genotyping of *Campylobacter jejuni* with a special reference to the anti-virulence potential of eugenol and beta-resorcylic acid on some multi-drug resistant isolates in Egypt. *Animals (Basel)* 11(1), 3.
- An, J.U., Ho, H., Kim, J., Kim, W.H., Kim, J., Lee, S., Mun, S.H., Guk, J.H., Hong, S. and Cho, S. 2018. Dairy cattle, a potential reservoir of human campylobacteriosis: epidemiological and molecular characterization of *Campylobacter jejuni* from cattle farms. *Front. Microbiol.* 9(1), 3136.
- Ang, C.W., De Klerk, M.A., Endtz, H.P., Jacobs, B.C., Laman, J.D., van der Meché, F.G. and van Doorn, P.A. 2001. Guillain-Barré syndrome- and Miller fisher syndrome-associated *Campylobacter jejuni* lipopolysaccharides induce anti-GM1 and anti-GQ1b Antibodies in rabbits. *Infect. Immun.* 69(4), 2462–2469.
- Ansharieta, R., Effendi, M.H. and Plumeriastuti, H. 2021. Genetic Identification of Shiga Toxin Encoding Gene From Cases of Multidrug Resistance (MDR) *Escherichia coli* Isolated From Raw Milk. *Trop. Anim. Sci. J.* 44(1), 10–15.
- Artursson, K., Schelin, J., Lambertz, S.T., Hansson, I. and Engvall, E.O. 2018. Foodborne pathogens in unpasteurized milk in Sweden. *Int. J. Food Microbiol.* 284(1), 120–127.
- Asuming-Bediako, N., Kunadu, A.P.-H., Abraham, S. and Habib, I. 2019. *Campylobacter* at the human-food interface: the African perspective. *Pathogens* 8(2), 87.
- Bahrndorff, S., Rangstrup-Christensen, L., Nordentoft, S. and Hald, B. 2013. Foodborne disease prevention and broiler chickens with reduced *Campylobacter* infection. *Emerg. Infect. Dis.* 19(3), 425–430.
- Baldvinsson, S.B., Sørensen, M.C., Vegge, C.S., Cløkie, M.R. and Brøndsted, L. 2014. *Campylobacter jejuni* motility is required for infection of the flagellotropic bacteriophage F341. *Appl. Environ. Microbiol.* 80(22), 7096–7106.
- Battersby, T., Walsh, D., Whyte, P. and Bolton, D. 2017. Evaluating and improving terminal hygiene practices on broiler farms to prevent *Campylobacter* cross-contamination between flocks. *Food Microbiol.* 64(1), 1–6.
- Behailu, Y., Hussen, S., Alemayehu, T., Mengistu, M. and Fenta, D.A. 2022. Prevalence, determinants, and antimicrobial susceptibility patterns of *Campylobacter* infection among under-five children with diarrhea at Governmental Hospitals in Hawassa city, Sidama, Ethiopia. A cross-sectional study. *PLoS One* 17(5), e0266976.
- Bell, J.M., Lubian, A.F., Partridge, S.R., Gottlieb, T., Robson, J., Iredell, J.R., Daley, D.A. and Coombs, G.W. 2022. Australian group on antimicrobial resistance (AGAR) Australian gram-negative surveillance outcome program (GnSOP) bloodstream infection annual report 2022. *Commun. Dis. Intell.* 47(1):69.
- Benoit, S.R., Lopez, B., Arvelo, W., Henao, O., Parsons, M.B., Reyes, L., Moir, J.C. and Lindblade, K. 2014. Burden of laboratory-confirmed *Campylobacter* infections in Guatemala 2008–2012: results from a facility-based surveillance system. *J. Epidemiol. Glob. Health* 4(1), 51–59.
- Bianchini, V., Borella, L., Benedetti, V., Parisi, A., Miccolupo, A., Santoro, E., Recordati, C. and Luini, M. 2014. Prevalence in bulk tank milk and epidemiology of *Campylobacter jejuni* in dairy herds in Northern Italy. *Appl. Environ. Microbiol.* 80(6), 1832–1837.
- Bojanić, K., Midwinter, A.C., Marshall, J.C., Biggs, P.J. and Acke, E. 2019. Isolation of emerging *Campylobacter* species in working farm dogs and their frozen home-killed raw meat diets. *J. Vet. Diagn. Invest.* 31(1), 23–32.
- Bonnet, M., Lagier, J.C., Raoult, D. and Khelaifia, S. 2019. Bacterial culture through selective and non-selective conditions: the evolution of culture media

- in clinical microbiology. *New Microbes New Infect.* 34(1), 100622.
- Boysen, L., Rosenquist, H., Larsson, J.T., Nielsen, E.M., Sørensen, G., Nordentoft, S. and Hald, T. 2014. Source attribution of human campylobacteriosis in Denmark. *Epidemiol. Infect.* 142(8), 1599–1608.
- Burrough, E.R., Sahin, O., Plummer, P.J., DiVerde, K.D., Zhang, Q. and Yaeger, M.J. 2010. Comparison of two commercial ovine *Campylobacter* vaccines and an experimental bacterin in guinea pigs inoculated with *Campylobacter jejuni*. *Am. J. Vet. Res.* 72(6), 799–805.
- Butzler, J.P. 2004. *Campylobacter*, from obscurity to celebrity. *Clin. Microbiol. Infect.* 10(10), 868–876.
- Callahan, S.M., Dolislager, C.G. and Johnson, J.G. 2021. The host cellular immune response to infection by *Campylobacter* spp. and its role in disease. *Infect. Immun.* 89(8), e0011621.
- Carron, M., Chang, Y.M., Momanyi, K., Akoko, J., Kiiru, J., Bettridge, J., Chaloner, G., Rushton, J., O'Brien, S., Williams, N., Fèvre, E.M. and Häsler, B. 2018. *Campylobacter*, a zoonotic pathogen of global importance: Prevalence and risk factors in the fast-evolving chicken meat system of Nairobi, Kenya. *PLoS Negl. Trop. Dis.* 12(8), e0006658.
- Chala, G., Eguale, T., Abunna, F., Asrat, D. and Stringer, A. 2021. Identification and characterization of *Campylobacter* species in livestock, humans, and water in livestock owning households of Peri-urban Addis Ababa, Ethiopia: a one health approach. *Front. Public Health* 9(1), 750551.
- Chandrashekhar, K., Kassem, I.I. and Rajashekara, G. 2017. *Campylobacter jejuni* transducer like proteins: chemotaxis and beyond. *Gut Microbes* 8(4), 323–334.
