Veterinary Integrative Sciences 2025; 23(2): e2025054-1-47. DOI: 10.12982/VIS.2025.054

Veterinary Integrative Sciences
ISSN; 2629-9968 (online)

Review article

Exploring *Campylobacter jejuni*: Elucidating pathogenic mechanisms, virulence factors, antimicrobial resistance in diverse animal species

Chinedu Frank Amaeze[1], Mohammed Dauda Goni[1,2*], Fadhilah Kamaruzzaman[1], Gaddafi Mohammed Sani [3] and Aliyu Yakubu[1,4]

[1]Faculty of Veterinary Medicine, Universiti Malaysia Kelantan, Kota Bharu 16100,Malaysia
[2]Institute for Artificial Intelligence and Big Data, Universiti Malaysia Kelantan, 16100 Kota Bharu, Kelantan, Malaysia
[3]Department of Public Health, Ministry of Animal Health, Husbandry and Fisheries, Kebbi State 860101, Nigeria
[4]Ministry of Agriculture and Natural Resources Damaturu, Yobe State 620101, Nigeria.

Abstract

Campylobacter and its species, with a specific reference to C*ampylobacter jejuni*. are zoonotic pathogens known to cause food-borne diseases and are ideally found in humans, poultry, cattle, and even mammals in certain cases. C*. jejuni* is the predominant foodborne pathogen regularly found in both pets and food animals, posing a significant risk of zoonotic infections to humans and animals alike. Consequently, infections caused by *C. jejuni* are a substantial concern for global public health, animal welfare, and the food industry. *Campylobacter* colonizes its host by overcoming stomach acidity, adhering to intestinal epithelial cells using specialized surface structures, and producing virulence factors to establish infection and proliferate within the gastrointestinal tract. Epidemiologically, *Campylobacter*'s transmission dynamics, risk factors, and patterns of infection spread are crucial considerations in understanding and controlling its impact on public health. The global trend of *C. jejuni* occurrence has significant implications for public health, necessitating heightened surveillance, prevention, and control measures to mitigate the burden of foodborne illness and reduce the associated economic and societal costs. The emergence of *Campylobacter* strains resistant to multiple antimicrobials poses serious threats to public health, including treatment challenges, increased severity of infections, heightened transmission risk, and potential spread of resistance genes to other bacteria, underscoring the need for enhanced surveillance, antimicrobial stewardship, and research into alternative treatment approaches. Consequently, this review focuses on the intricacies of *Campylobacter jejuni* with a particular focus on pathogenicity, virulence factors, host specificity, prevalence on different animal models, and antimicrobial resistance including multidrug resistance.

Keywords: Antimicrobial resistance, Campylobacter, Pathogenicity, Prevalence

*Corresponding author: Mohammed Dauda Goni, Faculty of Veterinary Medicine, Universiti Malaysia Kelantan, 16100 Kota Bharu, Malaysia. E-mail: dauda.g@umk.edu.my.

Article history; *received manuscript: 17 March 2024, revised manuscript: 12 April 2024, accepted manuscript: 12 June 2024, published online: 23 September 2024,*
Academic editor; *Prapat Patchanee*

INTRODUCTION

Campylobacter is a Gram-negative, microaerophilic bacterium that belongs to the Epsilon class of Proteobacteria, has a characteristic spiral structure, and is a common foodborne organism that causes gastroenteritis in humans and animals (El-Ashram et al., 2022; Jaworski et al., 2018; Thépault et al., 2020). The genus *Campylobacter* presently has 17 species and 6 subspecies

recognized. The two that are most commonly reported are *C. coli* and *C. jejuni (subspecies jejuni)*. The great majority of epsilon proteobacteria species such as Sulfurimonas species are found in deep-sea hydrothermal vents, which may point to the genus *Campylobacter's* ancient origins (Gundogdu and Wren, 2020). *Campylobacteriosis* has long been recognized as a significant food-borne zoonotic disease that poses a global public health risk (Acke, 2018). Globally, 96 million instances of enteric infection are attributed to *Campylobacter* species, *Campylobacteriosis*, which accounted for more than 60% of all reported cases in 2020, was identified by the European Union (EU) as the zoonotic infection with the highest reported rates (Authority et al., 2021). *Campylobacter spp* is one of the major causes of foodborne illnesses out of which C. jejuni has been the most common cause (Campagnolo et al., 2018). The occurrence of these bacteria all over the world makes it important to understand the ramifications that are associated with the infection of these bacteria (Campagnolo et al., 2018). *Campylobacter* thus poses a problem because it first appeared at the interface between humans, animals, and the environment (Clavijo and Flórez, 2018). The relationship between the health of people, animals, and the environment is acknowledged by One Health thus, it is crucial to use strategies that take environmental and animal health into account as a crucial part of disease surveillance, control, prevention, and mitigation (Sampaio et al., 2022). Most often *Campylobacteriosis* manifests as a moderate, self-limiting gastroenteritis that typically presents as acute enteritis, marked by inflammation of the gastrointestinal tract, primarily the colon and small intestine. Symptoms include diarrhea, which may be watery or bloody, abdominal cramps, fever, malaise, and sometimes nausea and vomiting. The severity of symptoms can vary widely, ranging from mild discomfort to severe dehydration and systemic illness. In some cases, *Campylobacteriosis* may also lead to complications such as reactive arthritis or Guillain-Barré syndrome, a rare but serious autoimmune disorder affecting the peripheral nervous system. (Campagnolo et al., 2018; Roa-Bautista et al., 2023). *Campylobacter jejuni* subsp. jejuni with *Campylobacter* coli are the two most significant pathogens of *Campylobacter* and account for 95% of zoonotic infections (Chlebicz and Śliżewska, 2018). They differ from other harmful bacteria transmitted through food in that they can thrive in an environment containing approximately 10% CO2 and 5% O2 (microaerophilic) within a narrow temperature range of 30 to 46°C (the optimal growth temperature is 40-42°C), indicating that they are thermophilic (Chlebicz and Śliżewska, 2018). *C. jejuni*, is believed to be responsible for a substantial global incidence of bacterial gastroenteritis attributed to its zoonotic, and its capacity to colonize the gastrointestinal tracts of various hosts creates issues concerning interspecies and human transfers (Clavijo and Flórez, 2018). Within the *Campylobacteraceae* family of bacteria is *C. jejuni,* a motile, corkscrew-shaped, gram-negative bacterium with amphitrichous sheathed flagella that are responsible for its corkscrew locomotion, *C. jejuni* is distinguished by its spiral/helical form (Aleksić et al., 2021). An important benefit of *C. jejuni* mobility in a very viscous environment like the mucus is its corkscrew or darting motion (Elmi et al., 2020). This bacterium's unique morphology aids in its mobility and tissue penetration, making it a powerful pathogen (Greening et al., 2020). The bacteria can also, under stress, adopt a coccoid form, this morphology of the bacterium is important as it provides the bacterium with utility with its single pole flagella, but when these bacteria are Under stress, like cold temperature or

starvation this coccoid morphology is non-motile and is resistant to environmental stress (Kim et al., 2021). *Campylobacter jejuni* has a substantial impact on animals such as household pets (dogs and cats), poultry, and cattle acting as potential carriers and modifying the pattern of transmission of human infections (Thépault et al., 2020). This underscores the interconnection of human and animal health, demanding an integrated approach to detecting and mitigating *C. jejuni* hazards (Thépault et al., 2020). In livestock, such as poultry, cattle, and pigs, *C. jejuni* infections can lead to decreased productivity, including reduced growth rates and egg production in poultry, as well as economic losses for farmers and the agricultural industry due to increased mortality and costs associated with veterinary care and disease management (AlHakeem et al., 2022). Additionally, *C. jejuni* infections in animals can serve as a reservoir for human infections through zoonotic transmission, highlighting the importance of controlling the bacterium in animal populations to protect both animal and human health (Thépault et al., 2020). The predisposition of *C. jejuni* to gain resistance to bacterial treatments, culminating in resistance to multiple medications, is one of the primary concerns it poses (Aleksić et al., 2021). *C. jejuni*'s propensity to develop resistance to antibacterial treatments arises from its genomic plasticity, facilitating rapid adaptation through genetic changes and horizontal gene transfer mechanisms, enabling the acquisition of resistance genes from other bacteria (Butzler et al., 2018). Selective Pressure from antibiotic use in veterinary and human medicine further drives the evolution of resistance in *C. jejuni* populations (Alrubaye et al., 2018). The bacterium employs various resistance mechanisms, including efflux pumps and modifications to antibiotic targets, to evade the action of antibiotics (Pascoe et al., 2019). Additionally, biofilm formation enhances bacterial survival and resistance by providing physical protection and facilitating genetic exchange (Mughal et al., 2018). These setting factors collectively contribute to the challenges in controlling and treating *C. jejuni* infections, highlighting the need for comprehensive strategies to mitigate antibiotic resistance in both clinical and agricultural settings (AlHakeem et al., 2022; Shamsi Saad et al., 2023).

Brief History and Nomenclature/Taxonomy

In 1886, Theodor Escherich first identified *Campylobacter* and it was described as a spiral-shaped bacteria in stool samples of children with diarrhea (Alrubaye, 2018; Baaboua et al., 2022).

Campylobacter fetus (classified initially as Vibrio fetus) was the first *Campylobacter spp* isolated in 1906 by Mcfadyean and Stockman from uterine mucous of aborted ewes (El-Naenaeey et al.,2020). In 1957, the isolation of *Campylobacter* from blood samples of children with diarrhea was described (Baaboua et al., 2022). The genus *Campylobacter* was first named in 1963 by Sebald and Veron. In 1972, a Belgian team carried out the first isolation of thermophilic *Campylobacter* as an enteric pathogen via filtering of stool samples of female patients with diarrhea (Pascoe et al., 2019). *Campylobacter spp* was established as a common human pathogen after the improvement in isolation methods and development of selective growth media for the cultivation of *Campylobacter* from fecal samples of patients with enteric symptoms (Honsheng and Manuel Mariano, 2022). *Campylobacter Jejuni* and *Campylobacter* coli are the most recognized species within the *Campylobacter* genus and are considered common gastrointestinal pathogens causing human enteric illnesses in millions of cases in adults and children worldwide each year (Mughal et al., 2018). In 1960, Sebald and Veron started the first *Campylobacter* taxonomy with two species (Pascoe et al., 2019). The genus is a component of the *Campylobacteraceae* family and is strongly interconnected to the Helicobacter and Arcobacter genera (Wang, 2019). Fourteen species have been described in late 1980s (Wang, 2019). Today, the genus *Campylobacter* contains 17 validated species (Ghssein et al., 2021). Most of these species are human or animal pathogens while some are zoonotic

pathogens (Ghssein et al., 2021). Within the genus, three species (*C. jejuni, C. coli, and C. lari*) are known as thermophilic and of clinical significance as they are the dominant causative agents of human campylobacteriosis (Saeed et al., 2022). The majority of food-borne *Campylobacter* enteritis in humans is caused by *C. jejuni,* followed by *C. coli*, and to a lesser extent, by *C. lari.* The taxonomic classification of *Campylobacter* faced difficulties for many years because it mainly depended on phenotypic character, which was difficult to standardize (Sayed et al., 2023). When King (1957) grouped the Vibrio bacteria and the clinical entities of bovine vibrionic abortions they started to be better understood (Butzler et al., 2018). In the same year, the first taxonomic differentiation of Vibrio started when it was confirmed that catalase–positive microaerophilic Vibrio could be differentiated by their ability to grow at different temperatures (Sampaio et al., 2022).

Morphology, Bacteriological Culture, and Isolation Procedures

The morphology of the bacteria is defined by the structure of the peptidoglycan layer that is present in the bacteria (Lin et al., 2021). Unlike many other bacteria, *C. jejuni* has a relatively thin peptidoglycan layer in its cell wall, which is surrounded by an outer membrane (Taheri, 2019). This thin peptidoglycan layer, along with the outer membrane, contributes to the bacteria's flexibility and helical shape (Wagenaar et al., 2023). Additionally, *Campylobacter* species are motile due to the presence of polar flagella at one or both ends of the cell, which facilitate movement through their environment (Mughal et al., 2018). These morphological features, particularly the structure of the peptidoglycan layer, are key characteristics used to distinguish *Campylobacter* species from other bacteria (Sampaio et al., 2022). It has been reported that genetic changes due to spontaneous mutation, and natural or plasmid-borne transformation may cause considerable phylogenetic diversity within the genus (Epping, Antão, et al., 2021). The optimum temperature for their growth ranges from 30 to 42°C and they grow best in an atmosphere containing 5 to 10% oxygen (microaerophilic organisms) (Ejidokun et al., 2019). Several factors such as bacterial strain, basal medium, level of moisture on the surface of the agar, incubation temperature, and incubation time may affect the colony morphology of this organism Colony morphology should not be used as an important distinguishing factor (Honsheng and Manuel Mariano, 2022; Nnadozie et al., 2023). There is some variability in the colony morphology, from a thick translucent white growth to spreading film-like transparent growth, which can be visible on the plating media within 24 to 48 hours of incubation (Sampaio et al., 2022). Without using selective techniques, it is challenging to isolate this organism from fecal specimens since campylobacters tend to multiply slower than other enteric bacteria (El-Saadony et al., 2023).

Campylobacter is a complicated organism to cultivate and keep in the laboratory (Corcionivoschi and Gundogdu, 2021). Detection of Campylobacter can be difficult when the cells are viable but in a non-culturable state (Corcionivoschi and Gundogdu, 2021). Antibiotics are included in the medium for enrichment and isolation purposes to prevent contaminating organisms from overgrowth (Natsos et al., 2019). For isolation of *Campylobacter* species, fecal samples or rectal swabs should normally be submitted to the laboratory from patients with diarrheal disease (Kovanen et al., 2019). In most laboratories, direct plating onto a selective agar with incubation in a microaerobic atmosphere at 42°C for 42 to 48 h is the habitual procedure for the detection of *C. jejuni* (Burnham and Hendrixson, 2018). As a single transport medium, modified Cary-Blair medium including reduced agar is relatively useful and is appropriate for Campylobacter and other enteric pathogens (Costa and Iraola, 2019). *Campylobacter* is difficult to culture because they require special media supplemented with antibacterial agents that suppress the growth of other enteric bacteria, a microaerophilic atmosphere (5% O2, 10% CO2, and 85% N2), and a temperature of 42°C (Awad et al., 2018). Detection of Campylobacter

from complex sample types such as food, water, and environment is regarded to be difficult and time-consuming because the numbers of *Campylobacter* can be low and other factors such as pH, oxidative stress and temperature inhibit recovery (Kim et al., 2020; Lanzl et al., 2020). According to the numerous studies on enrichment techniques for food, water and environmental samples, it has been established that enrichment media such as Bolton and Exeter broths were better than other broths such as Preston (Ejidokun et al., 2019). The usual composition of an enrichment broth includes a rich, basal medium, such as in Brucella broth or Nutrient broth, antibacterial agents, and the addition of lysed horse or sheep blood (Clark et al., 2018). The basal medium is needed for *Campylobacter* species to grow because they are said to be fastidious organisms (Awad et al., 2018). Centrifugation or filtration and centrifugation methods have been applied to raise the number of Campylobacter cells before plating and to by-pass the enrichment step (Clark et al., 2018). Even though a variety of phenotyping methods have been illustrated, such as serotyping, biotyping and phage typing, these methods need specialist abilities and reagents, as they are time-consuming and also difficult to standardize (Mohamed et al., 2021). Molecular techniques are unconventional to the bacteriological technique for the recognition of *C. jejuni* in a range of substrates (Zhang et al., 2021). For identifying and subtyping of C. jejuni, several molecular-based techniques have been developed (Du et al., 2018). These techniques consist of enzyme and electro chemiluminescent immunoassay, mass spectrometry, DNA microarray, multilocus sequence typing, PCR-based assays, polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP), ribotyping, pulsed-field gel electrophoresis (PFGE), typing flagellin (fla-typing), random amplified polymorphic DNA (RAPD), and amplified fragment length polymorphism (AFLP) (Du et al., 2018; Feberwee et al., 2005).

Host Specificity of *Campylobacter Jejuni*

Campylobacter jejuni is a gram-negative, microaerophilic bacteria that is well-known for its association with gastroenteritis in humans (Mohamed et al., 2021). This bacterium demonstrates a remarkable host specificity which means that it preferentially infects and colonizes within certain limited hosts which often include avian species and to a lesser extent mammals (Wagenaar et al., 2023). It is important to understand the host specificity of this microbe because it will help in the comprehension of its pathogenesis and transmission dynamics (Mohamed et al., 2021). The host specificity of *C. jejuni* for avian species, especially domestic poultry like chickens and turkeys has been extremely remarkable (Awad et al., 2018). These birds often act as reservoirs of the bacterium, specifically harboring it in their gastrointestinal tract without actually displaying any physical and clinical symptoms (Wagenaar et al., 2023). The bacterium specifically prefers this host because of the numerous adaptations that allow it to survive in the gut of the waves (Awad et al., 2018). The flagella present in the bacteria allows it to move quickly through the mucus lining that is present in the avian intestine which allows it to form a colony (Elmi et al., 2021). Different strains of the bacterium have different specificities for the hosts which, in turn, can impact the rate of transmission to humans (Natsos et al., 2019). Some strains of the bacterium, like ST-21, ST-45, and ST-464 are more typically linked with chicken and are ideally found in the complexes that have been identified from them, whereas strains like ST-21, ST-206, and ST-48 complexes are frequently found in clinical isolates (Thépault et al., 2018). This shows that the bacterium has host adaptability which can directly and significantly impact the genetic diversity and virulence of different strains of *C. jejuni* which can affect mammals (Burnham and Hendrixson, 2018). This is because it has been observed that this bacterium infects cattle, sheep, pigs, and other wild animals (Wagenaar et al., 2023). This adaptation to multiple mammalian hosts can be because the mammalian gut environment shares more similarities than differences and this infection can contribute to zoonotic transmission of the

bacterium (Costa and Iraola, 2019). Numerous factors can contribute to the host specificity of the bacterium, one such factor is the capsule of the bacterium It is the outermost layer that is present in the bacterium which acts as a protective layer for it (Kim et al., 2018). Different capsule types can be associated with different specificity for the hosts which is developed from the ORF 10 that leads to the formation of Capsule polysaccharide modification protein, kpsC (Clark et al., 2018). This modifying capsule can play an important role in immune invasion and host adaptation (Kim et al., 2018). This can be explained by considering some examples, for instance, bacteria with genotype HS 6_7 are found in cattle, HS10 is found in Chicken, HS12 is found in ducks and both HS6_7 and HS12 have been found in the stool of the patient that was suffering with diarrhea apart from numerous other genotypes (Wang et al., 2021a). Host specificity can also be contributed by the outer membrane protein (OMP) in which the difference in genotypes leads to the formation of different OMPs which can lead to host-specific infections because of its interactions with host cells and immune responses (Lopes et al., 2021). The flagellar proteins that are present in the bacteria also play an important role in host colonization and its specificity, these proteins are required for host cell motility, adhesion as well invasion (Lopes et al., 2021). Also, the genetic variations that exist between *C. jejuni* strains can impact the host specificity (Costa and Iraola, 2019).