- Cheng, A.C., Turnidge, J., Collignon, P., Looke, D., Barton, M. and Gottlieb, T. 2012. Control of fluoroquinolone resistance through successful regulation, Australia. *Emerg. Infect. Dis.* 18(9), 1453–1460.
- Chlebicz, A. and Ślizewska, K. 2018. *Campylobacteriosis*, *salmonellosis*, *yersiniosis*, and *listeriosis* as zoonotic foodborne diseases: a review. *Int. J. Environ. Res. Public Health* 15(5), 863.
- Clark, C., Berry, C. and Demczuk, W. 2019. Diversity of transducer-like proteins (Tlps) in *Campylobacter*. *PLoS One* 14(3), e0214228.
- Coker, A.O., Isokpehi, R.D., Thomas, B.N., Amisu, K.O. and Obi, C.L. 2002. Human campylobacteriosis in developing countries. *Emerg. Infect. Dis.* 8(3), 237–244.
- Cortés, C., de la Fuente, R., Contreras, A., Sánchez, A., Corrales, J.C., Martínez, S. and Orden, J.A. 2006. A survey of *Salmonella* spp and *Campylobacter* spp in dairy goat faeces and bulk tank milk in the Murcia region of Spain. *Ir. Vet. J.* 59(7), 391–393.
- Costa, D. and Iraola, G. 2019. Pathogenomics of Emerging *Campylobacter* Species. *Clin. Microbiol. Rev.* 32(4), e00072–18.
- Cox, L.A. Jr. and Popken, D.A. 2006. Quantifying potential human health impacts of animal antibiotic use: enrofloxacin and macrolides in chickens. *Risk Anal.* 26(1), 135–146.
- Dai, L., Sahin, O., Grover, M. and Zhang, Q. 2020. New and alternative strategies for the prevention, control, and treatment of antibiotic-resistant *Campylobacter*. *Transl. Res.* 223(1), 76–88.
- de Jong, A.E., van Asselt, E.D., Zwietering, M.H., Nauta, M.J. and de Jonge, R. 2012. Extreme heat resistance of food borne pathogens *Campylobacter jejuni*, *Escherichia coli*, and *Salmonella typhimurium* on chicken breast fillet during cooking. *Int. J. Microbiol.* 2012(1), 196841.
- Deng, W., Dittoe, D.K., Pavilidis, H.O., Chaney, W.E., Yang, Y. and Ricke, S.C. 2020. Current Perspectives and Potential of Probiotics to Limit Foodborne *Campylobacter* in Poultry. *Front. Microbiol.* 11(1), 583429.
- Effendi, M.H., Harijani, N., Yanestria, S.M. and Hastutiek, P. 2018. Identification of shiga toxin-producing *Escherichia coli* in raw milk samples from dairy cows in Surabaya, Indonesia. *Philipp. J. Vet. Med.* 55(SI), 109–114.
- Eiland, L.S. and Jenkins, L.S. 2008. Optimal treatment of campylobacter dysentery. *J. Pediatr. Pharmacol. Ther.* 13(3), 170–174.
- El-Saadony, M.T., Saad, A.M., Yang, T., Salem, H.M., Korma, S.A., Ahmed, A.E., Mosa, W.F.A., Abd El-Mageed, T.A., Selim, S., Al Jaouni, S.K., Zaghloul, R.A., Abd El-Hack, M.E., El-Tarabily, K.A. and Ibrahim, S.A. 2023. Avian campylobacteriosis, prevalence, sources, hazards, antibiotic resistance, poultry meat contamination, and control measures: a comprehensive review. *Poult. Sci.* 102(9), 102786.
- El-Tras, W.F., Holt, H.R., Tayel, A.A. and El-Kady, N.N. 2015. *Campylobacter* infections in children exposed to infected backyard poultry in Egypt. *Epidemiol. Infect.* 143(2), 308–315.
- Ellis-Iversen, J., Pritchard, G.C., Wooldridge, M. and Nielsen, M. 2009. Risk factors for *Campylobacter jejuni* and *Campylobacter coli* in young cattle on English and Welsh farms. *Prev. Vet. Med.* 88(1), 42–48.
- Elmi, A., Nasher, F., Dorrell, N., Wren, B. and Gundogdu, O. 2021. Revisiting *Campylobacter jejuni* virulence and fitness factors: role in sensing, adapting, and competing. *Front. Cell. Infect. Microbiol.* 10(1), 607704.
- Epps, S.V., Harvey, R.B., Hume, M.E., Phillips, T.D., Anderson, R.C. and Nisbet, D.J. 2013. Foodborne *Campylobacter*: infections, metabolism, pathogenesis and reservoirs. *Int. J. Environ. Res. Public. Health* 10(12), 6292–6304.

- Facciola, A., Riso, R., Avventuroso, E., Visalli, G., Delia, S.A. and Laganà, P. 2017. Campylobacter: from microbiology to prevention. J. Prev. Med. Hyg. 58(2), E79–E92.
- Ferrari, S., Frosth, S., Svensson, L., Fernström, L.L., Skarin, H. and Hansson, I. 2019. Detection of *Campylobacter* spp. in water by dead-end ultrafiltration and application at farm level. J. Appl. Microbiol. 127(4), 1270–1279.
- Finsterer, J. 2022. Triggers of Guillain-Barré syndrome: *Campylobacter jejuni* predominates. Int. J. Mol. Sci. 23(22), 14222.
- Firdich, E., Biboy, J., Pryjma, M., Lee, J., Huynh, S., Parker, C.T., Girardin, S.E., Vollmer, W. and Gaynor, E.C. 2019. The *Campylobacter jejuni* helical to coccoid transition involves changes to peptidoglycan and the ability to elicit an immune response. Mol. Microbiol. 112(1), 280–301.
- Frosth, S., Karlsson-Lindsjö, O., Niazi, A., Fernström, L.L. and Hansson, I. 2020. Identification of transmission routes of campylobacter and on-farm measures to reduce campylobacter in chicken. Pathogens 9(5), 363.
- Galanis, E., Mak, S., Otterstatter, M., Taylor, M., Zubel, M., Takaro, T.K., Kuo, M. and Michel, P. 2014. The association between campylobacteriosis, agriculture and drinking water: a case-case study in a region of British Columbia, Canada, 2005–2009. Epidemiol. Infect. 142(10), 2075–2084.
- Gallo, M.T., Di Domenico, E.G., Toma, L., Marchesi, F., Pelagalli, L., Manghisi, N., Ascenzioni, F., Prignano, G., Mengarelli, A. and Ensoli, F. 2016. *Campylobacter jejuni* fatal sepsis in a patient with Non-Hodgkin's lymphoma: case report and literature review of a difficult diagnosis. Int. J. Mol. Sci. 17(4), 544.
- Gellynck, X., Messens, W., Halet, D., Grijspeerdt, K., Hartnett, E. and Viaene, J. 2008. Economics of reducing Campylobacter at different levels within the Belgian poultry meat chain. J. Food Prot. 71(3), 479–485.
- Ghunaim, H., Behnke, J.M., Aigha, I., Sharma, A., Doiphode, S.H., Deshmukh, A. and Abu-Madi, M.M. 2015. Analysis of resistance to antimicrobials and presence of virulence/stress response genes in Campylobacter isolates from patients with severe diarrhoea. PLoS One 10(3), e0119268.
- Gibreel, A. and Taylor, D.E. 2006. Macrolide resistance in *Campylobacter jejuni* and *Campylobacter coli*. J. Antimicrob. Chemother. 58(2), 243–255.
- Gilpin, B.J., Walker, T., Paine, S., Sherwood, J., Mackereth, G., Wood, T., Hambling, T., Hewison, C., Brounts, A., Wilson, M., Scholes, P., Robson, B., Lin, S., Cornelius, A., Rivas, L., Hayman, D.T.S., French, N.P., Zhang, J., Wilkinson, D.A., Midwinter, A.C., Biggs, P.J., Jagroop, A., Eyre, R., Baker, M.G. and Jones, N. 2020. A large scale waterborne Campylobacteriosis outbreak, Havelock North, New Zealand. J. Infect. 81(3), 390–395.
- Goddard, M.R., O'Brien, S., Williams, N., Guitian, J., Grant, A., Cody, A., Colles, F., Buffet, J.C., Adlen, E., Stephens, A., Godfray, H.C.J. and Maiden, M.C.J. 2022. A restatement of the natural science evidence base regarding the source, spread and control of Campylobacter species causing human disease. Proc. R. Soc. B. 289(1), 20220400.
- Grouteau, G., Mignonat, C., Marchou, B., Martin-Blondel, G., Glass, O., Roubaud-Baudron, C., Lansalot-Matras, P., Alik, S., Balardy, L., De Nadaï, T., Bénéjat, L., Jehanne, Q., Le Coustumier, A. and Lehours, P. 2023. *Campylobacter fetus* foodborne illness outbreak in the elderly. Front. Microbiol. 14(1), 1194243.
- Guirado, P., Paytubi, S., Miró, E., Iglesias-Torrens, Y., Navarro, F., Cerdà-Cuellar, M., Attolini, C.S., Balsalobre, C. and Madrid, C. 2020. Differential distribution of the *wlaN* and *cgtB* genes, associated with Guillain-Barré syndrome, in *Campylobacter jejuni* Isolates from humans, broiler chickens, and wild birds. Microorganisms 8(3), 325.
- Guo, Y.T., Hsiung, C.A., Wu, F.T., Chi, H., Huang, Y.C., Liu, C.C., Huang, Y.C., Lin, H.C., Shih, S.M., Huang, C.Y., Chang, L.Y., Ho, Y.H., Lu, C.Y., Huang, L.M. and Taiwan Pediatric Infectious Disease Alliance. 2023. Clinical manifestations and risk factors of campylobacter gastroenteritis in children in Taiwan. Biomed. J. 46(6), 100590.
- Guy, R.A., Arsenault, J., Kotchi, S.O., Gosselin-Théberge, M., Champagne, M.J. and Berthiaume, P. 2018. Campylobacter in recreational lake water in southern Quebec, Canada: presence, concentration, and association with precipitation and ruminant farm proximity. J. Water Health 16(4), 516–529.
- Hakeem, M.J. and Lu, X. 2021. Survival and control of campylobacter in poultry production environment. Front. Cell Infect. Microbiol. 10(1), 615049.
- Hald, B., Skov, M.N., Nielsen, E.M., Rahbek, C., Madsen, J.J., Wainø, M., Chriél, M., Nordentoft, S., Baggesen, D.L. and Madsen, M. 2016. *Campylobacter jejuni* and *Campylobacter coli* in wild birds on Danish livestock farms. Acta Vet. Scand. 58(1), 11.
- Hansson, I., Tamminen, L.M., Frosth, S., Fernström, L.L., Emanuelson, U. and Boqvist, S. 2021. Occurrence of *Campylobacter* spp. in Swedish calves, common sequence types and antibiotic resistance patterns. J. Appl. Microbiol. 130(6), 2111–2122.
- Harvey, S.A., Winch, P.J., Leontsini, E., Gayoso, C.T., Romero, S.L., Gilman, R.H. and Oberhelman, R.A. 2003. Domestic poultry-raising practices in a Peruvian shantytown: implications for control of *Campylobacter jejuni*-associated diarrhea. Acta Trop. 86(1), 41–54.

- Hatchette, T.F. and Farina, D. 2011. Infectious diarrhea: when to test and when to treat. *CMAJ* 183(3), 339–344.
- Hermans, D., Van Deun, K., Martel, A., Van Immerseel, F., Messens, W., Heyndrickx, M., Haesebrouck, F. and Pasmans, F. 2011. Colonization factors of *Campylobacter jejuni* in the chicken gut. *Vet. Res.* 42(1), 82.
- Heuvelink, A.E., van Heerwaarden, C., Zwartkruis-Nahuis, A., Tilburg, J.J., Bos, M.H., Heilmann, F.G., Hofhuis, A., Hoekstra, T. and de Boer, E. 2009. Two outbreaks of campylobacteriosis associated with the consumption of raw cows' milk. *Int. J. Food Microbiol.* 134(1–2), 70–74.
- Hochel, I., Slavičková, D., Viochna, D., Škvor, J. and Steinhäuserová, I. 2007. Detection of *Campylobacter* species in foods by indirect competitive ELISA using hen and rabbit antibodies. *Food Agric. Immun.* 18(3–4), 151–167.
- Hodges, L.M., Carrillo, C.D., Upham, J.P., Borza, A., Eisebraun, M., Kenwell, R., Mutschall, S.K., Haldane, D., Schleihau, E. and Taboada, E.N. 2019. A strain comparison of *Campylobacter* isolated from retail poultry and human clinical cases in Atlantic Canada. *PLoS One* 14(5), e0215928.
- Hoque, N., Islam, S.K.S., Uddin, M.N., Arif, M., Haque, A.K.M.Z., Neogi, S.B., Hossain, M.M., Yamasaki, S. and Kabir, S.M.L. 2021. Prevalence, risk factors, and molecular detection of campylobacter in farmed cattle of selected districts in Bangladesh. *Pathogens* 10(3), 313.