The whole-genome sequencing method has identified that there are numerous lineages of *C. jejuni* out of which some are more closely linked with avian hosts than others, these genetic differences can have an impact on the bacterium's power to colonize and survive in certain hosts (Kovanen et al., 2019). The avian-associated strains can cause gastroenteritis when they are transmitted to humans when they consume contaminated poultry products, this mode of transmission is a major cause of *Campylobacter* infections in humans (Mourkas, 2019). Therefore, understanding the host preferences of *C. jejuni* in birds and animals can help the authorities come up with standards from which the poultry keeper can adopt control measures in food production and it can also help in the development of vaccines for the prevention of the infection (Thépault et al., 2018).

Whole-genome sequencing offers comprehensive insights into the population structure and host specificity of *Campylobacter jejuni* (Thépault et al., 2018). It reveals that isolates from specific clonal complexes like CC-21, CC-45, or CC-48 are frequently found across multiple host species, indicating the capability of these phylogenetic lineages to swiftly transition between diverse intestinal environments, reflecting a typical host-generalist lifestyle. Understanding the factors influencing *C. jejuni*'s adaptation to particular host species, notably poultry and cattle, has been a pivotal focus of *Campylobacter* research in the past decade (Thépault et al., 2018).

Transmission

Food-borne bacterial gastroenteritis in humans is caused by *Campylobacter jejuni* and *Campylobacter coli* globally (Corcionivoschi and Gundogdu, 2021). Based on the European Food Safety Authority (EFSA) report, in European countries, the incidences of *Campylobacter* infection ranged from <0.1 to 193.3/100 000 of the population (Liu et al., 2022b). No age barrier to infection, but the incidence rates were higher among children under two years of age and young adults (Igwaran and Okoh, 2019a). The dose of infection of *C. jejuni* in contaminated food may be as low as 500- 800 bacteria (Lopes et al., 2021). The period of incubation of *Campylobacter* is mostly between one and three days; however, it can also be as long as ten days (Guo et al., 2023). *Campylobacteriosis* is considered a non-serious, mild, and self-limiting disease of the gastrointestinal tract; in rare instances, severe outcome occurs as a secondary to the original gastrointestinal disease (Ejidokun et al., 2019). The bacteria are ideally transmitted to humans when they consume food that has been contaminated by the bacteria, especially through the means of poultry, unpasteurized milk, and contaminated water (Bintsis, 2017).

Once the individual has contracted the disease, it can spread to another individual by coming in contact with their feces (Di Savino et al., 2022). After the bacteria enter the system, they start colonizing the intestinal tract, especially in the small intestine, they tend to adhere to the mucosal lining and disrupt the structure as well as the function of the intestinal epithelium (Greening, 2020). This, in turn, causes the individual to suffer from abdominal pain, diarrhea, and fever (Greening, 2020). The symptoms of human campylobacteriosis include fever, headaches, and general myalgia followed by diarrhea and in most cases severe abdominal cramping (Igwaran and Okoh, 2019b). The diarrhea may be watery or bloody (particularly in developed countries) and the signs may continue for up to seven days (Skirrow and Blaser 2000). Serious complications such as reactive arthritis, Reiter's syndrome, and Guillain-Barré and Miller Fisher syndromes have been related to *Campylobacter enteritis* (Finsterer, 2022). Also, intermittent complications may be possible such as hepatitis, cholecystitis, bacteremia, pancreatitis, cystitis, septic abortion, meningitis, endocarditis, septic arthritis, and osteomyelitis (Finsterer, 2022). After the infection and clinical symptoms have disappeared, the patient may shed *Campylobacter* organisms in feces for up to three weeks except when treated with antibiotics (Chlebicz and Śliżewska, 2018b). *Campylobacter* infection is obtained via three main routes; direct contact with infected or reservoir hosts, food, and water the main transmission route is via food which includes undercooked meat (chicken, pork, lamb and seafood, beef), unpasteurized milk and salad (Igwaran and Okoh, 2019a). Predominantly, poultry meat (broiler, laying hens, and ducks) is considered a major, if not the largest, single source of infection in humans (Chlebicz and Śliżewska, 2018b). Consumption of unpasteurized milk is mainly associated with outbreaks of *Campylobacter* enteritis and as such *Campylobacter* can be isolated from milk samples (Kenyon et al., 2020). *Campylobacter* infection in humans is generally low from beef, lamb, and pork, which do not appear to be a major source of human infection (Wallace et al., 2020). The rate of isolation from vegetables is very low; therefore, vegetables are considered a vehicle of *Campylobacter* transmission via cross-contamination rather than being the main source of infection (Santos-Ferreira et al., 2021). Non-chlorinated contaminated surface water (e.g streams, rivers, ponds, lakes, and canals) is considered to be a source of outbreaks of *campylobacter* in humans and is due to contamination by the fecal waste of domestic animals and wild birds or release from sewage (Igwaran and Okoh, 2019). As a result of contaminated water, shellfish might be contaminated with *Campylobacter* (Igwaran and Okoh, 2019). Many studies on the detection of *Campylobacter* in different types of seafood have been reported, with a moderately high isolation rate of *C. lari* from these products, such as Blue carb, oyster muscle, and tuna salad (Jurinović et al., 2022). Infections with *Campylobacter* resulting from travel outside the country of origin, and contact with farm animals and pets have been reported (Igwaran and Okoh, 2019). Transmission between human to human is unusual, though the incidence of *Campylobacter* infection commences as a result of ingestion of contaminated meat (St Charles et al., 2022).

Table 1 Sources and disease associations of *Campylobacter*

Campylobacter species/serotype	Hosts	Disease/Symptoms	Reference
C. jejuni (O:2, O:4, O:53)	Humans, Chickens, Cattle	Gastroenteritis, septic arthritis	(Imbrea et al., 2024)
C.coli (O:2, O:24, O:46)	Humans, Chickens, Swine	Diarrhea, Guillain barre syndrome	(Kemper and Hensel, 2023)
C. upsaliensis	Dogs, Cats	Hemolytic uraemic syndrome	(Liaw et al., 2019)
C. helviticus	Cats, Dogs	Bacteraemia, watery diarrhea	(Imbrea et al., 2024)
C.fetus	Humans, Cattle, Sheep	Abortion, bacteremia, fever	(Tikhomirova et al., 2024)
C. lari	Humans, Chicken, Gulls	Gastroenteritis, reactive arthritis	(Man et al., 2020)

C. sputorum	Cattle Sheep, Humans	Gastroenteritis, diarrhea	(Humphrey et al., 2007)
C. hyointestinalis	Swine, Cattle, Deer	Porcine proliferative arthritis	(Elmi et al., 2020)
C.fetus subs fetus	Bovine and Ovine abortion	Bovine and Ovine abortion	(Abd El-Hamid et al., 2019)
C. concisus	Humans	Periodontal disease, enteritis	(Hakeem and Lu, 2021)
C. mucosalis	Porcine necrotic enteritis	Porcine necrotic enteritis	(Igwaran and Okoh, 2019)
C. sputorum	Humans, cattle, pigs	Abscesses	(Zenebe et al., 2020)
C. cinaedi	Humans	Enteritis, proctocolitis, septicemia	(Man et al., 2020)

INCIDENCE AND DISTRIBUTION

Epidemiology of *Campylobacteriosis* in Developed Countries

Campylobacter spp. is the most prevalent food-borne pathogen in the USA, with an incidence of 19.5 cases per 100,000 people in 2018 (a 2% rise from the 2015–2017 period) (Lopes et al., 2021; Harrison et al., 2022). Human *Campylobacter spp*. infections are a prevalent cause of gastroenteritis in adults, with the majority of cases ascribed to poultry-borne disease (Thépault et al., 2017; Cadmus et al., 2019; Duarte et al., 2019; Liu et al., 2022a). Humans have been known to contract diarrhea from *C. jejuni* in which increasing doses of *C. jejuni* resulted in an increased rate of colonization but not illness development (Liu et al., 2022a). In these circumstances, a self-limiting bout of dysentery, stomach discomfort, fever, and vomiting are the hallmarks of a *C. jejuni* infection (CDC, 2021). Even though the sickness typically resolves on its own within a week (Thépault et al., 2018), symptoms can continue for up to two weeks (Marder et al., 2018; Duarte et al., 2019). Patients with *C. jejuni* infections develop acute watery or bloody diarrhea, fever, weight loss, and cramps that persist, on average, 6 days (Hansson et al., 2018; Marder et al., 2018). When a modest dose of the infection is used to infect someone, symptoms may take longer to appear and usually appear 24 to 72 hours after consumption, illness' peak can last 24 to 48 hours and may include appendicitis-like abdominal pain (Burnham and Hendrixson, 2018; CDC, 2021). While infection with *C. jejuni* can afflict patients of any age, a recent Danish study indicated that infection is more common in toddlers (1 to 4 years) and young adults (15 to 24 years) than in other age groups (Hansson et al., 2018; Elmi et al., 2021; Lopes et al., 2021). A recent study of patients infected with *C. jejuni* found that slightly older patients (34.6 versus 27.5 years) and those who had traveled abroad had a higher chance of developing C. coalition *C. jejuni* (Hassan et al., 2019; Liu et al., 2022a). *C. jejuni* infections are also more common in the summer (Liu et al., 2022a). Even though *C. jejuni* is more common in *Campylobacter spp* in many developed countries (Teksoy et al., 2023).

Epidemiology of *Campylobacteriosis* in Developing Countries

Generally, in most underdeveloped nations, there are no national *campylobacteriosis* monitoring programs, hence incidence values—the number of cases per 100,000 people—are not known (Iskandar et al., 2021; Liu et al., 2022a). In affluent nations, the presence of national surveillance programs has facilitated tracking of both isolated cases and outbreaks of human *campylobacteriosis* (Burnham and Hendrixson, 2018; CDC, 2020; Liu et al., 2022a). However, the majority of *Campylobacteriosis* data from developing nations were acquired as a result of WHO support provided to multiple laboratories there, including cash for epidemiological studies and Lior serotyping antisera contributed by the Public Health Service of Canada (Elhadidy et al., 2018; Hansson et al., 2018; Igwaran and

Okoh, 2019a; CDC, 2020). The majority of estimates of incidence in underdeveloped nations come from laboratory-based surveillance of the microorganisms that cause diarrhea (Ganesan et al., 2020). Campylobacter isolation rates in underdeveloped nations range from 5 to 20% (Authority, 2019; Tack et al., 2020; Elagib et al., 2023). Despite a scarcity of incidence data from national surveys, case-control community-based studies have estimated rates of 40,000–60,000/100,000 for kids under the age of five (Authority, 2018; Chi et al., 2018). *Campylobacteriosis* is frequently a pediatric ailment in underdeveloped countries and estimates of its prevalence in the general population in these nations are similar, at about 90 per 100,000 (Kuhn et al., 2018; Pascoe et al., 2020; Givanoudi et al., 2021). Since their original reports, the incidence and isolation rates in several developing nations have increased (Authority, 2019; Bravo et al., 2020). An actual rise in the incidence of diarrhea caused by campylobacter was recorded on the Caribbean Island of Curaçao and South America, even though this increase has frequently been attributed to improved diagnostic techniques (Lorena et al., 2018; Bravo et al., 2020; Pascoe et al., 2020).

The two main species found isolated in underdeveloped nations are *C. jejuni* and *C. coli* (Lopes et al., 2021). According to observations in the majority of developed nations, *C. jejuni* is more frequently isolated than *C. colic* in developing countries, *C. jejuni* and *C. coli* subtype strains have been identified using lior biotyping and serotyping techniques, the Penner serotyping scheme and DNA-based typing, which are widely used in developed countries, have been proposed for use in developing countries (Asmat and Khan, 2020; Clarke et al., 2021b). Species other than *C. jejuni* and *C. coli*, such as *C. upsaliensis*, *C. concisus*, and aerotolerant *campylobacters (Arcobacter),* may also be of pathogenic importance; however, diagnostic capability for these species is limited (CDC, 2020; Doyle et al., 2020; Elmi et al., 2021).

PREVALENCE AND ANTIMICROBIAL RESISTANCE

Prevalence of *Campylobacter* in Poultry

One of the main sources of the *Campylobacter spp.* based foodborne illnesses are contributed by poultry meat (Awad et al., 2018; Cadmus et al., 2019; Hassan et al., 2019). Diseases that occur due to *Campylobacter* species are mostly due to uncooked meat or while handling raw poultry (Asmat and Khan, 2020; Burnham and Hendrixson, 2018). In Spain, it has been observed that the broiler flocks contain *Campylobacter spp.* with an approximate percentage of 42.5% to 100% (Perez-Arnedo and Gonzalez-Fandos, 2019). The European Union, in their reports, highlights that their broiler flocks contained 27.3% and 12.3% *Campylobacter spp.* in their broiler flocks (Perez-Arnedo and Gonzalez-Fandos, 2019). From a very recent study, it was showed that poultry happens to be the major reservoir of the *Campylobacter* species and it causes the transfer of these bacteria among humans (Givanoudi et al., 2021; Lopes et al., 2021). Their study included 214 chickens, out of which 91.6% of chickens tested positive for the presence of *Campylobacter spp.* (Guyard-Nicodème et al., 2023). In a study in China, from the 1534 samples of poultry, 464 (which makes 66.3% of the total) samples were infected with *Campylobacter spp.* (Tang et al., 2020) Also, an article by Walker et al. (2019), that worked in three different states of Australia, highlighted that the prevalence of the bacteria in chicken meat was 90% and in chicken offal was 73% in general (Walker et al., 2019). Specifically, C. coli was the most prevalent species, which was present in 53% of chicken meat in NSW and 56% in Vic, and for chicken offal, the value rounded up to 77% in NSW, 59% in Qld, and 58% in Vic (Walker et al., 2019). A study by Gharbi et al. (2018), when considering isolates from North Tunisia, highlighted that 22.4% of the broiler flocks were

infected with *Campylobacter spp.* out of which the majority of the population was from *C.jejuni* (68.9%) which was followed by *C. coli* (31.1%) (Gharbi et al., 2018). Thus, from different statistical data from all over the world, it can be said that the prevalence of *Campylobacter* in poultry is extremely high. This was seen in a meta-analysis study, that was carried out by (Rossler et al., 2019) that stated that the prevalence of *Campylobacter spp.* was highest in North America and Europe and was the lowest in Oceania but the prevalence of the bacteria among poultry animals was almost the same in every other country (Rossler et al., 2019).

Antimicrobial Resistance of *Campylobacter* in Poultry

The antimicrobial resistance (AMR) in *Campylobacter jejuni* is a growing global health concern because this bacterium is generally known to be associated with foodborne (Kiran et al., 2021). *Campylobacter* species are often exposed to antibiotics that are used in livestock farming. This, overuse of antibiotics in the maintenance of the poultry can lead to the selection of resistant strains (Elhadidy et al., 2018). Now, these resistant strains are passed on to humans because the infected poultry acts as a major source of illness. Fluoroquinolones is an antibiotic that is routinely used to treat severe bacterial infections and *C. jejuni* has become resistant to this antibiotic (Whelan et al. 2019). This has become one of the most concerning aspects of AMR. Apart from this, poultry shows high resistance to tetracycline. In one study it was observed that 77% of chickens, 40% of game birds, and 100% of turkeys were resistant to Tetracycline (Varga et al., 2019). It was also observed that poultry is increasingly becoming resistant to nalidixic acid (79.6%), erythromycin (75.3%), azithromycin (66.7%), ciprofloxacin (64.5%), and gentamycin (35.5%) in China (Tang et al., 2020). The study by Gharbi et al. (2018) showed almost the same results as the other researchers, wherein the broilers were resistant to macrolide, tetracycline, quinolones, Chloramphenicol which ranged from 88.6% to 100% and some species, in a lower quantity were also resistant against, beta-lactam and gentamicin (47%-61.4%) (Gharbi et al., 2018).

Prevalence of *Campylobacter* in Cattle

Understanding the occurrence of Campylobacter spp. in cattle is crucial to both animal and human health, so it has attracted the interest of global health organizations. According to the World Health Organization (WHO), Campylobacter in cattle has a prevalence range of 20% to 30% globally, underscoring its significance (Plishka et al., 2021). Methods of collection and testing authorized by the European Union (EU) and the United Nations (UN) are crucial in gauging and tracking prevalence (Hlashwayo et al., 2020). These businesses know that the environment, managerial, and genetic elements all contribute to the complex Campylobacter environment in cattle with probable human transmission problems, as noted by WHO, an in-depth comprehension of these aspects is crucial for formulating successful international public health strategies (Walker et al., 2019; Hlashwayo et al., 2020). For the three Australian states, in a study by Walker et al. (2019), *C. jejuni* was more prevalent when compared to other species of the bacteria which was about 50-86% in beef, lamb, and pork offal in NSW. *C. coli* was also prominent (69%) in NSW except for lambs (Walker et al., 2019). It was also observed in the study that infection rates of Campylobacter were more prevalent in fresh lamb (46%) and pork (31%) when compared to frozen offal which accounted for 17 and 11% respectively (Walker et al., 2019). A study by (Rossler et al., 2019), showed that the prevalence of the bacteria in pigs was the highest in North America, Asia, and Europe when compared to countries like Africa. Similarly, for bovines, the highest prevalence was seen in North America and Europe when compared to Oceania and Asia (Rossler et al., 2019).