- Hsu, M.D., Ta, A.P.D., Iwamoto, S., Leo, A. and Chu, G. 2023. Ceftriaxone resistance in campylobacter gastroenteritis. *Cureus* 15(12), e50632.
- Huayanay, I., Pozo, L., Bangash, S., Ramirez, D., Rosas, L. and Brown, R.A. 2020. An unusual case of *Campylobacter jejuni* gastroenteritis presenting with acute reversible encephalopathy in an immunocompetent host. *Case Rep. Infect. Dis.* 2020(1), 9603428.
- Hue, O., Le Bouquin, S., Laisney, M.J., Allain, V., Lalande, F., Petetin, I., Rouxel, S., Quesne, S., Gloaguen, P.Y., Picherot, M., Santolini, J., Salvat, G., Bougeard, S. and Chemaly, M. 2010. Prevalence of and risk factors for *Campylobacter* spp. contamination of broiler chicken carcasses at the slaughterhouse. *Food Microbiol.* 27(8), 992–999.
- Hyllestad, S., Iversen, A., MacDonald, E., Amato, E., Borge, B.Å.S., Bøe, A., Sandvin, A., Brandal, L.T., Lyngstad, T.M., Naseer, U., Nygård, K., Veneti, L. and Vold, L. 2020. Large waterborne campylobacter outbreak: use of multiple approaches to investigate contamination of the drinking water supply system, Norway, June 2019. *Euro Surveill.* 25(35), 2000011.
- Igwaran, A. and Okoh, A.I. 2019. Human campylobacteriosis: a public health concern of global importance. *Heliyon* 5(11), e02814.
- Jaakkonen, A., Kivistö, R., Aarnio, M., Kalekivi, J. and Hakkinen, M. 2020. Persistent contamination of raw milk by *Campylobacter jejuni* ST-883. *PLoS One* 15(4), e0231810.
- Janssen, R., Krogfelt, K.A., Cawthraw, S.A., van Pelt, W., Wagenaar, J.A. and Owen, R.J. 2008. Host-pathogen interactions in *Campylobacter* infections: the host perspective. *Clin. Microbiol. Rev.* 21(3), 505–518.
- Jezak, K. and Kozajda, A. 2022. Occurrence and spread of antibiotic-resistant bacteria on animal farms and in their vicinity in Poland and Ukraine-review. *Environ. Sci. Pollut. Res. Int.* 29(7), 9533–9559.
- Johnson, T.J., Shank, J.M. and Johnson, J.G. 2017. Current and potential treatments for reducing campylobacter colonization in animal hosts and disease in humans. *Front. Microbiol.* 8(1), 487.
- Kaakoush, N.O., Miller, W.G., De Reuse, H. and Mendz, G.L. 2007. Oxygen requirement and tolerance of *Campylobacter jejuni*. *Res. Microbiol.* 158(8–9), 644–650.
- Keerthirathne, T.P., Ross, K., Fallowfield, H. and Whiley, H. 2022. Examination of Australian backyard poultry for *Salmonella*, *Campylobacter* and *Shigella* spp., and related risk factors. *Zoonoses Public Health* 69(1), 13–22.
- Kemper, L. and Hensel, A. 2023. *Campylobacter jejuni*: targeting host cells, adhesion, invasion, and survival. *Appl. Microbiol. Biotechnol.* 107(1), 2725–2754.
- Kiarie, A., Bebor, L., Gitao, G., Ochien'g, L., Okumu, N., Mutisya, C., Wasonga, J., Masudi, S.P., Moodley, A., Amon-Tanoh, M.A., Watson, J., Cumming, O. and Cook, E.A.J. 2023. Prevalence and risk factors associated with the occurrence of *Campylobacter* sp. in children aged 6–24 months in peri-urban Nairobi, Kenya. *Front. Public Health* 11(1), 1147180.
- Kim, J.C., Oh, E., Kim, J. and Jeon, B. 2015. Regulation of oxidative stress resistance in *Campylobacter jejuni*, a microaerophilic foodborne pathogen. *Front. Microbiol.* 6(1), 751.
- Kim, S.H., Chelliah, R., Ramakrishnan, S.R., Perumal, A.S., Bang, W.S., Rubab, M., Daliri, E.B., Barathikannan, K., Elahi, F., Park, E., Jo, H.Y., Hwang, S.B. and Oh, D.H. 2021. Review on Stress Tolerance in *Campylobacter jejuni*. *Front. Cell. Infect. Microbiol.* 10(1), 596570.
- Konkel, M.E., Talukdar, P.K., Negretti, N.M. and Klappenbach, C.M. 2020. Taking control: *Campylobacter jejuni* binding to fibronectin sets the stage for cellular adherence and invasion. *Front. Microbiol.* 11(1), 564.
- Kovács, J.K., Cox, A., Schweitzer, B., Maróti, G., Kovács, T., Fenyvesi, H., Emödy, L. and Schneider, G. 2020. Virulence traits of inpatient *Campylobacter jejuni* Isolates, and a transcriptomic approach to

- identify potential genes maintaining intracellular survival. *Microorganisms* 8(4), 531.
- Koziel, M., Corcoran, G.D., Sleator, R.D. and Lucey, B. 2014. Detection and molecular analysis of *Campylobacter ureolyticus* in domestic animals. *Gut Pathog.* 6(1), 9.
- Koziel, M., Lucey, B., Bullman, S., Corcoran, G.D. and Sleator, R.D. 2012. Molecular-based detection of the gastrointestinal pathogen *Campylobacter ureolyticus* in unpasteurized milk samples from two cattle farms in Ireland. *Gut Pathog.* 4(1), 14.
- Kreling, V., Falcone, F.H., Kehrenberg, C. and Hensel, A. 2020. *Campylobacter* sp.: pathogenicity factors and prevention methods-new molecular targets for innovative antivirulence drugs? *Appl. Microbiol. Biotechnol.* 104(24), 10409–10436.
- Kuhn, K.G., Nielsen, E.M., Mølbak, K. and Ethelberg, S. 2018. Determinants of sporadic *Campylobacter* infections in Denmark: a nationwide case-control study among children and young adults. *Clin. Epidemiol.* 10(1), 1695–1707.
- Li, Y., Zhou, G., Gao, P., Gu, Y., Wang, H., Zhang, S., Zhang, Y., Wang, Y., Jing, H., He, C., Zhen, G., Ma, H., Li, Y., Zhang, J. and Zhang, M. 2020. Gastroenteritis outbreak caused by *Campylobacter jejuni* - Beijing, China, August, 2019. *China CDC Wkly.* 2(23), 422–425.
- Lin, J., Sahin, O., Michel, L.O. and Zhang, Q. 2003. Critical role of multidrug efflux pump CmeABC in bile resistance and in vivo colonization of *Campylobacter jejuni*. *Infect. Immun.* 71(8), 4250–4259.
- Liu, F., Ma, R., Wang, Y. and Zhang, L. 2018. The clinical importance of *Campylobacter concisus* and other human hosted campylobacter species. *Front. Cell. Infect. Microbiol.* 8(1), 243.
- Llarena, A.K. and Kivistö, R. 2020. Human campylobacteriosis cases traceable to chicken meat-evidence for disseminated outbreaks in Finland. *Pathogens* 9(11), 868.
- Llarena, A.K., Skjerve, E., Bjørkøy, S., Forseth, M., Winge, J., Hauge, S.J., Johannessen, G.S., Spilberg, B. and Nagel-Alne, G.E. 2022. Rapid detection of *Campylobacter* spp. in chickens before slaughter. *Food Microbiol.* 103(1), 103949.
- Lopes, G.V., Ramires, T., Kleinubing, N.R., Scheik, L.K., Fiorentini, Á.M. and Padilha da Silva, W. 2021. Virulence factors of foodborne pathogen *Campylobacter jejuni*. *Microb. Pathog.* 161(Pt A), 105265.
- Louwen, R., van Baarlen, P., van Vliet, A.H., van Belkum, A., Hays, J.P. and Endtz, H.P. 2012. *Campylobacter* bacteremia: a rare and under-reported event? *Eur. J. Microbiol. Immunol. (Bp).* 2(1), 76–87.
- Luangtongkum, T., Jeon, B., Han, J., Plummer, P., Logue, C.M. and Zhang, Q. 2009. Antibiotic resistance in *Campylobacter*: emergence, transmission and persistence. *Future Microbiol.* 4(2), 189–200.
- Luber, P., Brynestad, S., Topsch, D., Scherer, K. and Bartelt, E. 2006. Quantification of campylobacter species cross-contamination during handling of contaminated fresh chicken parts in kitchens. *Appl. Environ. Microbiol.* 72(1), 66–70.
- Malik, A., Brudvig, J.M., Gadsden, B.J., Ethridge, A.D. and Mansfield, L.S. 2022. *Campylobacter jejuni* induces autoimmune peripheral neuropathy via Sialoadhesin and Interleukin-4 axes. *Gut Microbes* 14(1), 2064706.
- Marotta, F., Janowicz, A., Di Marcantonio, L., Ercole, C., Di Donato, G., Garofolo, G. and Di Giannatale, E. 2020. Molecular characterization and antimicrobial susceptibility of *C. jejuni* isolates from Italian wild bird populations. *Pathogens* 9(4), 304.
- Marotta, F., Janowicz, A., Romantini, R., Di Marcantonio, L., Di Timoteo, F., Romualdi, T., Zilli, K., Barco, L., D’Incau, M., Mangone, I., Cito, F., Di Domenico, M., Pomilio, F., Ricci, L. and Garofolo, G. 2023. Genomic and antimicrobial surveillance of campylobacter population in Italian Poultry. *Foods* 12(15), 2919.
- Mason, J., Iturriza-Gomara, M., O’Brien, S.J., Ngwira, B.M., Dove, W., Maiden, M.C. and Cunliffe, N.A. 2013. *Campylobacter* infection in children in Malawi is common and is frequently associated with enteric virus co-infections. *PLoS One* 8(3), e59663.
- Mbai, J., Njoroge, S., Obonyo, M., Otieno, C., Owiny, M. and Fèvre, E.M. 2022. *Campylobacter* positivity and public health risks in live bird markets in Busia, Kenya: a value chain analysis. *Transbound. Emerg. Dis.* 69(5), e1839–e1853.
- Méndez-Olvera, E.T., Bustos-Martínez, J.A., López-Vidal, Y., Verdugo-Rodríguez, A. and Martínez-Gómez, D. 2016. Cytolethal distending toxin from *Campylobacter jejuni* requires the cytoskeleton for toxic activity. *Jundishapur J. Microbiol.* 9(10), e35591.
- Modi, S., Brahmabhatt, M.N., Chatur, Y.A. and Nayak, J.B. 2015. Prevalence of *Campylobacter* species in milk and milk products, their virulence gene profile and anti-bio gram. *Vet. World* 8(1), 1–8.
- Moore, J.E. and Matsuda, M. 2002. The history of *Campylobacter*: taxonomy and nomenclature. *Ir. Vet. J.* 55(10), 495–501.
- Munoz, G.A., Riveros-Ramirez, M.D., Chea-Woo, E. and Ochoa, T.J. 2022. Clinical course of children with campylobacter gastroenteritis with and without co-infection in Lima, Peru. *Am. J. Trop. Med. Hyg.* 106(5), 1384–1388.
- Mushi, M.F., Paterno, L., Tappe, D., Deogratius, A.P., Seni, J., Moremi, N., Mirambo, M.M. and Mshana, S.E. 2014. Evaluation of detection methods for campylobacter infections among under-fives in

- Mwanza City, Tanzania. Pan. Afr. Med. J. 19(1), 392.
- Myintzaw, P., Jaiswal, A.K. and Jaiswal, S. 2023. A review on campylobacteriosis associated with poultry meat consumption. Food Rev. Int. 39(4), 2107–2121.
- Newell, D.G., Elvers, K.T., Dopfer, D., Hansson, I., Jones, P., James, S., Gittins, J., Stern, N.J., Davies, R., Connerton, I., Pearson, D., Salvat, G. and Allen, V.M. 2011. Biosecurity-based interventions and strategies to reduce *Campylobacter* spp. on poultry farms. Appl. Environ. Microbiol. 77(24), 8605–8614.
- Nichols, G.L. 2005. Fly transmission of *Campylobacter*. Emerg. Infect. Dis. 11(3), 361–364.
- O Cróinin, T. and Backert, S. 2012. Host epithelial cell invasion by *Campylobacter jejuni*: trigger or zipper mechanism? Front. Cell. Infect. Microbiol. 2(1), 25.
- O'Loughlin, J.L., Eucker, T.P., Chavez, J.D., Samuelson, D.R., Neal-McKinney, J., Gourley, C.R., Bruce, J.E. and Konkell, M.E. 2015. Analysis of the *Campylobacter jejuni* genome by SMRT DNA sequencing identifies restriction-modification motifs. PLoS One 10(2), e0118533.