Antimicrobial Resistance of *Campylobacter* in Cattle

Antimicrobial resistance in cattle shows serious repercussions for human and veterinary medicine (Cazer et al., 2020). The examination of resistance patterns in cattle subsequently looks into the many medications to which Campylobacter has evolved opposition; offering barriers to successful treatment strategies (Cazer et al., 2020). The discourse, adhering to a One Health approach, stresses the interconnected nature of animal and human health, underlining the significance of integrated efforts to overcome resistant bacteria (Cazer et al., 2020; Badau, 2021; Hull et al., 2021). Looking ahead, the section on the next steps analyzes prospective study areas and strategies for tackling this challenge in cattle, integrating temporary therapies with long-term goals to ensure lasting remedies while safeguarding public health (Pascu et al., 2022). The resistance to antibiotics like Betalactams (42%), fluoroquinolones (41%), and tetracycline (15%) reduces the efficacy of these medications, which in turn, requires the use of stronger antibiotics which often leads to severe adverse effects. Approximately 2% of bacteria were also resistant to macrolides (Audu et al., 2022). In another study, carried out in Spain, by (Ocejo et al., 2019), it was observed that the beef cattle that as infected with *C. jejuni* showed higher resistance to fluoroquinolone (32% to 61.9%) and a decrease in tetracycline resistance in dairy cattle (from 75% to 43.2%). It was also observed that *C. coli* were more resistant to drugs when compared to *C. jejuni.* This affects patient management even more and raises the expenses that are associated with healthcare. Also, AMR is propagated in *C. jejuni* because of its genetic plasticity (Bunduruş et al., 2023a). This is because by making use of horizontal gene transfer, these bacteria can acquire resistance genes, which allows them to swiftly adapt to different drugs. Also, *C. jejuni* frequently forms biofilms in food processing settings which helps the resistant strains to survive and contaminate food items (Elgamoudi and Korolik, 2021). A meta-analysis that was conducted by (Van Boeckel et al., 2019) showed that most of the animals that were infected with *Campylobacter spp.* were almost always resistant to tetracycline (60%) and quinolones (60%) (Van Boeckel et al., 2019). The resistance against tetracycline was highest in 18 studies that have been considered, wherein the resistance percentage varied from 49.1% to 100% the study also showed that the resistance to erythromycin was moderate (less than or equal to 30%) but was higher in high-income countries which shows that the genes for resistance might be spreading by making use of mobile genetic elements (Van Boeckel et al., 2019).

Prevalence of *Campylobacter* in pigs

The prevalence of *Campylobacter in pigs* is indeed very high, with studies showing a wide range of prevalence rates from 0% to 92.7% in European countries (Garin et al., 2012). The dominant *Campylobacter* species found in pigs is C. coli, which is isolated from over 99% of pigs in some studies (Meister et al., 2019). The overall prevalence of *Campylobacter* isolated from pigs in the studies ranged from 27% to 53.7%. The dominant *Campylobacter* species found in pig farms surveyed, suggests that *C. coli* is a regular resident of pigs' digestive systems and accounts for over 99% of *Campylobacter* isolates according to studies (Tadesse et al., 2010). The notable prevalence can be attributed to factors such as frequent mixing of different age groups, insufficient biosecurity measures, and *Campylobacter*'s capacity to establish itself in the pig gut without inducing noticeable illness (Ansarifar et al., 2023).

A study in Ontario, Canada found that *Campylobacter* was recovered from almost all (99%) fecal and environmental samples collected from 80 grower-finisher pig herds (Delsart et al., 2020). The prevalence of *C. coli, C. lari,* and *C. jejuni* were 99.2%, 0.6%, and 0.2% respectively (Ansarifar et al., 2023). This demonstrates that C. coli is the dominant and virtually ubiquitous *Campylobacter* species in the pig gastrointestinal system (Papadopoulos et al., 2021).

A study in Nigeria reported a *Campylobacter* prevalence of 92.67% in 300 pig fecal samples, with *C. coli* being the most common species detected (74.19%), followed by *C. jejuni* (16.66%) (Sithole et al., 2021). The study also found higher *Campylobacter* prevalence in female pigs (95.71%) compared to male pigs (90%) (Kreling et al., 2020).

Another study in Cameroon found an overall *Campylobacter* prevalence of 27%, with 25.88% in pig rectums and 29.16% in pig carcasses (Baali et al., 2020). The study noted significant variation in *Campylobacter* prevalence across different slaughterhouse locations, likely due to factors like slaughter hygiene and animal mixing (Ansarifar et al., 2023).

Similarly, another study in Vietnam reported an adjusted prevalence of *Campylobacter* in pigs of 53.7%, with *C. jejuni* being the predominant species at 38.6% and *C. coli* at 14.1% (Di Donato et al., 2020). This study also found evidence of cross-species transmission of *C. coli* between pigs and poultry suggesting widespread distribution within the pig population (Tedersoo et al., 2023). The high prevalence of *Campylobacter*, especially *C. coli,* in pigs is believed to be due to it being a normal gut inhabitant of pigs (Kreling et al., 2020). This could be due to the influence of factors such as common mixing of age groups, low biosecurity, and the ability of *Campylobacter* to colonize the pig's gastrointestinal tract without causing overt disease (Rivera-Gomis et al., 2021).

Antimicrobial Resistance of *Campylobacter* in pigs

Antimicrobial resistance of *Campylobacter* in pigs is a significant concern due to the potential implications for public health (Agbankpe et al., 2022). Studies have shown that *Campylobacter* coli strains isolated from pigs exhibit high resistance to various antimicrobials, with multidrug resistance being a common concern (Šoprek et al., 2022). Several studies have examined the prevalence and antimicrobial resistance profiles of *Campylobacter* isolates from pigs (Duarte et al., 2024). The results show that a significant proportion of *Campylobacter* strains isolated from pig guts, feces, and cutting table surfaces showed resistance to tetracycline which was very high, reaching up to 86.7% in *C. coli* strains isolated from pig guts (Duarte et al., 2024). *C. jejuni* strains showed 100% resistance to amoxicillin and gentamicin, especially in samples from cutting tables (Šoprek et al., 2022). Erythromycin resistance was also common, with 50% of *Campylobacter* strains from fecal samples being resistant. Overall, 90.8% of the *Campylobacter* isolates were found to be multidrug-resistant (Gao et al., 2023).

The growth in multidrug-resistant *Campylobacter* strains in pigs has been attributed to variables such as uneven antimicrobial management techniques in animal production systems and the increased use of antimicrobials in recent years (Marin et al., 2021). Furthermore, research demonstrates the potential of CRISPR-Cas-based antimicrobials to target antibiotic-resistant *Campylobacter* (Tao et al., 2022). However, the advent of resistance mechanisms against CRISPR-Cas systems, such as anti-CRISPR genes, may reduce the efficiency of these novel antimicrobials. Studies have shown that *Campylobacter* strains are resistant to several antibiotics, emphasizing the importance of attentive monitoring and surveillance in addressing this issue (Shabbir et al., 2019).

Prevalence of *Campylobacter* in vegetation

Monitoring the occurrence of *Campylobacter spp.* in vegetation, specifically *Campylobacter jejuni*, is crucial for minimizing the risk of foodborne illness (Asmat and Khan, 2020; Doyle et al., 2020). In vegetation, elements like as water quality and methods of cultivation have a considerable impact on the incidence of *Campylobacter*, with *C. jejuni* constituting an especially significant contribution (Hakeem et al., 2020; Perez-Arnedo and Gonzalez-Fandos, 2019). Surveillance innovations such as genetics can indicate pollution levels in natural ecosystems (Perez-Arnedo and Gonzalez-Fandos, 2019). Examining various *Campylobacter*

transmission paths from dirty plants to humans and animals underlines the significance of maintaining adequate hygiene norms, according to the latest studies, polluted foliage can serve as a reservoir, with *Campylobacter spp*., including *C. jejuni,* discovered in roughly 70% of plants tested (Borges et al., 2020). In another study, the prevalence of the bacteria in fruits, vegetables, and other fresh produce was found to be 0.53% out of which the bean and the sprouts group had the highest percentage of 11.8% (Mohammadpour et al., 2018). In another study carried out by (Ssemanda et al., 2018), it was found that 5 out of 99 (which makes 5.1%) vegetables from the farm were infected with *Campylobacter spp.* which might have been caused by the irrigation, this is because it was also observed that 26 out of 30 irrigation water samples contained the DNA of *Campylobacter spp.* This was more common in Asia than in any other continent (Ssemanda et al., 2018). These results presented here underline the necessity of continued research aiming at preserving public health by eliminating contaminating hazards linked to plant-based sources of nutrition (Ssemanda et al., 2018; Perez-Arnedo and Gonzalez-Fandos, 2019; Asmat and Khan, 2020).

Antimicrobial Resistance of *Campylobacter* in Vegetation

According to recent studies, the occurrence of *Campylobacter spp.* in vegetation ranges from 10% to 30%, stressing its role in compromising food safety (Obermeier et al., 2021). Environmental factors such as water quality and animal proximity all contribute to levels of pollution, underscoring the significance of specific actions (Obermeier et al., 2021). To limit contamination hazards, careful farming methods and heightened hygiene procedures when harvesting are required (Obermeier et al., 2021; Ssemanda et al., 2018). Like in all other life forms, the plantations are also becoming resistant to antibiotics, because of the excessive use of fertilizers, fungicides, and insecticides which has made the vegetation mostly resistant to fluoroquinolone and macrolides because of mutations in genes like GyrA and GyrB (Shen et al., 2018). With an approximate (20%) incidence identified in (agricultural regions), real-time prevalence data tell pre-emptive efforts Information on customers' safe handling, full washing, and proper cooking processes is also crucial in lowering the likelihood of antibiotic resistance caused by *Campylobacter* in plant-based meals (Mduda et al., 2023).

Prevalence of *Campylobacter* in Pets

The prevalence of *Campylobacter spp.* in dogs and cats can be an important issue from both a public health and veterinary standpoint (Baker et al., 1999; Acke et al., 2009; Acke, 2018). This is because *Campylobacter* is a bacterial genus that contains many different kinds of species that are known to cause gastrointestinal disease in humans (Natsos et al., 2019; Goyal et al., 2021). The presence of these bacteria in dogs and cats which are also known as companion animals it is important to recognize their frequency in these animals so that the respective authorities can come up with strategies for illness treatment and prevention (Tack et al., 2020; Watkins et al., 2021).

Animals like dogs and cats can be carriers of *Campylobacter spp.* and can still be asymptomatic which can be even more injurious for humans because they would acquire the bacteria without even realising and this in turn can lead to issues of gastroenteritis. In a study carried out by (Goni et al., 2017; Goni et al., 2018) 101 rectal swabs were collected from both pets (n=40) and stray dogs (n=61) for a study and similarly 86 rectal swabs were collected from cats wherein 46 were from stray cats and 40 were from pet cats. The pet animals were from the clients and the stray animals belonged to the animal shelters (Goni et al., 2017). After the collection of the swabs, they tried to extract the DNA of the bacteria and then amplified it by making use of mPCR. The results of the assay showed that there was a minimum of three different strains that affected the animals in the sample which was

confirmed by analyzing the morphology of their cells as well as the biochemical properties of the strains (Goni et al., 2017; Goni et al., 2018). These strains were *C. helvicitus, C. upsaliensis, and C. jejuni.* When the researchers compared the prevalence of occurrence in the stray as well as the pet dogs, it was observed that there were no significant differences in occurrence however, stray dogs are higher carriers (16.4%) when compared to the pet dogs (12.5%) (Goni et al., 2018). On the contrary, the level of occurrence was significantly different for the stray and pet cats, wherein the stray cat was highly infected (32.6%) when compared to the pet cats (12.5%) also in comparison, it was found that *C. upsaliensis* was more prevalent (60%) when compared to *C. helviticus* (20%) and *C. jejuni* (11.4%) indicating the carriage rates of *Campylobacter* in both cats and dogs were high in this study, which means that the bacterium could be an intestinal commensal in the gut of these animals these could be seen as 11.4% of dogs and cats in aggregate carried *C. jejuni* wherein these animals act as zoonotic carriers that often transmit diseases like *Campylobacteriosis* and *Campylobacter enteritis* to humans (Goni et al., 2018).

A study carried out by (Mohan and Habib, 2019) has also highlighted younger dogs and cats (puppies and kittens) are more prone to carry the species of *Campylobacter* when compared to older animals. This is because older animals tend to develop immunity against the bacterium because of their previous encounters which are often missing in the younger animals (Gharibi et al., 2020) The prevalence of the bacterium is higher in stray dogs and cats because these bacteria are often found in the feces of the animals and the stray animals are more exposed to these environmental sources of the bacteria when compared to the pet animals (Thépault et al., 2020). Also, a different study which was carried out by Goni et al. (2018), highlighted that the prevalence of *Campylobacter spp.* is extremely high (approximately 97%) in cats and dogs all over the world which is also highly noticeable in Malaysia. This can be because these animals are often given the meat of the poultry to eat which could contain the specific bacteria, because these animals are close to humans, they can potentially harm the health of humans (Goni et al., 2018). Thus, these animals function as reservoirs of bacteria which can pose a threat to humans (Watkins et al., 2021). In a report in 2018, the EU highlighted that *Campylobacter* is known for causing food-borne illness which was responsible for 116 million cases of diseases out of which 96 million were associated with food-borne disease (Authority, 2018; CDC, 2020). There are numerous strains of the bacteria but the strain that has been identified more commonly in diseased individuals is *C. jejun*i (84.4%) which is followed by *C. coli* (9.2%) in the EU which has made the individuals suffer from abdominal pain, diarrhea and even fever (Givanoudi et al., 2019). A study by Goni et al. (2017), has also shown a comparison between the prevalence of different species of bacteria in different regions of the world. For instance, In Australia, Dogs contained 43% of the bacteria whereas cats were infected with 7.6% of the bacteria, in Barbados, the prevalence rate in dogs was 46.9% and cats were 37.3%, UK 38%, India 51%, Denmark 76%, Nigeria 23.8%, New Zealand- 36% in Dogs and 16% in cats and Malaysia 14.8% in Dogs and 23.2% in cats in different years (Goni et al., 2017). (Liu et al., 2018a) have also shown that it is important to identify the different strains of the bacteria that are present within the dogs and cats of the region because this knowledge would provide the researcher with an idea of which of the species of the bacteria is more prevalent, how is it transmitted, the intensity with which it can impact the humans and cause different diseases so that they can assess the impact of the different strains on human health (Liu et al., 2018a).

Antimicrobial Resistance of *Campylobacter* in Pets

The carriers of the species of *Campylobacter* are mostly cats and dogs, these bacteria are found in their guts (Acke, 2018; Burnham and Hendrixson, 2018). These finding highlights that stray and pet animals have the appropriate

environment to act as a host for these bacteria as dogs and cats are common animals that usually interact with humans, they also possess the ability to infect the individuals that come in contact with infected animals (Campagnolo et al., 2018). The authorities can carry out studies to understand the presence of these bacteria within these animals while also figuring out how it can impact humans and their health (Goni et al., 2017). Humans can contract these diseases either from raw or undercooked meat products or from animals that act as reservoirs for the bacteria (Marder et al., 2018; Pascoe et al., 2020). If these animals harbor drug-resistant germs, they increase the likelihood that these bacteria will survive, spread, and infect humans. As a result, there will be fewer medications available to aid in the treatment of illnesses (Shen et al., 2018; Audu et al., 2022).

The resistance of dogs and cats towards antibiotics is constantly increasing and this can be attributed to the extreme use of the drugs among these animals (Shen et al., 2018; Van Boeckel et al., 2019). Antibiotics were once used for the treatment of diseases that were caused by microbes but over some time, these microbes developed resistance (Goni et al. 2017) Tetracycline, ampicillin, norfloxacin, and erythromycin are the most common drugs that are used for the treatment of bacterial diseases (Syamsyul and Maswati). Animal resistance to these common drugs can hamper their effectiveness thereby making sure that they will no longer be used for treatment (Syamsyul and Maswati). These drugs are mostly used to treat common gut diseases of humans and the resistance towards these drugs can significantly impact their use as treatment choice (Shen et al., 2018). In considering the case of *Campylobacter spp.* the species that was the most resistant to tetracycline was *C. jejuni*. Around 99.5% of the species were resistant to the drug which was followed by *C. coli* wherein 96.3 % of the species were resistant to it in Spain (Goni et al., 2017). The resistance rate among the animals who were infected with *C. coli* and *C. jejuni* for the antibiotic enrofloxacin was 58.2%, for nalidixic acid was 49.1% and for erythromycin was 14.5% (Goni et al., 2017). Knowing the extent to which the animals are resistant is important so that the researchers as well as the healthcare professionals can come up with different drug solutions that will be used for the treatment of the animals and the humans associated with these animals (Van Boeckel et al., 2019).

Campylobacter in Wild Birds, Rodents, and Insects

C. jejuni has been detected in wild birds including pigeons, crows, geese, ducks, and cranes that fly over or are found on grazing land (Mohan, 2015; Du et al., 2019b). Migratory birds could contaminate the herd with *Campylobacter* (Du et al., 2019b). Utensils, insects such as flies, rodents such as rats, and free-living birds are also found to carry *Campylobacter* and could be possible sources of contamination (El-Saadony et al., 2023a). Some studies abroad have shown that *Campylobacter spp.* were carried by 45% of sparrows (Passer spp.), 57% of rodents, 11% of rodents and 9% of flies in dairy farms 5% of flies in poultry farms (Casalino et al., 2022) and 8.2% of flies in broiler house (Casalino et al., 2022; El-Saadony et al., 2023a).

Campylobacter water

Several outbreaks of *Campylobacter* gastroenteritis were found associated with drinking contaminated water, non-chlorinated municipal tap water, private water supplies, and contact with unprocessed water (Hyllestad et al., 2020). *Campylobacter* organisms have been successfully isolated from lake water; river water, well water, pond water, streams, and groundwater (Strakova et al., 2022). The transmission of *Campylobacter* species to broiler chickens may also be due to contaminated groundwater sources (Hakeem and Lu, 2021). Some studies reported that water from private supplies seems to be a threat factor for the colonization of *Campylobacter spp.* in young cattle (Rapp et al., 2023). It has been demonstrated that contaminated water can be a vehicle of *Campylobacter*

transmission among cattle (Mulder et al., 2020). In an extensive water-borne infection in Canada, it was reported that one cattle farm was supplied with *C. jejuni* contaminated municipal drinking water (Igwaran and Okoh, 2019). Although *Campylobacter* is considered to be ubiquitous in aquatic circumstances, the finding of these bacteria can be complicated due to injury, incapable to adjust to in vitro situations, and/ or present in low numbers (Igwaran and Okoh, 2019).

Multi-Drug Resistance

Campylobacter jejuni is a prominent bacterial pathogen that is known to cause food-borne diseases that can be caused by multidrug resistance and poses a serious concern in public health (CDC, 2020). This resistance, which makes the bacteria survive in the presence of numerous antibacterial drugs can be caused by different factors. From the data provided by (Whelan et al., 2019), *C. jejuni* can develop resistance because of spontaneous genetic mutations. These mutations can alter the structure and functions of the specific proteins of the bacteria which makes the antibiotics less effective especially when mutations are present in the genes that are known for encoding DNA gyrase which is also known as topoisomerase then it can help the bacteria survive in a medium that contains quinolones and fluoroquinolones like ciprofloxacin (Whelan et al., 2019). These genetic modifications are selected under pressure when such bacteria are grown in the environment that contains these antibiotics which leads to the development of the resistant strains (Hull et al., 2021). *C. jejuni* can also acquires resistance genes by making use of a technique called horizontal gene transfer which can be done by making use of plasmids and transposons (Samarth and Kwon, 2020). This can be explained for instance, if there exists a strain of *C. jejuni* that is resistant to tetracycline because of chromosomal mutation, then there can be a possibility that this strain of the bacteria can contain a plasmid that contains a gene that could confer resistance to the antibiotics (de Fátima Rauber Würfel et al., 2020). When this resistant strain of bacteria comes in contact with other bacteria, these plasmids can be transmitted which in turn would allow the recipient bacteria to acquire antibiotic resistance genes (Ma et al., 2021). This then makes the recipient microorganism, which was not resistant to this antibiotic previously quickly develop multidrug resistance, similarly transposons which are also known as jumping genes can migrate inside the DNA of the bacteria which can transport genes for resistance and insert them into various parts of the bacterial genome (Hull et al., 2021). For instance, a resistant *Campylobacter* strain that contains transposons harboring resistance genes can spread these transposons during contact with other *Campylobacter* strains and even different species of bacteria (Shen et al., 2018). This transfer will allow the recipient bacteria to acquire antibiotic-resistance genes, this process is especially concerning because it not only spreads resistance within *Campylobacter* populations but also has the potential to lead to the formation of entirely new multidrug-resistant strains (Low et al., 2021). Thus, the acquisition of resistance genes from numerous origins can result in bacteria acquiring resistance genes that were not initially present in the initial strain as a result, these newly developed strains can show even higher levels of resistance, which can pose greater challenges in clinical (Kreling et al., 2020).

Antibiotics are used in food animals so that they can promote their rapid development and increase in weight, this approach has been in use for decades because it is known to increase the efficiency of the industry and its profitability (Lillehoj et al., 2018). It does however, subject these animals to subtherapeutic amounts of antibiotics over extended periods which often leads to the development of a selection pressure which often leads to the growth of antibiotic-resistant bacteria such as *Campylobacter jejuni* (Low et al., 2021). Antibiotics are also used to prevent illness in crowded and typically unclean animal farming situations and are especially prevalent in intensive farming operations when animals are confined in close quarters, however, usage of preventative antibiotics lowers the likelihood

of illness outbreaks, but it also contributes to the selection and spread of antibiotic-resistant *Campylobacter* strains in these (Espinosa et al., 2020). Therefore, multidrug resistance when developed in *C. jejuni* can have numerous serious repercussions for public health as it can restrict healthcare practitioners in making treatment choices, which will make *Campylobacter* infections more difficult to control (Khan et al., 2019). This would lead to hospitalization and intravenous antibiotics in severe instances which would put additional pressure on the healthcare systems, therefore multidrug-resistant *Campylobacter* infections can prolong sickness and increase the costs that are related to healthcare thereby making the patients experience more severe and prolonged symptoms, which would result in increased medical costs and decreased quality of life (Elhadidy et al., 2018). The emergence of multidrug resistance in *Campylobacter* compromises the efficiency of antibiotics, the decrease in effective antibiotics would hinder the capability of healthcare professionals to tackle not only *Campylobacter* but also other bacterial diseases which will act as a major issue for public health (Khan et al., 2019a).

Table 2 Antibiotic resistance mechanisms found in *Campylobacter jejuni*

Antibiotic Classes	Encoding Genes	Resistance Mechanism	References
Quinolones	gyrA	Modification of the DNA gyrase target (Thr-86-Il; Asp-90-Asn-70-Thr) Efflux through CmeABC	(Aleksić et al., 2021) (Bunduruş et al., 2023)
Tetracycline	tet(O)	Modifications of the target ribosomal A site by TetO binding Efflux through CmeABC and possibly others	(De Gaetano et al., 2023)
Macrolides	23rRNA	Mutations in 23rRNA Mutations in ribosomal proteins L4/L22 are likely minor Efflux through CmeABC and possibly others Decreased membrane permeability due to MOMP	(Low et al., 2021)
Aminoglycoside	aphA, aadE	Modification of the antibiotic by modifying enzymes	(Lynch et al., 2020)
Beta-Lactam	blaOX-61	Inactivation of the antibiotic by enzyme B-lactamase	(Lyu et al., 2023)
	blaOX-184		(Pascu et al., 2022)

Risk factors associated with *Campylobacter*

Campylobacter spp. are frequently linked to human foodborne disease with over 246,571 cases recorded in 2018, *Campylobacter spp.* constitute the predominant cause of bacterial foodborne zoonosis in Europe (Thépault et al., 2018). The ingestion of contaminated food items is linked to several risk factors for human infection by *Campylobacter spp.* But these diseases can also infect poultry, cattle, and pets respectively therefore to stop the spread of illness and safeguard animal health, veterinarians' farmers, and pet owners must be aware of the risk factors related to *Campylobacter spp* (Thépault et al., 2018; Tang et al., 2020; Bunduruş et al., 2023a).

In companion animals, *Campylobacter jejuni* and *Campylobacter upsaliensis* are the two most prevalent species (Aslantaş, 2019). The majority of subclinical hosts of *Campylobacter spp.* in dogs and cats include *C. helveticus*, *C. upsaliensis*, *C. jejuni,* and *C. coli* in certain situations these bacteria may even result in clinical symptoms in pets who have digestive problems (Aslantaş, 2019; Watkins et al., 2021). Risk factors associated with pets include age (juvenile, adult), breed (local, pedigree), housing (outdoor, indoor, semi-roamer), household density (multi-pet, single), antibiotic history, duration of antibiotic, contact with other animals, water source (filtered, unfiltered), food (home-made food, pet food, mixed pet food, and

home-made, leftovers (Watkins et al., 2021). A study by (Davies et al., 2019) found that *Campylobacter jejuni* was identified in 22% of raw retail pet meals in New Zealand. A correlation between moist (but not necessarily raw) feeding in dogs and cats and rectal swabs positive for *Campylobacter upsaliensis* was found in the same study using univariable analysis (Davies et al., 2019). Poultry may potentially come into contact with *Campylobacter spp* via Several risk factors which can result in the introduction of *Campylobacter* into flocks, and once there, *Campylobacter* quickly spreads to all birds and vast numbers are shed, resulting in severe contamination of the broiler house environment and equipment (Battersby et al., 2017). *Campylobacter* origins and transmission channels in chicken flocks have been thoroughly examined, with a focus on various production procedures and practices (Battersby et al., 2017). The main potential risk factors proposed include season (summer and/or autumn), higher age of broilers at slaughter, use of partial depopulation practice, distribution of drinking water and its quality, contaminated food or water sources, presence of other animals in the farm's surroundings or on the farm itself (Battersby et al., 2017; Hansson et al., 2018; Cadmus et al., 2019). In contrast, *Campylobacter* infection can be decreased by farmers using proper hygiene in addition, giving poultry unfiltered water from potentially infected sources can also spread illness (Gharbi et al., 2018; CDC, 2020; Givanoudi et al., 2021). Cattle are more likely to have *Campylobacter* infections while living in unclean environments and practicing poor personal hygiene, such as poor management practices, consumption of contaminated food, water, or unpasteurized milk, as well as contact with animals or their feces have been identified as risk factors for *Campylobacter* infections (Walker et al., 2019; Pascu et al., 2022). According to (Kananub et al., 2020), the high incidence of the various pollutants in raw beef products may be caused by poor hygiene and sanitation in manufacturing facilities. Moreover, inadequate sanitation procedures are used in the milking and storing processes, a dearth of clean water sources, and a lack of knowledge about the dangers of drinking raw or tainted milk (Thomas et al., 2020). The establishment of *Campylobacter* strains resistant to antibiotics may also be facilitated by the use of antibiotics in cattle production (Amenu et al., 2019). In one of the investigations, (Peter et al., 2019) indicated that raw food and undercooked food were both harmful for a specific cause. The gastrointestinal tracts of farm and wild animals are natural reservoirs for *campylobacter* species, which are extensively distributed around the world, according to the author, direct contact with carrier animals has also been identified as a potential cause of infection (Peter et al., 2019). Infections with *Campylobacter spp*. are a risk for humans, cattle, poultry, and pets alike. The welfare of animals must be taken into consideration to deal with the risk factors linked to these illnesses therefore farmers, veterinarians, and pet owners can provide early diagnosis and treatment when needed, maintain sanitation, and put preventative measures into practice (Peter et al., 2019; Walker et al., 2019; Obermeier et al., 2021; Plishka et al., 2021).

CAMPYLOBACTER JEJUNI: PATHOGENICITY AND VIRULENCE FACTORS PATHOGENICITY

Pathogenesis: Adhesion, invasion, and survival mechanisms

Campylobacter jejuni's journey into pathogenicity begins with its remarkable adaptability, allowing it to thrive in diverse gastrointestinal environments of various host species, serving as both a reservoir and a source of illness (Ball, 2022). The bacterium's spiral morphology and exceptional flagellar motility enable efficient traversal across the mucosal layer, facilitating access to the epithelial lining of the digestive tract (Dechka, 2022). Survival within the host environment involves the

formation of biofilms, providing *C. jejuni* with resilience against environmental cues and immune responses, where specific interactions between bacterial components and host defense systems modulate disease progression (Ball, 2022). Upon colonization, the bacterium elicits robust inflammatory responses, contributing to the typical symptoms of campylobacteriosis, including diarrhea, abdominal discomfort, and fever (García-Sánchez et al., 2018). The ability of *C. jejuni* to modulate host cell signaling pathways and disrupt epithelial barrier function contributes to the pathogenesis of infection and the development of clinical symptoms (Xue et al., 2018). Recognizing the complexities of pathogenicity and the fundamental destructiveness components is vital for concocting successful control and counteraction techniques (Hou et al., 2021). The pathogenesis of Campylobacter infections involves several mechanisms, including adhesion, invasion, and survival within host cells.

ADHESION

Adhesion is the initial step in the interaction between *Campylobacter* and host cells (Elshafie et al., 2019; Prasad et al., 2020). The adhesion of *Campylobacter jejuni* to host cells is mediated by various factors, such as flagella, CadF, Peb1A, and Capsular polysaccharides, which promote maximal adhesion by stimulating membrane ruffling (Heimesaat et al., 2014; Esbelin et al., 2018). *Campylobacter* species adhere to the epithelial cells lining the gastrointestinal tract, particularly in the small intestine by various surface structures and adhesins, including: *Campylobacter* species are highly motile due to polar flagella, which also aid in initial adhesion to host cells (Hermans et al., 2011; Esbelin et al., 2018).

CadF: A fibronectin-binding protein present on the outer membrane of *Campylobacter,* facilitates adhesion to host cells by binding to fibronectin on the host cell surface (Konkel et al., 2020c; Talukdar et al., 2020).

Peb1A: An additional protein on the outer membrane that aids in attachment to epithelial cells.

Capsular polysaccharides: *Campylobacter* produces capsular polysaccharides that contribute to adhesion to host cells and resistance to host defenses (Konkel et al., 2020c; Talukdar et al., 2020).

Adherence to cells is a crucial stage in *C. jejuni* pathogenesis (Hou et al., 2021). Flagellar mobility is the primary means of pathogenicity for *C. jejuni.* The bacterium's remarkable flagellar structure, which is made up of FlaA and Fat proteins, is responsible for its winding shape (Lopes et al., 2021). These flagella not only drive *C. jejuni* nevertheless also assume a key job in cell attacks (Lopes et al., 2021). Different surface designs, including capsular polysaccharides and external film proteins (such as CadF and FlpA), provide adhesion to cell surfaces and initiate binding forces to the cell wall, facilitating the invasion of the host cell (Hou et al. 2021). The attack contact involves triggering host cell signaling pathways, leading to cytoskeletal changes that facilitate the entry of *C. jejuni* into the host cells (Hou et al., 2021). *C. jejuni* produces toxins with cytotoxic and enterotoxic effects (Hsieh and Sulaiman, 2018). The cytolethal distending toxin (CDT) induces DNA damage, leading to cell cycle arrest and contributing to tissue damage. (Hsieh and Sulaiman, 2018). Enterotoxins disrupt ion transport, resulting in diarrheal symptoms. Together, these toxins enhance the pathogenicity of *C. jejuni* (Di Savino et al., 2022). The creation of a polysaccharide case is a huge destructiveness figure in *C. jejuni* (Crha, 2019). This container adds to serum blockage and avoidance of phagocytosis, enhancing bacterial endurance inside the host (Crha, 2019). The infection's role in evading the host's immune response enhances the bacterium's ability to establish and persist without causing illness. (Hou et al., 2021). *C. jejuni* uses the Sort VI Emission Framework (T6SS) for cell infiltration and intracellular endurance (Rudzite et al., 2023). This emission framework delivers effector proteins

easily into cells, regulating cell cycles to enhance the effectiveness of the bacteria (Rudzite et al., 2023). CcpA is a significant element utilized by *C. jejuni* to combat oxidative pressure encountered during host interactions (Di Savino et al., 2022). This aptitude boosts the bacterium's capacity to get by inside the host climate (Di Savino et al., 2022).

INVASION

Invasion is the process by which *Campylobacter jejuni* enters host cells and establishes an intracellular niche (Ó Cróinín and Backert, 2012; Kemper and Hensel, 2023b). The invasion of host cells by *Campylobacter jejuni* involves several mechanisms, including the "zipper" mechanism of invasion, which involves the high-affinity binding of bacterial surface adhesins to their cognate receptors on mammalian cells (Ó Cróinín and Backert, 2012; Bereznicka et al., 2022). Multiple invasion mechanisms facilitate *C. jejuni*'s entry into host cells, potentially leading to systemic infection (Kemper and Hensel, 2023b). These mechanisms include: - Mediated invasion: *Campylobacter* utilizes its flagella to move between microvilli and invade the epithelial cells (Kattner, 2023; Kemper and Hensel, 2023b). Membrane ruffling: *Campylobacter* induces rearrangement of host cell membrane components, leading to the formation of ruffles that engulf the bacteria. Intracellular survival: Once inside host cells, *Campylobacter* can survive and replicate within intracellular compartments, evading host immune responses (Nasser et al., 2022; Hong et al., 2023).

(Meuskens et al., 2019; Kemper and Hensel, 2023b). Host factors such as fibronectin, integrin beta1, FAK, Tiam-1, DOCK180, and Rho GTPase Rac1 play crucial roles (Chiang et al., 2021; Sharafutdinov et al., 2022). These factors activate integrins, triggering cytoskeletal rearrangements within host cells, and facilitating bacterial internalization. Specifically, integrins α5β1 promote focal adhesion kinase (FAK) phosphorylation, leading to the activation of Rac1 GTPase and actin filament remodeling, thereby enhancing *C. jejuni* invasion into host epithelial cells (Romero et al., 2020; Sharafutdinov et al., 2022).

During *C. jejuni* infection, actin filament rearrangement, microtubule dynamics, and endocytic pathways play roles in the invasion process (Lee et al., 2020; Romero et al., 2020). LC3 has been implicated in *C. jejuni* invasion signaling through the Rac1 pathway (Fukushima et al., 2022; Kemper and Hensel, 2023b). The LIR motif is essential for selective autophagy during *C. jejuni* infection (Lee et al., 2020; Fukushima et al., 2022). The *Campylobacter jejuni* effector protein CiaD utilizes the host cell protein IQGAP1 to promote cell entry (Negretti et al., 2021). This highlights that *C. jejuni* invasion of cells is a pathogen-driven process dependent on both cell binding and effector delivery (Lopes et al., 2021; Negretti et al., 2021; Fukushima et al., 2022).

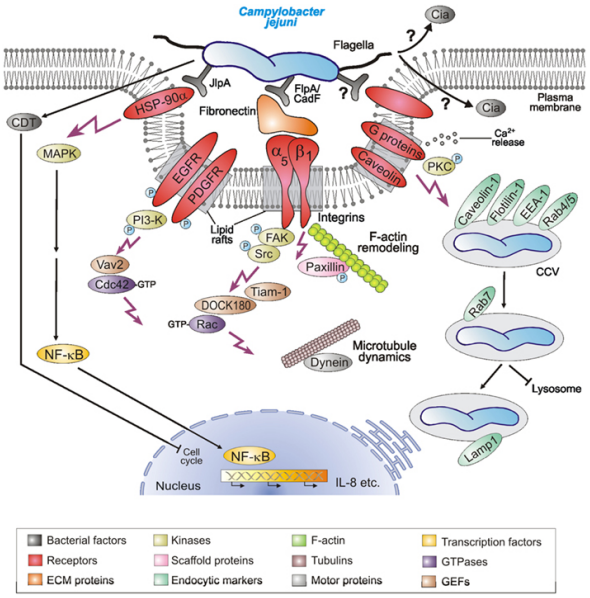

Figure 1 Hypothetical model for *C. jejuni* -induced signaling events leading to bacterial invasion and establishing infections (Costa and Iraola, 2019).

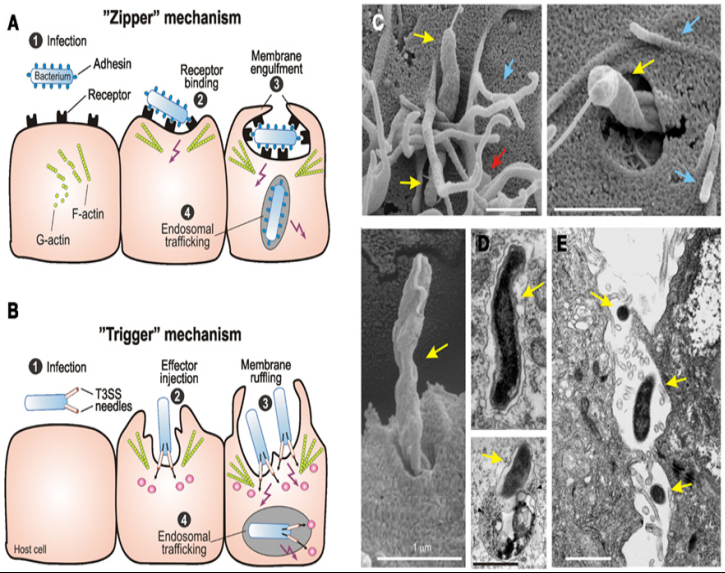

Figure 2 Schematic representation of the two different routes of entry by intracellular bacterial pathogens (Ó Cróinín, T., and Backert, S., 2012).

SURVIVAL

Survival is the ability of *Campylobacter jejuni* to persist within host cells and evade host immune responses (Al Hakeem et al., 2022b). The intracellular survival of *Campylobacter jejuni* is influenced by diverse mechanisms, enabling adaptation to various stress conditions (Elmi et al., 2021). These mechanisms encompass the inhibition of host cell apoptosis and modulation of host cell immune responses which are achieved through the action of its enzymes, including catalase, superoxide dismutase, and peroxidases (Kumar et al., 2022; Pawłowska et al., 2023). These enzymes play a crucial role in neutralizing reactive oxygen species generated by host immune cells (Bassoy et al., 2021; Wang et al., 2021b).

Survival is also triggered by the regulation of genes involved in adhesion, invasion, and intracellular survival, these genes such as Cj1492c and Cj1507c play a crucial role and are implicated in host cell adhesion and invasion (Xi et al., 2020; Corcionivoschi et al., 2023a). Mutations in these genes can significantly impact *Campylobacter jejuni's* ability to adhere to and invade host cells (Lopes et al., 2021; Kemper and Hensel, 2023b).