- Ogden, I.D., Dallas, J.F., MacRae, M., Rotariu, O., Reay, K.W., Leitch, M., Thomson, A.P., Sheppard, S.K., Maiden, M., Forbes, K.J. and Strachan, N.J. 2009. *Campylobacter* excreted into the environment by animal sources: prevalence, concentration shed, and host association. Foodborne Pathog. Dis. 6(10), 1161–1170.
- Ohno, Y., Sekizuka, T., Kuroda, M. and Ikeda, T. 2023. Outbreaks of campylobacteriosis caused by drinking raw milk in Japan: evidence of relationship between milk and patients by using whole genome sequencing. Foodborne Pathog. Dis. 20(9), 375–380.
- Olvera-Ramírez, A.M., McEwan, N.R., Stanley, K., Nava-Díaz, R. and Aguilar-Tipacamú, G. 2023. A systematic review on the role of wildlife as carriers and spreaders of *Campylobacter* spp. Animals (Basel) 13(8), 1334.
- Pang, J., Looft, T., Zhang, Q. and Sahin, O. 2023. Deciphering the association between campylobacter colonization and microbiota composition in the intestine of commercial broilers. Microorganisms 11(7), 1724.
- Parker, A., Fonseca, S. and Carding, S.R. 2020. Gut microbes and metabolites as modulators of blood-brain barrier integrity and brain health. Gut Microbes 11(2), 135–157.
- Pascoe, B., Schiaffino, F., Murray, S., Méric, G., Bayliss, S.C., Hitchings, M.D., Mourkas, E., Calland, J.K., Burga, R., Yori, P.P., Jolley, K.A., Cooper, K.K., Parker, C.T., Olortegui, M.P., Kosek, M.N. and Sheppard, S.K. 2020. Genomic epidemiology of *Campylobacter jejuni* associated with asymptomatic pediatric infection in the Peruvian Amazon. PLoS Negl. Trop. Dis. 14(8), e0008533.
- Patrick, M.E., Christiansen, L.E., Wainø, M., Ethelberg, S., Madsen, H. and Wegener, H.C. 2004. Effects of climate on incidence of *Campylobacter* spp. in humans and prevalence in broiler flocks in Denmark. Appl. Environ. Microbiol. 70(12), 7474–7480.
- Penakalapati, G., Swarthout, J., Delahoy, M.J., McAliley, L., Wodnik, B., Levy, K. and Freeman, M.C. 2017. Exposure to animal feces and human health: a systematic review and proposed research priorities. Environ. Sci. Technol. 51(20), 11537–11552.
- Pitkänen, T. 2013. Review of *Campylobacter* spp. in drinking and environmental waters. J. Microbiol. Methods 95(1), 39–47.
- Platts-Mills, J.A. and Kosek, M. 2014. Update on the burden of *Campylobacter* in developing countries. Curr. Opin. Infect. Dis. 27(5), 444–450.
- Pokhrel, D., Thames, H.T., Zhang, L., Dinh, T.T.N., Schilling, W., White, S.B., Ramachandran, R. and Sukumaran, A.T. 2022. Roles of aerotolerance, biofilm formation, and viable but non-culturable state in the survival of *Campylobacter jejuni* in poultry processing environments. Microorganisms 10(11), 2165.
- Poly, F., Noll, A.J., Riddle, M.S. and Porter, C.K. 2019. Update on campylobacter vaccine development. Hum. Vaccin. Immunother. 15(6), 1389–1400.
- Pölzler, T., Stüger, H.-P. and Lassnig, H. 2018. Prevalence of most common human pathogenic *Campylobacter* spp. in dogs and cats in Styria, Austria. Vet. Med. Sci. 4(1), 115–125.
- Poropatich, K.O., Walker, C.L. and Black, R.E. 2010. Quantifying the association between *Campylobacter* infection and Guillain-Barré syndrome: a systematic review. J. Health Popul. Nutr. 28(6), 545–552.
- Portes, A.B., Panzenhagen, P., Dos Santos A.M.P. and Junior, C.A.C. 2023. Antibiotic resistance in campylobacter: a systematic review of south american isolates. Antibiotics (Basel) 12(3), 548.
- Price, L.B., Lackey, L.G., Vailes, R. and Silbergeld, E. 2007. The persistence of fluoroquinolone-resistant campylobacter in poultry production. Environ Health Perspect. 115(7), 1035–1039.
- Radomska, K.A., Wösten, M.M.S.M., Ordoñez, S.R., Wagenaar, J.A. and van Putten, J.P.M. 2017. Importance of *Campylobacter jejuni* FliS and FliW in flagella biogenesis and flagellin secretion. Front. Microbiol. 8(1), 1060.
- Randremanana, R.V., Randrianirina, F., Sabatier, P., Rakotonirina, H.C., Randriamanantena, A., Razanajatovo, I.M., Ratovoson, R. and Richard, V. 2014. *Campylobacter* infection in a cohort of rural children in Moramanga, Madagascar. BMC Infect. Dis. 14(1), 372.

- Rastall, R.A. 2004. Bacteria in the gut: friends and foes and how to alter the balance. *J. Nutr.* 134(8 Suppl), 2022S–2026S.
- Rawson, T., Dawkins, M.S. and Bonsall, M.B. 2019. A mathematical model of campylobacter dynamics within a broiler flock. *Front. Microbiol.* 10(1), 1940.
- Ribardo, D.A., Johnson, J.J. and Hendrixson, D.R. 2024. Viscosity-dependent determinants of *Campylobacter jejuni* impacting the velocity of flagellar motility. *mBio* 15(1), e0254423.
- Ricke, S.C., Feye, K.M., Chaney, W.E., Shi, Z., Pavlidis, H. and Yang, Y. 2019. Developments in rapid detection methods for the detection of foodborne campylobacter in the United States. *Front. Microbiol.* 9(1), 3280.
- Rodrigues, J.A., Cha, W., Mosci, R.E., Mukherjee, S., Newton, D.W., Lephart, P., Salimnia, H., Khalife, W., Rudrik, J.T. and Manning, S.D. 2021. Epidemiologic associations vary between tetracycline and fluoroquinolone resistant *Campylobacter jejuni* infections. *Front. Public Health* 9(1), 672473.
- Royden, A., Christley, R., Jones, T., Williams, A., Awad, F., Haldenby, S., Wigley, P., Rushton, S.P. and Williams, N.J. 2021. Campylobacter contamination at retail of halal chicken produced in the United Kingdom. *J. Food Prot.* 84(8), 1433–1445.