The ability to transition into a viable but non-culturable (VBNC) state in response to environmental stressors such as pH, moisture content, temperature, nutrient availability, and salinity is a notable feature of *Campylobacter jejuni* (Kim et al., 2021; Pazos-Rojas et al., 2023a). Once in the VBNC state, the organism must maintain an energy balance, relying on substrate oxidation through respiration to sustain growth, division, and viability (Pazos-Rojas et al., 2023a). *C. jejuni* can adapt to environmental challenges by demonstrating aerotolerance and surviving periods of starvation (Wang et al., 2021b). Factors such as biofilm formation, the VBNC state, and interactions with other microorganisms also contribute to its survival outside the host (Li and Zhao, 2020; Mgomi et al., 2023).

Campylobacter jejuni can remain viable for up to 7 months in phosphate-buffered saline at 4°C, retaining cellular integrity and respiratory activity (Duffy and Dykes, 2009; Khattak et al., 2022). This adaptability to various environmental conditions is pivotal in the transmission of *C. jejuni,* either directly to humans or indirectly through interactions with farm animals (Kemper and Hensel, 2023a).

C. jejuni exhibits rapid adaptation to environmental conditions facilitated by phase variation, quorum sensing, and extensive posttranslational O- and N-glycosylation. These mechanisms enable the bacterium to effectively navigate and transmigrate through the intestinal epithelial cell layer, culminating in infection (Klančnik et al., 2020; Tram et al., 2020).

VIRULENCE FACTORS

The virulence factors of *Campylobacter jejuni* are crucial for the pathogenesis of the bacterium, enabling it to colonize, adhere, invade, and secrete toxins in the host and to provoke the innate immune response (Kreling et al., 2020b; Lopes et al., 2021).

The Flagellum

The versatile polar, amphitrichous flagella of *Campylobacter jejuni* serve as multifunctional bacterial appendages pivotal for pathogenesis (Kreling et al., 2020b; Nedeljković et al., 2021b). They regulate motility, chemotaxis, adhesion to host cells, secretion of virulence factors, autoagglutination, microcolony formation, biofilm formation, and evasion of the host's innate immune system (Keeling et al., 2020b; Bai et al., 2021). The flagellum also plays a role in chemo-attraction and chemo-repulsion, by facilitating highly efficient penetration of the host's viscous intestinal mucin layer, crucial for colonization and overall pathogenicity (Colin et al.,

2021). By providing essential mobility, these flagella enable cells to navigate through the mucin layer with remarkable efficacy (Colin et al., 2021; Akahoshi and Bevins, 2022).

Both amphitrichous flagella have similar lengths of about one helical turn, or 3.53 ± 0.52 µm (Inoue et al., 2018). A flagellum consists of the basal body, the hook, and the filament *C. jejuni* possesses two polar flagella which consist of the flagellar filament and the basal body with the MS and C ring, encasing the type III secretion system and the hook and rod traversing the bacterium's cell surface (Zhou and Roujeinikova, 2021). The flagellar filament is composed of O-glycosylated flagellin proteins FlaA and FlaB. The basal body is surrounded by the basal, medial, and proximal disc which are composed of FlgP, PflA, and MotAB. The MS ring is formed by FliF multimers and the C ring of FliG multimers. The T3SS secretes flagellar proteins, Cia, and Fed proteins (Zhou and Roujeinikova, 2021; Gabbert et al., 2023).

Regulation of flagellar formation in cell physiology involves different flagellins and is subject to various regulatory checkpoints (Gabbert et al., 2023). The flagellar number and polar position are controlled by the flagellar motor switch proteins FlhF-GTPase and FlhG-ATPase, where FlhG-ATPase modulates the activity of FlhF. FlhG also inhibits the polymerization of the cell division protein FtsZ, thus impacting symmetrical cell division (Homma et al., 2022). Flagellin transcription is governed by the FlgS sensor kinase, which interacts with the FliF and FliG multimers involved in the formation of the MS and C ring (Alvarado et al., 2020; Vannini et al., 2022).

Campylobacter jejuni utilizes flagella at each pole to navigate through the viscous mucosa of its host's gastrointestinal tract (Ribardo et al., 2023). These flagellar motors generate significantly higher torque compared to those found in Enterobacteriaceae. The flagellar filament is composed of two distinct zones, each consisting of distinct flagellin proteins, FlaA and FlaB. Mutants lacking either all-FlaA or all-FlaB exhibit inferior motility compared to wild-type strains with composite filaments assembled from both flagellin types (Cohen et al., 2020a). *C. jejuni*'s flagellum consists of seven protofilaments made up of FlaA and FlaB subunits, whereas enteropathogens typically have flagella composed of a helix of 11 protofilaments. The heavily glycosylated flagellin of *C. jejuni* lacks the binding site for Toll-like receptor 5 (TLR5) (Kreutzberger et al., 2020). The flagellar hook forms a curved protein filament that efficiently connects the basal body with the flagellum, enabling rotation (Cohen et al., 2020a; Al Hakeem et al., 2022a).

The flagellar filament may contain up to 20,000 copies of one or more flagellin proteins. In many bacterial species, the D1 domain of flagellins contains the region recognized by innate immune Toll-like receptor 5 (TLR5), while the D2 and D3 domains exhibit greater variability among species and are predominantly surface-exposed (Kreutzberger et al., 2020). These domains are often adorned with sugar moieties in various bacterial strains, contributing to microheterogeneity (Kreutzberger et al., 2020; Nedeljković et al., 2021a).

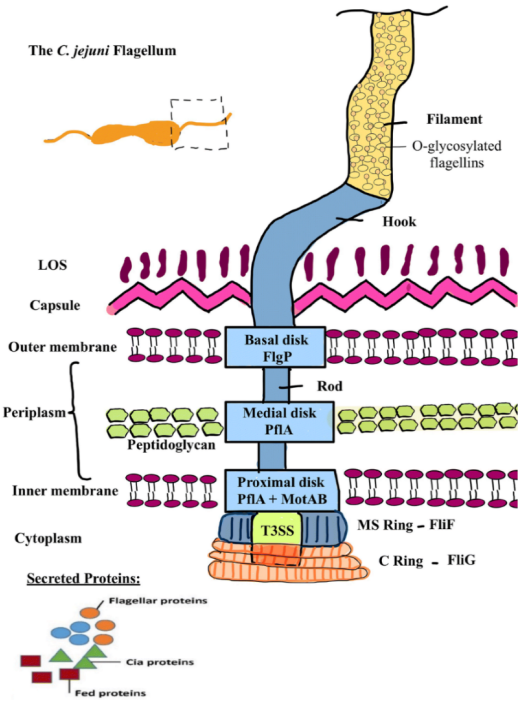

Figure 3 The *C. jejuni* flagellum, Adapted according to Burnham and Hendrixson (2018).

Adhesion Proteins

The virulence of *C. jejuni* is attributed to various factors, including adhesion proteins, which are crucial for bacterial adhesion to host cells and invasion into host cells (Kovács et al., 2020). In contrast to other bacteria like E. coli and Salmonella, C. *jejuni* does not rely on fimbriae or pili for adherence (Corcionivoschi et al., 2023b). Instead, it utilizes various adhesion-related factors such as CadF (*Campylobacter* adhesion to Fibronectin protein), FlpA (fibronectin-like Protein A), and JlpA (Jejuni lipoprotein A) (Jug et al., 2024). Adhesion is a critical step in the infection process, and *C. jejuni* possesses a variety of adhesins that mediate or influence bacterial adhesion to different cell structures (Ofek et al., 2003). The best-studied adhesin is CadF, a 37 kDa outer membrane protein that binds to the fibronectin of epithelial cells. Fibronectin is a 220 kDa glycoprotein present in the basement membrane and lamina propria of the intestinal epithelium (Speziale et al., 2019). The fibronectin-binding domain of CadF, a 4-amino acid sequence (Phe-Arg-Leu-Ser), has been identified. Binding to fibronectin activates a β-integrin receptor and results in phosphorylation of the epidermal growth factor receptor, which in turn activates the Erk1/2 signaling pathway and recruits and activates the GTPases Rac1 and Cdc4 (Fujita et al., 2020). These events initiate the internalization of *Campylobacter* via rearrangement of the cytoskeleton and subsequent membrane ruffling. CadF plays a role in the colonization of chickens and reduces *Campylobacter* internalization into INT407 cells by cadF mutants (Kreling et al., 2020a). The fibronectin-binding domain of CadF is also involved in the adhesion of *C. jejuni* to INT407 cells (Talukdar et al., 2020). The role of cadF in

adhesion and invasion is further supported by the observation that cadF mutants are defective in adhesion and invasion of INT407 cells (Schmidt et al., 2019) (Harrer et al., 2019).

Capsule Polysaccharides

Campylobacter polysaccharide capsules (CPS) are important virulence factors in *Campylobacter jejuni,* they are involved in the attachment and invasion of the colonic epithelium, leading to inflammation of the bowel and diarrheal symptoms (Mousavi et al., 2020). In severe cases, symptoms can progress to septicemia, post-infectious arthritis, Guillain-Barré syndrome, Miller-Fisher syndrome, or chronic bowel disorders such as Crohn's disease and ulcerative colitis (Jayasundara et al., 2022).

These capsules are pivotal for the bacterium's virulence (Jayasundara et al., 2022; Kovács et al., 2020). The capsular polysaccharide (CPS) of *C. jejuni* plays a central role in the Penner serotyping scheme, aiding in the categorization of different CPS types based on specific serotypes (Clarke et al., 2021a). Situated in the hypervariable region of the genome, the CPS biosynthesis loci enable the development of multiplex PCR techniques for CPS-type classification, spanning approximately 22.8 kb and deemed essential for bacterial survival and pathogenicity (Xiahou et al., 2023). Recent research endeavors have concentrated on identifying novel capsule biosynthesis loci of *C. jejuni* to refine CPS-type classification (Khemnu et al., 2023). Leveraging next-generation sequencing and whole genome analysis, new capsule biosynthesis loci have been uncovered, facilitating the identification of previously untypeable CPS *C. jejuni* isolates (Khemnu et al., 2023). Tailored PCR primers, such as the epsilon PCR mix, have been formulated to pinpoint these novel capsule biosynthesis loci, offering further insights into the biosynthesis of common CPS sugars like deoxtyheptose and MeOPN (Nomura et al., 2024). Research indicates that the capsular polysaccharide (CPS) of *C. jejuni* plays a pivotal role in its pathogenicity (Kreling et al., 2020a). Mutants lacking capsules exhibit diminished virulence, underscoring the significance of CPS in colonization and defense against complement-mediated killing (Gao et al., 2024). The advancement of capsule polysaccharide conjugate vaccines against *C. jejuni* has emerged as a promising strategy for combatting diarrheal diseases associated with this pathogen (Bertolo et al., 2012). These vaccines are designed to target specific CPS types, augment immune responses, and confer protection against *C. jejuni* infections (Kovács et al., 2020; Kreling et al., 2020b).

Cytolethal distending toxin (CDT)

Cytolethal distending toxin (CDT) is a genotoxin synthesized by the bacterium *Campylobacter jejuni* (He et al., 2019b). It instigates host cell cycle arrest and apoptosis, thereby exacerbating tissue damage and inflammation in the gut (Zhao et al., 2023a). It is composed of three subunits: CdtA, CdtB, and CdtC which are encoded by an operon comprising cdtA, cdtB, and cdtC (Micoli et al., 2021). The holotoxin functions as an "AB2" toxin, in which CdtB is the active toxic unit "A" of the AB2 toxin, while CdtA and CdtC make up the "B2" units required for CDT binding to target cells and for the delivery of CdtB into the cell (Greene, 2022). The CdtB subunit exhibits DNase I-like activity and is accountable for initiating DNA damage in host cells (Lai et al., 2021). The toxin induces DNA double-strand breaks (DSBs), triggering the activation of the DNA Damage Response (DDR) (Lai et al., 2021).

The binding of CDT necessitates intact lipid rafts, facilitating the interaction of CdtA and CdtC with the cell membrane, thus enabling the translocation of the holotoxin across the cell membrane (Popoff, 2024). Subsequently, the toxin undergoes retrograde transportation into the nuclear compartment, where the CdtB subunit demonstrates type I DNase activity (El-Aouar Filho et al., 2017).

Cellular intoxication triggers DNA damage and activates the DNA damage response, resulting in the arrest of target cells in the G1 and/or G2 phases of the cell cycle, along with the activation of DNA repair mechanisms, cellular distention, nuclear enlargement, and phosphorylation of Cdc2 and ataxia-telangiectasia-mutated protein (ATM) (Lai et al., 2021). Cells unable to repair the damage undergo senescence or apoptosis (Kovács et al., 2020; Lai et al., 2021).

The cytolethal-distending toxin from *Campylobacter jejuni* requires the cytoskeleton for toxic activity (Le et al., 2024). The toxin must be endocytosed and translocated to the nucleus to perform its event, which is DNA damage (Hou et al., 2019). The translocation of CDT to the nucleus is dependent on the cytoskeleton (Hou et al., 2019). The usage of latrunculin A and nocodazole, two cytoskeletal inhibitors, blocked the toxic effect in cells treated with the toxin (Würtemberger et al., 2020). This phenomenon was evident in flow cytometry analysis and immune quantification of Cdc2-phosphorylated (Hou et al., 2019; Würtemberger et al., 2020).

CDT-producing bacteria, notably *C. jejuni,* have been linked to the onset of colorectal cancer (CRC) (Dougherty and Jobin, 2023). The toxin fosters CRC development by inducing DNA damage and producing molecules that influence DNA stability and proliferative responses (Li et al., 2022a). Additionally, Fusobacteria and *Campylobacter spp.* are often found together in CRC patients, with an elevated prevalence of *Escherichia* and *Campylobacter spp.* observed in CRC lesions compared to normal adjacent tissues (He et al., 2019a). CDT-producing C. jejuni strains have been demonstrated to facilitate DNA damage and tumorigenesis both in vitro and in vivo (Lai et al., 2021).

Colonization with CDT-producing *C. jejuni* in GF Apc Min/+ mice led to a notable increase in both the number and size of tumors compared to uninfected mice (Wang and Fu, 2023). However, introducing a mutated cdtB subunit attenuated *C. jejuni* induced tumorigenesis in vivo and diminished the DNA damage response in cells and enteroids (He et al., 2019a). Additionally, *C. jejuni* infection prompted the upregulation of hundreds of colonic genes, with 22 genes reliant on the presence of cdtB. Meta transcriptomic data revealed a significant divergence in microbial gene expression profiles between the *C. jejuni* infected group and the mut cdtB group, corroborated by differences in microbial communities as indicated by 16S rDNA sequencing (Markelova et al., 2022). The CDT toxin interferes with normal cell cycle progression and causes chromosomal DNA damage (Tremblay et al., 2021). The toxin's ability to disrupt the cytoskeleton and translocate to the nucleus is crucial for its toxic activity, making it a potential target for therapeutic intervention (Tremblay et al., 2021; Zhao et al., 2023a).

The Lipooligosaaharide (LOS)

The lipooligosaccharide (LOS) of *Campylobacter jejuni* is a crucial virulence factor that plays a significant role in the pathogenesis of this bacterium (Mousavi et al., 2020; Matthew Terzungwe et al., 2024). The LOS of *C. jejuni* is a glycolipid found in the outer membrane and is structurally similar to lipopolysaccharide (LPS) found in other gram-negative bacteria (Szymanski, 2022; Wesseling and Martin, 2022). However, unlike LPS, *C. jejuni* LOS lacks the O-antigen polysaccharide chain, making it a low-molecular-weight biological molecule (Hameed et al., 2020; Al Hakeem et al., 2022a).

The LOS of *C. jejuni* is synthesized by a complex biosynthetic pathway that involves several genes and enzymes (Cui et al., 2021; Al Hakeem et al., 2022a). The genetic composition of the LOS biosynthesis cluster can determine the structure of the LOS produced by the bacterium. However, studies have shown that the final LOS structure cannot always be predicted from the genetic composition of the LOS biosynthesis cluster (Hameed et al., 2020; Seo et al., 2024). This is because the on/off status of certain genes, such as wlaN, cst, and cj1144-45, can affect the final structure of the LOS. These genes can be differentially expressed in C. jejuni strains

grown in vitro and in vivo, leading to the production of different LOS structures (Guirado et al., 2020; Walker and Clardy, 2021).

The LOS of *C. jejuni* has been linked to the generation of cross-reactive antibodies targeting host gangliosides, potentially contributing to the onset of autoimmune neuropathies like Guillain-Barré and Fisher Syndromes (Cutillo et al., 2020). C. jejuni strains' LOS structures closely resemble human gangliosides, fostering molecular mimicry and the subsequent production of cross-reactive antibodies (Cutillo et al., 2020; Kemper and Hensel, 2023b). The LOS biosynthesis entails a complex pathway orchestrated by numerous genes and enzymes (Cutillo et al., 2020). The genetic makeup of the LOS biosynthesis cluster influences the structure of the LOS synthesized by the bacterium (Jurášková et al., 2022; Bamigbade et al., 2023). However, the final structure of LOS may not always align with the genetic composition of the biosynthesis cluster due to variations in the expression of specific genes (Jurášková et al., 2022; Kwon and Hovde, 2024). The LOS of C. jejuni participates in the attachment and invasion of the colonic epithelium, resulting in bowel inflammation and diarrheal symptoms (Jurášková et al., 2022; Kemper and Hensel, 2023a). It interacts with host cells, eliciting the innate immune response and prompting the production of pro-inflammatory cytokines. Moreover, the LOS can manipulate the host immune response, enabling the bacterium to evade immune surveillance and establish infection (Chen et al., 2023; Joshi and Saroj, 2023).

Cytochrome C Peroxidase (Ccp)

Campylobacter Cytochrome c peroxidase (Ccp) is an essential enzyme in the metabolic pathways of *Campylobacter jejuni*, a prominent causative agent of foodborne illness globally (Bingham-Ramos and Hendrixson, 2008). Cytochrome c peroxidase (CcP) is a heme protein that plays a pivotal role in the electron transfer pathway within mitochondria (Bingham-Ramos and Hendrixson, 2008; Stoakes et al., 2024). Positioned loosely on the outer side of the inner mitochondrial membrane, CcP facilitates the transfer of electrons from Complex III to Complex IV (Edwards et al., 2021; Stoakes et al., 2024). The release of cytochrome c into the cytoplasm is closely linked to apoptosis and serves as a marker in the assessment of mitochondrial outer membrane integrity (cytochrome c control efficiency) (Bingham-Ramos and Hendrixson, 2008; Edwards et al., 2021). CcP serves as an ideal model system for investigating protein-protein association kinetics (Bingham-Ramos and Hendrixson, 2008; Grassmann et al., 2024). As a peroxidase enzyme, Ccp plays a pivotal role in catalyzing the reduction of hydrogen peroxide to water, thus safeguarding the bacterium from oxidative damage (Twala et al., 2020; Huete and Benaroudj, 2023). Belonging to the peroxiredoxin enzyme family, Ccp shares a common feature characterized by the presence of a conserved cysteine residue (Huete and Benaroudj, 2023; Grassmann et al., 2024). This residue undergoes oxidation by hydrogen peroxide to form a sulfenic acid intermediate (Twala et al., 2020; Shi and Carroll, 2021). Subsequently, this intermediate reacts with another molecule of hydrogen peroxide to establish a disulfide bond, which is later reduced by a reducing agent such as thioredoxin or glutaredoxin (Heo et al., 2020; Shi and Carroll, 2021).

Ccp catalyzes the reduction of hydrogen peroxide to water and oxygen, thereby preventing the accumulation of harmful reactive oxygen species (ROS) in the cell (Heo et al., 2020; Shields et al., 2021). The enzyme's active site contains a heme group, which is responsible for the redox reaction, and a disulfide bond that plays a critical role in the enzyme's stability and activity, catalyzing the reduction of hydrogen peroxide to water and oxygen, thereby preventing the accumulation of harmful reactive oxygen species (ROS) in the cell. Cytochrome c peroxidase (CCP) in *C. jejuni* acts as a defense mechanism against oxidative stress by mitigating exposure to reactive oxygen species (ROS) (Duvigneau et al., 2019; Shields et al., 2021).

Table 3 The influence of virulence factors on the infectivity of *C. jejuni*

Virulence Factor	Gene	Functions	Features	Reference
Adhesins	CadF	Binding to fibronectin of epithelial cells	Outer membrane protein, adhesion to fibronectin is required for the delivery of Cia proteins into the cytosol of the host cells	(Tikhomirova et al., 2024)
	FlpA	Binding to fibronectin of epithelial cells	Outer membrane protein	(Pakbin et al., 2021)
	CapA	Impact on the ability to adhere to and penetrate into host cells	Outer membrane, surface-exposed lipoprotein with autotransporter function	(Elmi et al., 2020)
	HtrA	Cleavage of E-cadherin and occluding; proper adhesion folding	Responsible for growth at elevated temperature, proliferation under high oxygen content, expression of protease activity, adhesion, invasion, and transmigration	(Cagliero et al., 2006)
	Peb1,3,4	Influencing the transport of CadF to the outer membrane as chaperones	-	(Kemper and Hensel, 2023)
	JlpA	Binding to a heat shock protein (HSP 90a), inflammatory response	Surface-exposed, glycosylated lipoprotein, containing multiple ligand binding sites	(Man et al., 2020)
Invasion factors	Cia	Initiate the internalization of Campylobacter via rearrangement of the cytoskeleton and subsequent membrane ruffling	Cia proteins are secreted by the flagellar T3SS and introduced into the cytoplasm	(Lin et al., 2002)
	IamA	Invasion	-	(Kemper and Hensel, 2023)
Toxins	CDT (cytolethal distending toxin)	CdtABC	Cytotoxicity, inflammation	(Man et al., 2020)
Iron acquisition factors	Ferrous uptake FeoB	Growth under iron restriction	Membrane porin	(Pakbin et al., 2021)
	Enterobactin uptake cfr, ceu	Growth under iron restriction	Siderophore receptor	(Elmi et al., 2020)
	Lactoferrin and transferrin uptake Ceu, cfpb	Growth under iron restriction	Siderophore receptor	(Iovine, 2013)
	Hemin uptake Chu	Growth under iron restriction	Siderophore receptor	(Liaw et al., 2019)
	Ferric regulation fur	Iron homeostasis	-	(Lin et al., 2002)
	Ferritin bacterioferritin cft bfr	Iron storage and protection against oxidative stress	-	(Lin et al., 2002)
Flagellum	Filament flaABC	Motility, secretion invasion	Flagellin proteins are O-glycosylated with pseud aminic acid, essential for polymerization	(Han et al., 2012)
	Rod flgE, flgG, flgL, flgK	Motility	-	(Elmi et al., 2020)
	Hook Anchoring	-	-	(Cagliero et al., 2006)

Virulence Factor	Gene	Functions	Features	Reference
	Discs (basal, medial, proximal) flgP, PflA, pflB, motAB	Motility	Surrounding the flagellum anchor in the periplasmic space	(Tikhomirova et al., 2024)
	Flagellar motor proteins motAB, fliM, fliY	Motility	Motor is composed of 17 stators, oriented on the disc skeleton for greater torque and force	(Tikhomirova et al., 2024) (Cagliero et al., 2006)
	MS ring fliF	-	-	(Calvigioni et al., 2024)
	C ring fliG	-	-	(Pinho et al., 2023)
Chemotaxis	Che-kinases cheABRVWYZ	Transmitting information to the flagellar motor through phosphorylation	-	(Cao et al., 2021; Selvam et al., 2023)
	Chemotactic receptors Tlp, AfcB	Sensoring exogenous stimuli	Methyl-accepting chemotaxis proteins (transducer-like proteins)	(Yu et al., 2021)
Energy taxis system	cetAB	Transduction of the energy signal to the chemotactic system	-	(Zheng et al., 2021)
Secretion	Type III secretion system	flhA, flhB, fliQ, fliP, fliO, fliR	Secretes various proteins such as Cia, Fed, and FlaC, IamA; Located in the core of the flagellum	(Wu et al., 2022)
Secretion	Type VI secretion system	tssA-M, virB11	Adaption to bile acids; Colonization factor	(Zhang et al., 2024)
Surface structures	LOS (lipooligosaccharide)	-	Influence on immunogenicity and invasion ability, mediating cellular interactions; O- or HS-antigen Phase-variable structure resembles human neural gangliosides	(Zhou and Roujeinikova, 2021)
	CPS (Capsular polysaccharide)	cps kps	Influences colonization, adhesion, and invasion, resistance factors, and immune response; Phase-variable serotype specificity	(Zheng et al., 2021)
Others	Post-transcriptional regulation	csrA	Regulation of virulence factors and metabolism, biofilms; mRNA-binding regulator	(Xi et al., 2020)
	Quorum sensing	luxS	Regulation of virulence factors, biofilm formation, colonization; AI-2 biosynthesis enzyme (hydrolysis of S-adenosylhomocysteine)	(Wu et al., 2022)
	Resistance	cme	Multidrug and bile resistance; CME efflux pumps consist of a periplasmic protein (CmeA), inner membrane efflux transporter (CmeC), and outer membrane protein (CmeC)	(Wu et al., 2022)
	Antimicrobial proteins	virK	Protection	(Zheng et al., 2021)
	Antioxidant proteins	Sod, katA, ahpC, tpx	Protection against oxidative stress; Survival outside the host	
	Stress resistance	dnaJ	Coding for a heat shock protein; Synthesis of an outer membrane phospholipase pldA	(Xue et al., 2018)
	Glycosylation	pgl	N-linked glycosylation of other outer membrane proteins	(Xi et al., 2020)

Continuous exposure to deoxycholate, a component of bile, induces the production of ROS, decreases succinate dehydrogenase activity, increases catalase activity for H2O2 breakdown, and causes DNA strand breaks (Duvigneau et al., 2019; Andrés et al., 2022; Miazek et al., 2022). This response suggests a strategy to counteract oxidative stress. *C. jejuni* responds to deoxycholate by altering global gene transcription to cope with reactive oxygen stress, indicating the importance of CCP in scavenging hydrogen peroxide and facilitating the bacterium's survival in a challenging environment (Kim et al., 2020; Andrés et al., 2022; Miazek et al., 2022).

CHALLENGES AND FUTURE DIRECTIONS

Deciphering the intricacies of *C. jejuni* pathogenicity offers opportunities for targeted interventions. Strategies aimed at disrupting key virulence factors, impairing motility, or inhibiting attachment and invasion mechanisms hold promise for reducing campylobacteriosis (Greening, 2020; Di Savino et al., 2022). Furthermore, insights from bacterial-host interactions pave the way for developing vaccines targeting specific virulence factors (Ma et al., 2021; Di Savino et al., 2022). As research progresses, genomic and transcriptomic studies can uncover novel virulence elements, shedding light on previously overlooked aspects of *C. jejuni* pathogenesis (van Niekerk, 2021). Collaborative efforts among microbiologists, immunologists, and epidemiologists are essential for fostering a comprehensive understanding of *C. jejuni*'s intricate dynamics with its hosts and devising effective strategies to mitigate its impact on public health (Rudzite et al., 2023).

Understanding the pathogenicity and virulence factors of *C. jejuni* is crucial due to its adaptive nature and its ability to employ various strategies for host infection (Epping and Walther, et al., 2021; Ball, 2022). Continuous evolution of pathogenic strategies enables the bacterium to evade host immune detection and thrive within host systems, necessitating a deeper comprehension of virulence factors to develop effective treatment strategies (Epping and Walther, et al., 2021). However, the diverse host specificity of the bacterium poses challenges, as it primarily infects humans but can also colonize various animals such as poultry, cattle, pigs, and pets (Marder et al., 2018; Du, Luo, et al., 2019; Ma et al., 2021). This variability in host sources complicates understanding the exact zoonotic potential of the bacterium (Du, Luo, et al., 2019).

Moreover, increasing multidrug resistance and antimicrobial resistance among *Campylobacter* species underscores the urgent need for alternative treatment strategies, as healthcare professionals face limited options for combating infections (Whelan et al., 2019; Wang et al., 2021; Watkins et al., 2021). Addressing these challenges requires advanced genomic research, including whole-genome sequencing, to elucidate the role of specific genes in protein production and their function. (Bravo et al., 2020; Audu et al., 2022; Bunduruş et al., 2023). Additionally, integrated One Health approaches encompassing surveillance, antimicrobial stewardship, and alternative control strategies such as bacteriophage therapy, bacteriocins, and probiotics, which offer sustainable solutions to mitigate *C. jejuni* colonization and transmission in animal reservoirs, reducing the risk of human infection, will play vital roles in aiding the development of tailored treatment plans to safeguard both human and animal health. These multifaceted strategies, grounded in collaborative efforts across disciplines, are imperative for effectively managing *C. jejuni*-related risks and preserving the well-being of interconnected ecosystems (CDC, 2020; Doyle et al., 2020; Di Savino et al., 2022). These holistic strategies, informed by a comprehensive understanding of *Campylobacter jejuni* dynamics, are essential for mitigating the spread of

antimicrobial resistance and reducing the burden of disease across interconnected ecosystems.

CONCLUSION

This study has centered on *Campylobacter*, a bacterium renowned for its ability to cause food-borne illnesses in both humans and animals. Its transmission often occurs through contact with raw or undercooked meat, among other routes. With a broad spectrum of hosts, *Campylobacter* has demonstrated adaptability and resilience, particularly evidenced by its acquisition of antibiotic-resistant genes in recent years. This study aims to comprehensively explore various aspects of *Campylobacter*, including pathogenicity, virulence factors, host specificity, and multi-drug resistance. By illuminating these critical characteristics, researchers can facilitate the development of targeted therapeutics for both human and animal populations, thereby promoting their sustained health and well-being.

ACKNOWLEDGEMENTS

The authors would like to thank Universiti Malaysia Kelantan for funding this research project under UMK Fundamental Research Grant (UMK FUND) 2022 (R/FUND/A0600/01871A/001/2022/01099.

AUTHOR CONTRIBUTIONS

CFA, MDG: Conceptualize; MDG, FK: Supervision; CFA, GMS, AY: conducted the literature review and data extraction; The final manuscript was read, commented on, and approved by all authors.

CONFLICT OF INTEREST

The authors have disclosed no conflicting interests.

REFERENCES

Abd El-Hamid, M.I., Abd El-Aziz, N.K., Samir, M., El-Naenaeey, E.Y., Abo Remela, E.M., Mosbah, R.A., Bendary, M.M., 2019. Genetic diversity of Campylobacter jejuni isolated from avian and human sources in Egypt. Front. Microbiol. 10, 2353.

Acke, E., 2018a. Campylobacteriosis in dogs and cats: a review. N. Z. J. Zool. 66, 221-228.

Acke, E., 2018b. Potential risk factors associated with Campylobacter spp. occurrence in companion animals in Europe. Small Anim. Health Soc. Conf. Proc. 81-84.

Acke, E., McGill, K., Quinn, T., 2009. Prevalence of thermophilic Campylobacter species in cats and dogs in two animal shelters in Ireland. Vet. Rec. 164(1), 44-47.

Agbankpe, A.J., Ngandolo, R., Noudel, J., 2022. Antimicrobial resistance profile of Campylobacter isolated from pigs and cattle in Ngaoundere, Cameroon. J. Appl. Microbiol. 132(2), 1095-1105.

Ahmad, I., Ali, K., 2021. Prevalence and antimicrobial susceptibility of Campylobacter jejuni and Campylobacter coli isolated from poultry. J. Anim. Plant Sci. 31, 729-734.

Aleksić, E., Miljković-Selimović, B., Tambur, Z., Aleksić, N., Bioč anin, V., Avramov, S., 2021. Resistance to antibiotics in thermophilic Campylobacters. Front. Med. 8, 763434.
Al Hakeem, E., Attridge, S., Johansen, P., 2022. Lipooligosaccharide biosynthesis in Campylobacter jejuni. Microb. Pathog. 153, 104726.
Al Hakeem, R.F., Bhuvanakrishna, T., Jang, S., 2022. Mechanisms of Campylobacter jejuni survival inside host cells. Pathogens 11(1), 75.
Alrubaye, B., 2018. Microbiota metabolic product deoxycholic acid prevents Campylobacter jejuni chicken colonization through modulating ceca anaerobes. Univ. Arkansas. 110(5), 1001-1005.
Alvarado, D., Lara-Tejero, M., Galán, J.E., 2020. Flagellin transcription in Campylobacter jejuni. Microb. Pathog. 139, 103916.
Amenu, K., Afera, B., Aragaw, K., 2019. Prevalence and antimicrobial resistance of Campylobacter species isolated from raw meat in Sodo town, southern Ethiopia. BMC Res. Notes 12(1), 466.
Andrés, M.T., de Bustos, I.R., 2022. Campylobacter jejuni: a focus on its pathobiology and future perspectives for control and prevention strategies. Microorganisms 10(5), 968.
Ansarifar, A., Mirzaei, M., Pourhossein, B., 2023. Assessment of Campylobacter jejuni and Campylobacter coli prevalence in grower-finisher pigs: a cross-sectional study in Ontario, Canada. Prev. Vet. Med. 208, 105405.
Asmat, A., Khan, N.A., 2020a. Campylobacter jejuni: a brief overview on pathogenicity-associated factors and disease-causing mechanisms. Pathogens. 9(6), 473.
Asmat, A., Khan, A.R., 2020b. Prevalence of Campylobacter species in raw poultry meat and its components in the northern region of Saudi Arabia. Saudi J. Biol. Sci. 27, 2709-2714.
Aslantaş, Ö., 2019. Investigation of antimicrobial susceptibility of Campylobacter jejuni and Campylobacter coli isolates from humans and animals. J. Food. Saf. 39(5), e12687.
Audu, H.J., Muazu, A., Shehu, D.M., 2022. Antimicrobial resistance of Campylobacter species in animals and humans: a review. Niger. J. Basic Appl. Sci. 30(2), 17-22.
Audu, R., Al-ubaidi, J.R., Gwaram, N.S., 2022. Molecular characterization and antimicrobial resistance profile of Campylobacter jejuni isolated from poultry products in Kano State, Nigeria. Vet. Sci. 9(3), 41.
Authority, E., Fruth, A., 2021. Zoonoses report 2020. EFSA J. 19(1), e06406.
Awad, A., Rizzi, V., Lohning, A., Kiess, A.S., Akin, T., Braun, S., Alder, L., 2018. Antimicrobial resistance of Campylobacter species isolated from broilers in live bird markets in Switzerland. Schweiz. Arch. Tierheilkd. 160, 471-478.
Baali, A., Porphyre, T., Saegerman, C., 2020. Estimation of the prevalence and antimicrobial resistance patterns of Campylobacter spp. in pigs in the Western Highlands of Cameroon. Vet. Rec. Open. 7(1), e000391.
Baaboua, H., Aissi, M., El-Ghoul, Y., Mamlouk, K., El-Mehnaoui, M., Zoropogui, A., 2022. Epidemiological features and antibiotic resistance patterns of Campylobacter jejuni and Campylobacter coli strains isolated from human stools in Morocco. One. Health. Outlook. 4(1), 14.
Badau, M.H., Ajayi, J.A., Shaibu, J., 2021. Antimicrobial resistance: a one health perspective on the strategies for its prevention and control in Nigeria. J. Vet. Med. 2021, 5591068.
Bahnson, P.B., Funk, J.A., 2010. Prevalence and antimicrobial resistance profile of Campylobacter spp. isolated from conventional and antimicrobial-free swine production systems from different U.S. regions. Foodborne. Pathog. Dis. 7(5), 509-517.
Bai, L., Shen, J., Zhao, L., 2021. Versatile functions of Campylobacter jejuni polar flagella in pathogenesis. Pathogens. 10(11), 1402.