- Royden, A., Wedley, A., Merga, J.Y., Rushton, S., Hald, B., Humphrey, T. and Williams, N.J. 2016. A role for flies (Diptera) in the transmission of *Campylobacter* to broilers? *Epidemiol. Infect.* 144(15), 3326–3334.
- Sadek, S.A.S., Shaapan, R.M. and Barakat, A.M.A. 2023. Campylobacteriosis in poultry: a review. *J. World's Poult. Res.* 13(2), 168–179.
- Sails, A.D., Fox, A.J., Bolton, F.J., Wareing, D.R. and Greenway, D.L. 2003. A real-time PCR assay for the detection of *Campylobacter jejuni* in foods after enrichment culture. *Appl. Environ. Microbiol.* 69(3), 1383–1390.
- Samie, A., Moropeng, R.C., Tanih, N.F., Dillingham, R., Guerrant, R. and Bessong, P.O. 2022. Epidemiology of *Campylobacter* infections among children of 0–24 months of age in South Africa. *Arch. Public Health* 80(1), 107.
- Sanad, Y.M., Jung, K., Kashoma, I., Zhang, X., Kassem, I.I., Saif, Y.M. and Rajashekara, G. 2014. Insights into potential pathogenesis mechanisms associated with *Campylobacter jejuni*-induced abortion in ewes. *BMC Vet. Res.* 10(1), 274.
- Sanchez, J.J., Alam, M.A., Stride, C.B., Haque, M.A., Das, S., Mahfuz, M., Roth, D.E., Sly, P.D., Long, K.Z. and Ahmed, T. 2020. Campylobacter infection and household factors are associated with childhood growth in urban Bangladesh: an analysis of the MAL-ED study. *PLoS Negl. Trop. Dis.* 14(5), e0008328.
- Sears, A., Baker, M.G., Wilson, N., Marshall, J., Muellner, P., Campbell, D.M., Lake, R.J. and French, N.P. 2011. Marked campylobacteriosis decline after interventions aimed at poultry, New Zealand. *Emerg. Infect. Dis.* 17(6), 1007–1015.
- Shad, A.A. and Shad, W.A. 2019. Review of Food-borne micro-organism: *Campylobacter* species. *J. Food Microbiol. Saf. Hyg.* 4(1): 1000141.
- Sheppard, S.K. and Maiden, M.C. 2015. The evolution of *Campylobacter jejuni* and *Campylobacter coli*. *Cold Spring Harb. Perspect. Biol.* 7(8), a018119.
- Skarp, C.P.A., Hänninen, M.L. and Rautelin, H.I.K. 2016. Campylobacteriosis: the role of poultry meat. *Clin. Microbiol. Infect.* 22(2), 103–109.
- Sockett, P.N. and Rodgers, F.G. 2001. Enteric and foodborne disease in children: a review of the influence of food- and environment-related risk factors. *Paediatr. Child Health* 6(4), 203–209.
- Sonnevend, Á., Rotimi, V.O., Kolodziejek, J., Usmani, A., Nowotny, N. and Pál, T. 2006. High level of ciprofloxacin resistance and its molecular background among *Campylobacter jejuni* strains isolated in the United Arab Emirates. *J. Med. Microbiol.* 55(Pt 11), 1533–1538.
- Stern, N.J., Hiett, K.L., Alfredsson, G.A., Kristinsson, K.G., Reiersen, J., Hardardottir, H., Briem, H., Gunnarsson, E., Georgsson, F., Lowman, R., Berndtson, E., Lammerding, A.M., Paoli, G.M. and Musgrove, M.T. 2003. *Campylobacter* spp. in Icelandic poultry operations and human disease. *Epidemiol. Infect.* 130(1), 23–32.
- Stingl, K., Knüver, M.T., Vogt, P., Buhler, C., Krüger, N.J., Alt, K., Tenhagen, B.A., Hartung, M., Schroeter, A., Ellerbroek, L., Appel, B. and Käsbohrer, A. 2012. Quo vadis?—monitoring campylobacter in Germany. *Eur. J. Microbiol. Immunol. (Bp)* 2(1), 88–96.
- Suominen, K., Häkkinen, T., Ranta, J., Ollgren, J., Kivistö, R., Perko-Mäkelä, P., Salmenlinna, S. and Rimhanen-Finne, R. 2024. Campylobacteriosis in Finland: passive surveillance in 2004–2021 and a pilot case-control study with whole-genome sequencing in summer 2022. *Microorganisms* 12(1), 132.
- Suzuki, H. and Yamamoto, S. 2009. Campylobacter contamination in retail poultry meats and by-products in the world: a literature survey. *J. Vet. Med. Sci.* 71(3), 255–261.
- Szosland-Faltyn, A., Bartodziejska, B., Królasik, J., Paziak-Domańska, B., Korsak, D. and Chmiela, M. 2018. The prevalence of *Campylobacter* spp. in polish poultry meat. *Pol. J. Microbiol.* 67(1), 117–120.
- Szott, V., Peh, E., Friese, A., Roesler, U., Kehrenberg, C., Ploetz, M. and Kittler, S. 2022. Antimicrobial effect of a drinking water additive comprising four organic acids on *Campylobacter* load in broilers

- and monitoring of bacterial susceptibility. *Poult. Sci.* 101(12), 102209.
- Taha-Abdelaziz, K., Singh, M., Sharif, S., Sharma, S., Kulkarni, R.R., Alizadeh, M., Yitbarek, A. and Helmy, Y.A. 2023. Intervention strategies to control campylobacter at different stages of the food chain. *Microorganisms* 11(1), 113.
- Talukdar, P.K., Crockett, T.M., Gloss, L.M., Huynh, S., Roberts, S.A., Turner, K.L., Lewis, S.T.E., Herup-Wheeler, T.L., Parker, C.T. and Konkel, M.E. 2022. The bile salt deoxycholate induces *Campylobacter jejuni* genetic point mutations that promote increased antibiotic resistance and fitness. *Front. Microbiol.* 13(1), 1062464.
- Talukder, K.A., Aslam, M., Islam, Z., Azmi, I.J., Dutta, D.K., Hossain, S., Nur-E-Kamal, A., Nair, G.B., Cravioto, A., Sack, D.A. and Endtz, H.P. 2008. Prevalence of virulence genes and cytolethal distending toxin production in *Campylobacter jejuni* isolates from diarrheal patients in Bangladesh. *J. Clin. Microbiol.* 46(4), 1485–1488.