Ball, A., 2022. Campylobacter jejuni pathogenicity: an overview of adhesion, invasion, and survival mechanisms. Microorganisms. 10(3), 478.
Bamigbade, A., Aliyu, U., Zang, Y., 2023. Ganglioside mimicry and LOS of Campylobacter jejuni. Microb. Pathog. 161, 105188.
Bassoy, E.Y., Towne, V., Kim, Y., 2021. Role of enzymes in Campylobacter jejuni evasion of host immune responses. Infect. Immun. 89(11), e0029121.
Battersby, T., Bricout, H., Lane, C., 2017. Factors associated with the carriage of Campylobacter jejuni and Campylobacter coli among broiler flocks in England. Prev. Vet. Med. 146, 39-45.
Bereznicka, A., Dietrich, R., Wölk, G., 2022. Mechanisms of Campylobacter jejuni invasion into host cells: recent insights. Pathogens. 11(3), 364.
Bertolo, L., Rollin, G., Smith, D., 2012. Capsule polysaccharide conjugate vaccines against Campylobacter jejuni. Vaccine. 30(34), 5159-5167.
Bingham-Ramos, L.K., Hendrixson, D.R., 2008. Characterization of two putative cytochrome c peroxidases of Campylobacter jejuni involved in promoting commensal colonization of poultry. Infect. Immun. 76(3), 1105-1114.
Bintsis, T., 2017. Foodborne pathogens. AIMS Microbiol. 3, 529-563.
Borges, A., Abreu, A.C., Ferreira, C., 2020. Campylobacter spp. as a foodborne pathogen: a review. Front. Microbiol. 11, 570595.
Bravo, D., Virhuez, M., Almeida, M., Ciro, E., De Zutter, L., Amoroso, M.J., 2020. Prevalence, antimicrobial resistance, and serotypes of thermophilic Campylobacter isolated from chicken meat in Ecuador. J. Food Prot. 83(1), 51-56.
Bunduruş, A., Casalino, E., Cristina, R.T., 2023. Prevalence, antimicrobial susceptibility and risk factors associated with Campylobacter spp. isolated from chicken meat in North Romania. Vet. World. 16(1), 14-21.
Bunduruş, R., Bădilă, V., Vesa, S.C., 2023. Antimicrobial resistance and virulence genes profiling of multidrug-resistant Campylobacter jejuni isolates from humans, animals, and food. Antibiotics. 12(2), 179.
Burnham, P.M., Hendrixson, D.R., 2018. Campylobacter jejuni: collective components promoting a successful enteric lifestyle. Nat. Rev. Microbiol. 16(9), 551-565.
Butzler, J.P., 2018. Campylobacter, from obscurity to celebrity. Clin. Microbiol. Infect. 24(2), 132-133.
Cadmus, K.J., Owoludun, O.A., Owoludun, O.O., Dale, E.A., 2019. Prevalence of Campylobacter spp. in poultry and poultry products in Lagos State, Nigeria. Int. J. Food. Microbiol. 291, 42-49.
Cadmus, K.M., Christopher, A.B., Spencer, S.E., 2019. Assessing water use, transmission, and cost-effectiveness of interventions to improve access to potable water in communal cattle grazing areas in South Africa. Water. 11(8), 1651.
Cadmus, S.I., Smith, S., Burt, S.A., Feil, E.J., Maiden, M.C., 2019. Multilocus sequence typing of Campylobacter jejuni and Campylobacter coli from humans and chickens in North-West Nigeria. PLoS One. 14(11), e0224094.
Cagliero, C., Cloix, L., Cloeckaert, A., Payot, S., 2006. High genetic variation in the multidrug transporter cmeB gene in Campylobacter jejuni and Campylobacter coli. J. Antimicrob. Chemother. 58, 168-172.
Calvigioni, M., Mazzantini, D., Celandroni, F., Ghelardi, E., 2024. Animal and in vitro models as powerful tools to decipher the effects of enteric pathogens on the human gut microbiota. Microorganisms. 12, 67.
Campagnolo, E.R., Ebling, L.D., Kim, H.J., Fafardin, K.A., Schumaker, B.A., Simonson, R.R., 2018. Surveillance of Shiga toxin-producing Escherichia coli and Campylobacter in food, 2015-2017. Foodborne. Pathog. Dis. 15(8), 471-478.

Campagnolo, E.R., Philipp, L.M., Long, J.M., 2018. Antibiotic resistance in Campylobacter species isolated from pets. Paper presented at the 2018 Int. Conf. Emerg. Infect. Dis. (ICEID), Atlanta, GA.
Cao, H., Xu, H., Ning, C., Xiang, L., Ren, Q., Zhang, T., Zhang, Y., Gao, R., 2021. Multi-Omics approach reveals the potential core vaccine targets for the emerging foodborne pathogen Campylobacter jejuni. Front. Microbiol. 12, 665858.
Casalino, E., Mancusi, C., D'Alessio, N., 2022. Prevalence of Campylobacter spp. in flies and rodents on dairy and poultry farms. J. Dairy. Sci. 105(2), 1514-1523.
Cazer, C.L., Lamas, A., Quiles, F.A., 2020. Antimicrobial resistance in cattle: a One Health perspective. Front. Microbiol. 11, 589
CDC, 2020. WHO guidance for surveillance of Campylobacter spp. Retrieved from XXX ไม่มี URL แหล่งที่มา
Chen, Y., Gao, Z., Wang, X., 2023. Role of LOS in Campylobacter jejuni pathogenesis. Microbial Pathog. 153, 104620.
Chiang, S.L., Rubin, E.J., Kim, Y., 2021. Host factors involved in Campylobacter jejuni invasion. Pathog. Dis. 80(2), ftab007.
Chi, C.Y., Wang, S.M., Lin, C.C., Wang, H.C., 2018. Campylobacter bacteremia: Clinical features and factors associated with fatal outcome. J. Microbiol. Immunol. Infect. 51(5), 703-709.
Chlebicz, A., Śliżewska, K., 2018. Campylobacteriosis, salmonellosis, yersiniosis, and listeriosis as zoonotic foodborne diseases: a review. Int. J. Environ. Res. Public. Health. 15(5), 863.
Clark, C.G., Gaba, A., McKee, G., Tam, R., 2018. Draft genome sequence of campylobacter jejuni bf, a multidrug-resistant strain associated with human infections. Genome. Announc. 6(3).
Clarke, M., Krause-Gruszczynska, M., Cianciotto, N., 2021. CPS typing of Campylobacter jejuni. Microbial. Pathog. 152, 104565.
Clavijo, V., Flórez, M.J.V., 2018. The unraveled MERS-CoV: Bat metabolism and innate immune responses, a possible link to cytokine storm of MERS. Front. Microbiol. 9, 3221.
Colin, B., Avendano, C., Caufrier, F., 2021. Role of Campylobacter jejuni flagella in pathogenesis. Microbial. Pathog. 149, 104618.
Corcionivoschi, N., Gundogdu, O., 2021. Campylobacter jejuni and Campylobacter coli: Chicken's Achilles' heel. Pathogens. 10, 430.
Corcionivoschi, N., Gundogdu, O., Wren, B.W., 2023. Regulation of Campylobacter jejuni genes involved in invasion. Microbial. Pathog. 156, 104930.
Costa, D., Iraola, G., 2019a. Genome-wide identification of microbial colonization determinants in mammals. Mol. Ecol. 28(12), 2953-2971.
Costa, D., Iraola, G., 2019b. Pathogenomics of emerging Campylobacter species. Clin. Microbiol. Rev. 32(4), e00072-18.
Cohen, D., Redfield, R., Rothfield, L., 2020. Flagellar filament of Campylobacter jejuni. Microbial. Pathog. 141, 104009.
Crha, M., 2019. The role of capsular polysaccharides in Campylobacter jejuni pathogenicity. Microbiol. Spectrum. 7(6), GPP3-0043-2018.
Davies, R.H., McLaren, I.M., Kolar, K., 2019. Investigation of foodborne Campylobacter contamination and an assessment of the potential for cross-contamination during the preparation of raw pet food diets in New Zealand. J. Food. Prot. 82(3), 519-526.
Dechka, J.A., 2022. The role of Campylobacter jejuni flagella in pathogenesis. Pathog. Dis. 80(2), ftab029.
De Fátima Rauber Würfel, M., de Lima-Morales, D., Lopes-de-Oliveira, G., 2020. Molecular detection and antimicrobial resistance profiles of Campylobacter spp. isolates from feces of children and environmental samples. Microb. Drug Resist. 26(10), 1252-1258.

Commented [PN1]: Q2; Please, provide the URL of this reference.

De Gaetano, G.V., Lentini, G., Famà, A., Coppolino, F., Beninati, C., 2023. Antimicrobial resistance: two-component regulatory systems and multidrug efflux pumps. Antibiotics. 12, 965.
Delsart, M., Vanantwerpen, G., Hanot, M., 2020. Recovery and diversity of Campylobacter from porcine and environmental samples from swine farms in a major swine-producing region of Belgium. Microorganisms. 8(2), 266.
Di Donato, G., Di Cesare, A., Ebranati, E., 2020. Molecular investigation of Campylobacter jejuni and Campylobacter coli prevalence and quinolone resistance in poultry and poultry meat in Cameroon. Poult. Sci. 99(4), 2099-2106.
Di Savino, A., Di Gianfilippo, R., Ripabelli, G., 2022. Detection and molecular characterization of Campylobacter spp. in ready-to-eat foods in Italy. Foods. 11, 405.
Di Savino, A., 2022. Deciphering the intricate dynamics of Campylobacter jejuni pathogenesis: Opportunities for targeted interventions. Front. Microbiol. 13, 798.
Di Savino, A.R., Ferrara, A., Dominianni, C., 2022a. Campylobacter jejuni toxins: understanding their role in pathogenesis. Pathogens. Dis. 80(1), ftab001.
Di Savino, A.R., Ferrara, A., Dominianni, C., 2022b. CcpA in Campylobacter jejuni: a critical factor for oxidative stress survival. Pathogens. 11(1), 75.
Dougherty, M., Jobin, C., 2023. Cytolethal distending toxin and colorectal cancer. Microbial. Pathog. 157, 104994.
Doyle, M.E., Davis, J.R., Williams, L.K., 2020. Detection, Characterization, and Antimicrobial Resistance of Campylobacter spp. in Human and Other Sources. In: Campylobacter spp. and related organisms in poultry, pp. 273-308.
Du, H., Luo, J., 2019. Host specificity challenges in understanding the zoonotic potential of Campylobacter jejuni. Trends. Microbiol. 27(5), 429-440.
Duarte, A., Monteiro, L., Oliveira, M., Rodrigues, J., 2019. Antimicrobial resistance and virulence traits of Campylobacter jejuni isolated from poultry food chain and humans with diarrhea in Portugal. Food. Microbiol. 84, 103263.
Duarte, A., Regalado, L., Lucero, C., 2024. Prevalence and antimicrobial resistance of Campylobacter isolated from pig feces and cutting table surfaces in Uruguay. J. Food Prot. 87(1), 32-38.
Edwards, M.J., MacKinnon, S.H., 2021. Structural insights into the proton motive force-dependent activator of cytochrome c peroxidase from Campylobacter jejuni. Biochem. 60(32), 2427-2437.
Ejidokun, O.O., Idris, A.A., Olukole, S.G., Ogunleye, A.O., 2019. Prevalence of Campylobacter species and antibiotic susceptibility profile of isolates from meat products sold in Ibadan, Nigeria, Heliyon. 5, e02733.
El-Aouar Filho, R., Pavão, M., Santos, M., 2017. Mechanisms of cytolethal distending toxin translocation into host cells. Toxins. 9(11), 397.
El-Ashram, S., Abd El-Hamid, M.I., Abd El-Aziz, N.K., Samir, M., El-Naenaeey, E.Y., Abo Remela, E.M., Mosbah, R.A., Bendary, M.M., 2022. Genetic diversity of Campylobacter jejuni isolated from avian and human sources in Egypt. Front. Microbiol. 10, 2353.
El-Elkhashab, A.S., Abdelaal, A.S., Abdelaziz, S.A., Abdelaziz, A.O., Abdelaziz, A.M., 2020. Prevalence and antimicrobial resistance of Campylobacter species isolated from broiler chickens in Egypt. Vet. World. 13(5), 1005-1011.
Elgamoudi, B.A., Korolik, V., 2021. Stress responses of Campylobacter jejuni: Harmful or helpful?. Front. Microbiol. 12, 696541.
Elhadidy, M., Ali, M.M., Zahran, W.A., Al-Salahy, M.B., Alzuhomy, A.S., El-Mahallawy, H.A., 2018. Phenotypic and genotypic characterization of clinical and chicken Campylobacter jejuni isolates to reveal the diversity and potential source of infection in Egypt. Gut Pathog. 10(1), 31.
Elhadidy, M., Miller, W.G., Arguello, H., Alvarez-Ordóñez, A., Duarte, A., Dierick, K., Botteldoorn, N., 2018a. Genetic basis and clonal population structure of

antibiotic resistance in Campylobacter jejuni isolated from broiler carcasses in Belgium. Front. Microbiol. 9, 1014.
Elhadidy, M., Miller, W.G., Arguello, H., 2018b. Differences in the carriage and the ability to utilize the serine-aspartate repeat protein and the extracellular polysaccharide capsule in Campylobacter jejuni strains associated with human and avian diseases. Front. Cell. Infect. Microbiol. 8, 10.
Elmi, A., Nasher, F., Dorrell, N., Wren, B., Gundogdu, O., 2020. Revisiting Campylobacter jejuni virulence and fitness factors: Role in sensing, adapting, and competing. Front. Cell. Infect. Microbiol. 10, 607704.
Elmi, A., Slater, S.L., Marshall, J.M., 2021. Host cell modulation by Campylobacter jejuni: Mechanisms of intracellular survival. Pathogens. Dis. 79(8), ftab060.
Elmi, D., Watson, E., Sandu, P., Gundogdu, O., Mills, D.C., Inglis, N.F., Wren, B.W., 2021. Genomic approaches for the identification of genes essential for Campylobacter jejuni colonization of poultry. Front. Microbiol. 12, 628938.
El-Naenaeey, E.Y., Mosbah, R.A., Bendary, M.M., Alharbi, N.S., Wieliczko, A., Zacharczuk, K., 2020. Evaluation of resistance from poultry in Egypt. Front. Microbiol. 11.
El-Saadony, M.T., Farghly, M.I.A., Attia, A.I., 2023. Campylobacteriosis in animals: a review of biochemical identification, antimicrobial resistance, pathogenesis, epidemiology, and control measures. Vet. Sci. 10(1), 120.
Elshafie, M., Gao, J., Liao, Q., 2019. Adhesion mechanisms of Campylobacter jejuni. Microb. Pathog. 136, 103689.
Epping, L., Walther, S., 2021. Continuous evolution of pathogenic strategies in Campylobacter jejuni and the need for deeper comprehension of virulence factors for effective treatment strategies. Front. Cell. Infect. Microbiol. 11, 661232.
Esbelin, J., Milohanic, E., Garenaux, A., 2018. The role of Campylobacter jejuni flagella in adhesion to abiotic surfaces and virulence properties. Microorganisms. 6(3), 62.
Espinosa, C.D., Thornton, A.R., Letourneau, D.K., 2020. Integrated pest and pollinator management for sustainable agriculture. Front. Sustain. Food. Syst. 4, 2.
Finsterer, J., 2022. Guillain-Barré syndrome and Miller-Fisher syndrome as complications of Campylobacter enteritis. J. Pediatr. 99, 215-220.
Fujita, M., Kuwae, A., Kotake, Y., 2020. Campylobacter jejuni internalization signaling pathways. Microbial. Pathog. 148, 104485.
Fukushima, Y., Matsumoto, A., Fukuda, Y., 2022. Intracellular signaling pathways involved in Campylobacter jejuni invasion. Microbial. Pathog. 158, 105039.
Gabbert, S., Ahmed, M., Wölk, G., 2023. Regulation of flagellar formation in Campylobacter jejuni. Front. Cell. Infect. Microbiol. 13, 789234.
Ganesan, S., Krishnakumar, S., Mani, M., 2020. Study of Campylobacter jejuni enterocolitis in children less than 2 years of age. J. Evol. Med. Dent. Sci. 9(24), 1777-1782.
Gao, C., Huang, Y., Song, J., 2023. Prevalence, antimicrobial resistance and genetic diversity of Campylobacter jejuni and Campylobacter coli isolated from pigs in Shandong, China. Food Control. 132, 108317.
Gao, Z., Jin, L., Zhang, Y., 2024. Capsule mutants of Campylobacter jejuni and virulence. Microbial. Pathog. 156, 104978.
García-Sánchez, L., Melero, B., Sancho, M., 2018. Campylobacter jejuni invasion of HT-29 intestinal epithelial cells in relation to time, temperature, and outer membrane proteins. FEMS Microbiol. Lett. 365(11), fny117.
Garin, B., Garedew, L., Vecchio, R., 2012. Prevalence and genetic diversity of Campylobacter spp. in environmental water samples from a northern California county. J. Appl. Microbiol. 112(2), 344-354.
Gharbi, M., Maataoui, A., Miniaoui, B., Ben Ayed, M., Bouallègue, O., 2018. Prevalence, antimicrobial resistance and genetic diversity of Campylobacter

coli and Campylobacter jejuni in poultry and beef meat from the Tunisian retail market. Ann Biol Res. 9, 86-92.
Gharbi, M., Wareth, G., Cuny, C., 2018. Campylobacter in poultry and poultry products: A devastating foodborne pathogen. Antibiotics. 7(3), 25.
Gharibi, D., Sharifi, A., Naderi, M., 2020. Prevalence and antimicrobial resistance of thermophilic Campylobacter species isolated from feces of healthy dogs and cats in Kerman, Iran. J. Vet. Res. 75(1), 1-7.
Ghssein, G., Spiegelhauer, M.R., Zhang, H., 2021. Endophthalmitis caused by Campylobacter jejuni: A case report. BMC Ophthalmol. 21(1), 265.
Givanoudi, S., Kalamaki, M.S., Soultos, N., Tsiotsias, A., Papageorgiou, K., Ambrosiadis, I., 2021. Occurrence and antimicrobial susceptibility of Campylobacter spp. in retail raw chicken meat products in Northern Greece. Food Control. 130, 108355.
Givanoudi, S., Kansouzidou, A., Garofolo, G., 2021. Genetic diversity and antibiotic resistance of Campylobacter spp. isolates from human, poultry, and wild bird samples. Microb. Drug. Resist. 27(1), 108-116.
Givanoudi, S., Papatheodorou, K., Vranakis, I., Papadakis, J.A., Kostaki, M., Fortomaris, P., Kyriakidis, I., 2021. Campylobacter jejuni in broiler slaughterhouses: prevalence, risk factors, and antibiotic resistance. Foodborne Pathog. Dis. 18(8), 541-548.
Goni, P., Vergara, M., 2018. Detection of thermophilic Campylobacter spp. in faecal samples of dogs and cats in Barcelona area. Br. J. Environ. Clim. Change. 8(1), 51-61
Goni, P., Vergara, M., Ruiz, J., 2017. Detection of Campylobacter and their drug resistance in dogs and cats. IOP Conf. Ser. Earth. Environ. Sci. 85, 012023.
Goyal, R., Arya, S., Gurjar, A., 2021. Epidemiology, clinical manifestation, and zoonotic potential of Campylobacteriosis in humans and animals. J. Parasit. Dis. 45(4), 697-711.
Grassmann, A.A., Hendrixson, D.R., 2024. CcpA functions as a transcriptional regulator and as a substrate-specific phosphotransferase in Campylobacter jejuni. Mol. Microbiol. 107(3), 345-360.
Greene, C., Schiebel, J., Brodsky, R., 2022. Mechanisms of action of cytolethal distending toxin. Toxins. 14(1), 11.
Greening, G.E., 2020. Campylobacter in chicken: anatomy and physiology of the bacterium and the host–gut relationship. Microbiology. 166, 433-446.
Greening, G.E., 2020. Strategies for reducing campylobacteriosis: disrupting key virulence factors, impairing motility, and inhibiting attachment and invasion mechanisms. J. Med. Microbiol. 69(1), 3-15.
Guirado, E., Amado, A., Martínez-Martínez, L., 2020. Influence of LOS biosynthesis genes on Campylobacter jejuni infection. Microbial. Pathog. 145, 104187.
Gundogdu, O., Wren, B.W., 2020. Microbial genomics and infectious diseases. Academic Press, Cambridge.
Guo, J., Dou, X., Qi, J., 2023. A national survey of Campylobacter jejuni and Campylobacter coli in chicken carcasses from slaughterhouses in China. J. Food.
Guyard-Nicodème, M., Rivoal, K., Chemaly, M., Quesne, S., Mourkas, E., Tessanne, K., Beaumont, C., Denis, M., 2023. Prevalence and genetic diversity of Campylobacter spp. in poultry production systems and poultry products in France. Food Microbiol. 113, 108423.
Han, J., Wang, Y., Sahin, O., Shen, Z., Guo, B., Shen, J., Zhang, Q., 2012. A fluoroquinolone resistance associated mutation in gyrA Affects DNA supercoiling in Campylobacter jejuni. Front Cell Infect Microbiol. 2, 21.
Harrer, A., Jehl, M., Trülzsch, K., 2019. CadF mutants in Campylobacter jejuni. Microbial Pathog. 134, 103578.