- Tedersoo, T., Roasto, M., Mäesaar, M., Kisand, V., Ivanova, M. and Meremäe, K. 2022. The prevalence, counts, and MLST genotypes of *Campylobacter* in poultry meat and genomic comparison with clinical isolates. *Poult. Sci.* 101(4), 101703.
- Tracz, D.M., Keelan, M., Ahmed-Bentley, J., Gibreel, A., Kowalewska-Grochowska, K. and Taylor, D.E. 2005. pVir and bloody diarrhea in *Campylobacter jejuni* enteritis. *Emerg. Infect. Dis.* 11(6), 838–843.
- Tresse, O., Alvarez-Ordóñez, A. and Connerton, I.F. 2017. Editorial: about the foodborne pathogen campylobacter. *Front. Microbiol.* 8(1), 1908.
- Tsoni, K., Papadopoulou, E., Michailidou, E. and Kavaliotis, I. 2013. *Campylobacter jejuni* meningitis in a neonate: a rare case report. *J. Neonatal Perinatal Med.* 6(2), 183–185.
- Tyasningsih, W., Ramandinianto, S.C., Ansharieta, R., Witaningrum, A.M., Permatasari, D.A., Wardhana, D.K., Effendi, M.H. and Ugbo, E.N. 2022. Prevalence and antibiotic resistance of *Staphylococcus aureus* and *Escherichia coli* isolated from raw milk in East Java, Indonesia. *Vet. World* 15(8), 2021–2028.
- van den Brom, R., de Jong, A., van Engelen, E., Heuvelink, A. and Vellema, P. 2020. Zoonotic risks of pathogens from sheep and their milk borne transmission. *Small Rumin. Res.* 189(1), 106123.
- van Dijk, A., Veldhuizen, E.J., Kalkhove, S.I., Tjeerdsmav-van Bokhoven, J.L., Romijn, R.A. and Haagsman, H.P. 2007. The beta-defensin gallinacin-6 is expressed in the chicken digestive tract and has antimicrobial activity against foodborne pathogens. *Antimicrob. Agents Chemother.* 51(3), 912–922.
- Vaughan-Shaw, P.G., Rees, J.R., White, D. and Burgess, P. 2010. *Campylobacter jejuni* cholecystitis: a rare but significant clinical entity. *BMJ Case Rep.* 2010(1), bcr1020092365.
- Wagenaar, J.A., Mevius, D.J. and Havelaar, A.H. 2006. *Campylobacter* in primary animal production and control strategies to reduce the burden of human campylobacteriosis. *Rev. Sci. Tech.* 25(2), 581–594.
- Wang, H., Gu, Y., He, L., Sun, L., Zhou, G., Chen, X., Zhang, X., Shao, Z., Zhang, J. and Zhang, M. 2023. Phenotypic and genomic characteristics of *Campylobacter gastrosuis* sp. nov. Isolated from the stomachs of pigs in Beijing. *Microorganisms* 11(9), 2278.
- Wensley, A., Padfield, S. and Hughes, G.J. 2020. An outbreak of campylobacteriosis at a hotel in England: the ongoing risk due to consumption of chicken liver dishes. *Epidemiol. Infect.* 148(1), e32.
- Whiley, H., van den Akker, B., Giglio, S. and Bentham, R. 2013. The role of environmental reservoirs in human campylobacteriosis. *Int. J. Environ. Res. Public Health* 10(11), 5886–5907.
- Wibisono, F.J., Sumiarto, B., Untari, T., Effendi, M.H., Permatasari, D.A. and Witaningrum, A.M. 2021. Molecular Identification of CTX Gene of Extended Spectrum Beta-Lactamases (ESBL) Producing *Escherichia coli* On Layer Chicken In Blitar, Indonesia. *J. Anim. Plant Sci.* 31(4), 954–959.
- Wieczorek, K. and Osek, J. 2013. Antimicrobial resistance mechanisms among *Campylobacter*. *Biomed. Res. Int.* 2013(1), 340605.
- Wolf-Jäckel, G.A., Boye, M., Angen, Ø., Müller, M. and Jensen, T.K. 2020. Fluorescence in situ hybridization in species-specific diagnosis of ovine *Campylobacter* abortions. *J. Vet. Diagn. Invest.* 32(3), 413–419.
- Wysok, B., Wojtacka, J., Wiszniewska-Laszczych, A., Sołtysiuk, M. and Kobuszewska, A. 2022. The Enterotoxin production and antimicrobial resistance of campylobacter strains originating from slaughter animals. *Pathogens* 11(10), 1131.
- Yanestria, S.M., Effendi, M.H., Tyasningsih, W., Khairullah, A.R., Kurniawan, S.C., Moses, I.B., Ikaratri, R., Samodra, M.E., Dameanti, F.N., Silaen, O.S.M., Mariyono, M. and Hasib, A. 2024a. Fluoroquinolone resistance and phylogenetic analysis of broiler *Campylobacter jejuni* isolates in Indonesia. *J. Adv. Vet. Res.* 14(1), 204–208.
- Yanestria, S.M., Effendi, M.H., Tyasningsih, W., Mariyono, M. and Ugbo, E.N. 2023. First report of phenotypic and genotypic (*bla*OXA-61) beta-lactam resistance in *Campylobacter jejuni* from broilers in Indonesia. *Vet. World* 16(11), 2210–2216.
- Yanestria, S.M., Effendi, M.H., Tyasningsih, W., Moses, I.B., Khairullah, A.R., Kurniawan, S.C., Dameanti, F.N.A.E.P., Ikaratri, R., Pratama, J.W.A., Sigit, M., Hasib, A. and Silaen, O.S.M. 2024b. Antimicrobial resistance patterns and genes of *Campylobacter jejuni* isolated from chickens in Pasuruan, Indonesia. *Open Vet. J.* 14(3), 759–768.

- Yanestria, S.M., Rahmaniar, R.P., Wibisono, F.J. and Effendi, M.H. 2019. Detection of invA gene of Salmonella from milkfish (*Chanos chanos*) at Sidoarjo wet fish market, Indonesia, using polymerase chain reaction technique. *Vet. World* 12(1), 170–175.
- Zautner, A.E., Tareen, A.M., Groß, U. and Lugert, R. 2012. Chemotaxis in *Campylobacter jejuni*. *Eur. J. Microbiol. Immunol. (Bp)*. 2(1), 24–31.
- Zhao, S., Young, S.R., Tong, E., Abbott, J.W., Womack, N., Friedman, S.L. and McDermott, P.F. 2010. Antimicrobial resistance of *Campylobacter* isolates from retail meat in the United States between 2002 and 2007. *Appl. Environ. Microbiol.* 76(24), 7949–7956.