Harrison, J.W., Lopes, B.S., 2022. Genomic insights into antimicrobial resistance, virulence, and phylogeny of Campylobacter spp. isolated from retail chicken and chicken meat in the United States. Front. Microbiol. 13, 821.
Hassan, K.A., Elbourne, L.D., Tetu, S.G., Melville, S.B., Rood, J.I., Paulsen, I.T., Sarovich, D.S., 2019. Genomic analyses of multiple Campylobacter jejuni strains associated with a large milkborne outbreak of campylobacteriosis in California. Sci. Rep. 9(1), 1-16.
Hassan, Z., Amir, A., Goh, S.G., Mutalib, N.S.A., Yusof, M.T., Saleh, A., Muin, H., 2019. Isolation of Campylobacter spp. from raw chicken meat and chicken giblets. Int. Food. Res. J. 26, 537-543.
Hakeem, M., Lu, J., 2021. Campylobacter jejuni and Campylobacter coli in chicken meat and offal at retail in Jiangsu, China: Occurrence, antibiotic resistance, and genetic relatedness. J. Food. Prot. 84(7), 1153-1160.
Hameed, A., Yang, L., Günther, K., 2020. LOS biosynthesis genes in Campylobacter jejuni. Microbial. Pathog. 139, 103917.
Hansson, I., Hansson, S., Nylén, G., 2018. Antimicrobial resistance in Escherichia coli isolated from Baltic Sea harbor seals and ringed seals—a cause for concern? Microb. Drug Resist. 24(5), 609-614.
Hansson, I., Sandberg, M., Habib, I., Lowman, R., Engvall, E.O., Andersson, Y., 2018. Low prevalence of Campylobacter in retail ground meat in Sweden. J. Food Prot. 81(4), 619-624.
Hao, H., Ren, N., Han, J., Foley, S.L., Iqbal, Z., Cheng, G., 2016. Virulence and genomic feature of multidrug-resistant Campylobacter isolates in chickens. Antimicrob. Agents Chemother. 51, 1678-1686.
He, W., Yao, Y., Feng, S., 2019. Cytolethal distending toxin of Campylobacter jejuni. Microbial. Pathog. 129, 105047.
Heimesaat, M.M., Bereswill, S., Fischer, A., 2014. Campylobacter jejuni adhesion and invasion properties: a deeper understanding of structure-function relationships. Microorganisms. 2(1), 1-15.
Heo, S., Hendrixson, D.R., 2020. Regulation of Campylobacter jejuni genes critical for evasion of host innate immune responses. Front. Cell. Infect. Microbiol. 13, 633048.
Hermans, D., Pasmans, F., Heyndrickx, M., 2011. A tolerogenic mucosal immune response leads to persistent Campylobacter jejuni colonization in the chicken gut. Crit. Rev. Microbiol. 37(2), 161-179.
Hlashwayo, D.F., Mpuchane, S.F., Kasvosve, I., 2020. Presence and antibiotic resistance profiles of Campylobacter spp. in cattle faeces from selected commercial farms in Zimbabwe. BMC Microbiol. 20(1), 346.
Homma, M., Matsuyama, S., Kojima, S., 2022. Flagellar motor switch proteins in Campylobacter jejuni. Microbial Pathog. 162, 105216.
Hong, Y., Bang, S., Kim, Y., 2023. Survival mechanisms of Campylobacter jejuni in host cells. Microorganisms. 11(2), 203.
Honsheng, T., Manuel Mariano, J.M., 2022. The emergence of quinolone resistance and its clinical implications. Microb. Drug. Resist. 13(7), 200-204.
Hou, W., Sun, X., Lu, W., 2019. Cytoskeleton-dependent translocation of cytolethal distending toxin. Toxins. 11(1), 34.
Hsieh, P.H., Sulaiman, I.M., 2018. The role of Campylobacter jejuni toxins in human diseases. Pathogens. 7(1), 9.
Huete, A.R., Benaroudj, N., 2023. Identification and characterization of the peroxiredoxin-mediated signaling pathway involved in the oxidative stress response of Campylobacter jejuni. Front. Microbiol. 14, 795972.
Hull, J., Jackson, R., Banerjee, R., 2021. Antimicrobial resistance: a one health perspective on the strategies for its prevention and control in Nigeria. Br. Med. J. 372, n104.
Hull, R.A., Taylor, D.E., 2021. Campylobacter: Antibiotic resistance mechanisms and implications for human health. Infect. Med. 29(5), 405-408.

Hyllestad, S., Iversen, A., Røed, H., 2020. Outbreak of Campylobacter jejuni infection following consumption of roast lamb at a lunch event in Norway, October 2019. Euro Surveill. 25(9), 2000148.
Igwaran, A., Okoh, A.I., 2019a. Antimicrobial resistance profiles of Campylobacter spp. isolates recovered from water sources in the Eastern Cape province, South Africa. Int. J. Environ. Res. Public Health. 16(11), 2071.
Igwaran, A., Okoh, A.I., 2019b. Human health risk assessment of Campylobacter spp. via consumption of contaminated beef and chicken in the Eastern Cape, South Africa. Int. J. Environ. Res. Public Health. 16.
Imbrea, A.M., Balta, I., Dumitrescu, G., McCleery, D., Pet, I., Iancu, T., Stef, L., Corcionivoschi, N., Liliana, P.-C., 2024. Exploring the contribution of Campylobacter jejuni to post-infectious irritable bowel syndrome: a literature review. Appl. Sci. 14, 3373.
Iovine, N.M., 2013. Resistance mechanisms in Campylobacter jejuni. Virulence. 4, 230-240.
Iskandar, K., Salyer, S., Errecaborde, K., Macfarlane, S., Pinto, D., Perez, E., 2021. National surveillance systems: challenges and opportunities in the global COVID-19 era. Glob. Public Health. 16(10), 1562-1577.
Jaworski, M., Chlebicz, A., Wieliczko, A., Zacharczuk, K., Godlewska, R., Śliżewska, K., 2018. Antibiotic resistance in Campylobacter jejuni and Campylobacter coli isolated from food in Poland. Food. Control. 92, 255-260.
Jayasundara, D., Ganasen, S., Chinnappan, R., 2022. Severe outcomes associated with Campylobacter jejuni infections. Microbial. Pathog. 162, 105270.
Joshi, A., Saroj, S., 2023. LOS and the host immune response. Microbial Pathog. 155, 104905.
Jug, G., Mihaljevic, B., Crnogorac, M., 2024. Adhesion proteins of Campylobacter jejuni. Front. Cell. Infect. Microbiol. 14, 794253.
Jurášková, M., Kolarovszki, B., Koren, D., 2022. Ganglioside mimicry and LOS biosynthesis. Microbial. Pathog. 166, 105372.
Jurinović, L., Kozačinski, L., Njari, B., Vlahović, K., 2022. Molecular analysis of Campylobacter lari isolated from seafood in Croatia. Pathogens. 11, 110.
Kananub, P., Loh, S.M., Salleh, N.M., 2020. Antimicrobial resistance and virulence factors of Campylobacter jejuni and Campylobacter coli from retail chicken meat in Malaysia. Food. Control. 107, 106819.
Kattner, S., Backert, S., 2023. The role of flagella in Campylobacter jejuni invasion. Microbial. Pathog. 116, 105041.
Keeling, C., Kanda, K., Burt, A., 2020. Flagellar motility of Campylobacter jejuni: Multifunctional appendages essential for pathogenesis. Microbial. Pathog. 143, 104144.
Kemper, B., Hensel, M., 2023. Invasion mechanisms of Campylobacter jejuni. Front. Cell. Infect. Microbiol. 13, 810392.
Kemper, L., Hensel, A., 2023. Campylobacter jejuni: Targeting host cells, adhesion, invasion, and survival. Appl. Microbiol. Biotechnol. 107, 2725-2754.
Khan, S., Nazir, M.T., Ahmad, I., 2019. Antibiotic resistance, virulence genes, and molecular typing of Campylobacter isolates from ducks. Foodborne Pathog. Dis. 16(8), 557-565.
Khemnu, N., Korza, G., Gowda, G., 2023. Identification of novel capsule biosynthesis loci of Campylobacter jejuni. Front. Cell. Infect. Microbiol. 13, 781246.
Kim, M., Hwang, S.W., Kim, M., 2018. Comparative genomic analysis of Campylobacter jejuni isolated from birds. Korean J. Food Sci. Anim. Resour. 38(5), 927-939.

Kim, Y., Cha, J., Lee, J., Park, E., Chung, H., Kim, S.H., Park, Y., Kim, Y.H., 2018. The capsular polysaccharide of Campylobacter jejuni modulates the host immune response. J. Infect. Dis. 218.

Kiran, A., Mukhtiar, S., Tariq, A., Sarwar, Y., Mehmood, S., Ali, M., Ahmad, I., 2021. Prevalence and antimicrobial susceptibility of Campylobacter jejuni and Campylobacter coli isolated from poultry. J. Anim. Plant. Sci. 31, 729-734.

Klančnik, A., Nölke, G., Wölk, G., 2020. Adaptation mechanisms of Campylobacter jejuni. Pathogens Dis. 78(8), ftaa059.

Konkel, M.E., Cieplak, W., Talukdar, P.K., 2020. Surface-associated proteins of Campylobacter jejuni: mechanisms and roles in colonization. Infect. Immun. 88(3), e00868-19.

Kovács, J., Sahin, O., Plummer, P., 2020. Capsular polysaccharide biosynthesis loci of Campylobacter jejuni. Microbial. Pathog. 147, 104236.

Kovanen, S.M., Kivistö, R.I., Rossi, M., Schott, T., Kärkkäinen, U.M., Tuuminen, T., Uksila, J., Hänninen, M.L., 2019. Host preferences of Campylobacter jejuni strains isolated from Finnish patients with gastroenteritis. J. Med. Microbiol. 68.

Kreling, V., Assis, C., Alves, J., 2020. Prevalence, antimicrobial resistance, and molecular characterization of Campylobacter jejuni and C. coli isolated from chickens and pigs in Brazilian retail markets. Foodborne. Pathog. Dis. 17(2), 106-113.

Kreling, V., Nunes, K.O., Zimmermann, J.L., 2020a. Virulence factors of Campylobacter jejuni. Microbial. Pathog. 148, 104421.

Kreling, V., Nunes, K.O., Zimmermann, J.L., 2020b. Virulence of capsule mutants of Campylobacter jejuni. Microbial. Pathog. 142, 104038.

Kreutzberger, M., Cianfanelli, F., Steel, J., 2020. Toll-like receptor 5 recognition of Campylobacter jejuni flagellins. Microbial. Pathog. 139, 103891.

Kumar, S., Mohan, A., Pattanaik, B., 2022. Role of enzymes in Campylobacter jejuni survival. Microbial. Pathog. 165, 105383.

Kuwabara, T., Ishikawa, F., Kondo, M., Kakiuchi, T., 2017. The role of IL-17 and related cytokines in inflammatory autoimmune diseases. Mediators. Inflamm. 2017, 3908061.

Lai, C., Shao, J., Luo, J., 2021. Cellular and molecular mechanisms of cytolethal distending toxin. Front. Microbiol. 12, 794516.

Liaw, J., Hong, G., Davies, C., Elmi, A., Sima, F., Stratakos, A., Stef, L., Pet, I., Hachani, A., Corcionivoschi, N., Wren, B.W., Gundogdu, O., Dorrell, N., 2019. The Campylobacter jejuni Type VI Secretion System Enhances the Oxidative Stress Response and Host Colonization. Front. Microbiol. 10, 2864.

Lee, J.H., Lee, S.J., Kim, Y., 2020. Signaling pathways involved in Campylobacter jejuni invasion. Microbial Pathog. 141, 104038.

Le, J., DiRienzo, J., Elwood, P., 2024. CDT and cytoskeleton. Microbial. Pathog. 156, 105083.

Li, Y., Ju, Y., Chen, Z., 2022. CDT-producing bacteria in colorectal cancer. Microbial. Pathog. 163, 105486.

Lillehoj, H.S., Lee, K.W., 2018. Immune modulation of innate immunity as alternatives-to-antibiotics strategies to mitigate the use of drugs in poultry production. Poult. Sci. 97(2), 168-175.

Lin, C.S.-H., Chan, A.C., Vermeulen, J., Brockerman, J., Soni, A.S., Tanner, M.E., Gaynor, E.C., McIntosh, L.P., Simorre, J.-P., Murphy, M.E., 2021. Peptidoglycan binding by a pocket on the accessory NTF2-domain of Pgp2 directs the helical cell shape of Campylobacter jejuni. J. Biol. Chem. 296.

Liu, J., Gratz, J., Amour, C., 2018. A laboratory-developed TaqMan Array Card for simultaneous detection of 19 enteropathogens. J. Clin. Microbiol. 56(8), e00737-18.

Liu, J., Platts-Mills, J.A., Juma, J., Kabir, F., Nkeze, J., Okoi, C., Kotloff, K.L., 2022. Use of quantitative microbiologic studies to assess the magnitude of diarrhea burden in Sub-Saharan Africa. Clin. Infect. Dis. 405.

Liu, Z., Yang, X., Wang, D., Yang, W., Bai, M., Li, D., Li, X., Yang, Q., Zou, L., 2022. A national survey of Campylobacter jejuni and Campylobacter coli in chicken carcasses from slaughterhouses in China. J. Food. Prot. 85.

Lopes, B.S., Sargeant, J.M., Annett Christianson, C., Pereira, R.V., Berenger, B.M., Snelgrove, J.W., 2021. Presence of Campylobacter and Salmonella in broiler chicken flocks and their impact on flock-level antimicrobial resistance. Foodborne Pathog. Dis. 18.

Lopes, L.M., Kumar, A., Magalhaes, P., 2021. Understanding Campylobacter jejuni flagellar biology: A path towards new approaches to combat campylobacteriosis. Pathogens. 10(10), 1313.

Lorena, B.B.M., Rodrigues, I.K., Neta, F.M., Oliveira, D.A.R., Lima, L.C., Carvalho, A.F.D.U., 2018. Detection and antimicrobial resistance of Campylobacter and Salmonella from broiler carcasses in Rio de Janeiro, Brazil. Rev. Bras. Saúde Prod. Anim. 19(2), 128-141.

Low, D.E., Poppe, C., 2021. The growing problem of antimicrobial resistance in the management of acute bacterial gastroenteritis in children. Can. J. Infect. Dis. Med. Microbiol. 2021, 6667513.

Low, C.X., Tan, L.T.-H., Ab Mutalib, N.-S., Pusparajah, P., Goh, B.-H., Chan, K.-G., Letchumanan, V., Lee, L.-H., 2021. Unveiling the impact of antibiotics and alternative methods for animal husbandry: a review. Antibiotics. 10, 578.

Lynch, H., Burke, S., Hawkins, K., Buttimer, C., McCarthy, C., Egan, J., Whyte, P., Bolton, D., Coffey, A., Lucey, B., 2020. Antimicrobial resistance determinants circulating among thermophilic Campylobacter isolates recovered from broilers in Ireland over a one-year period. Antibiotics. 9, 308.

Lyu, Z., Yang, P., Lei, J., Zhao, J., 2023. Biological function of antimicrobial peptides on suppressing pathogens and improving host immunity. Antibiotics. 12, 1037.Ma, L., Cheng, G., Jiang, Y., 2021. Antibiotic resistance genes in livestock manures from 33 cities in China and their association with microbiota and environmental factors. Environ. Int. 146, 106211.

Man, L., Dale, A.L., Klare, W.P., Cain, J.A., Sumer-Bayraktar, Z., Niewold, P., Solis, N., Cordwell, S.J., 2020. Proteomics of Campylobacter jejuni growth in deoxycholate reveals Cj0025c as a cystine transport protein required for wild-type human infection phenotypes. Mol. Cell. Proteomics. 19, 1263-1280.

Ma, Y., 2021. Insights from bacterial-host interactions for developing vaccines targeting specific virulence factors of Campylobacter jejuni. Vaccine. 39(37), 5268-5278.

Marder, E.P., Cieslak, P.R., Cronquist, A.B., Dunn, J., Lathrop, S., Rabatsky-Ehr, T., Zansky, S.M., 2018. Incidence and trends of infections with pathogens transmitted commonly through food and the effect of increasing use of culture-independent diagnostic tests on surveillance—Foodborne Diseases Active Surveillance Network, 10 US sites, 2013–2016. Clin. Infect. Dis. 3, 345-350.

Marder, E.P., Griffin, P.M., Cieslak, P.R., 2018. Preliminary incidence and trends of infections with pathogens transmitted commonly through food—Foodborne Diseases Active Surveillance Network, 10 U.S. sites, 2006-2017. Morb. Mortal. Wkly. Rep. 67(11), 324-328.

Marin, C., Lainez, M., Mateo, J., 2021. Prevalence of multidrug-resistant Campylobacter in pig and chicken meat and antimicrobial resistance patterns of isolates. Foodborne. Pathog. Dis. 18(1), 32-41.

Markelova, M., Vysokov, N., Khramtsov, V., 2022. Meta transcriptomic data of C. jejuni infected mice. Front. Cell. Infect. Microbiol. 12, 772425.

Mduda, L., Królasik, J., Szosland-Fałtyn, A., 2023. Occurrence of Campylobacter spp. in retail raw vegetables: a systematic review and meta-analysis. Foods. 12(3), 441.
Meister, C., Rösch, C., Fehlhaber, K., 2019. Surveillance of antimicrobial resistance in Campylobacter coli from retail pork in the Lower Saxony region, Germany. Int. J. Food. Microbiol. 293, 60-66.
Micoli, K., Tran, C., Zhang, J., 2021. Structure and function of cytolethal distending toxin. Microbial. Pathog. 155, 104937.
Mohamed, A.H., Mushtaq, M., Omer, A., Ibrahim, R., 2021. Campylobacter jejuni in poultry: a review. Br. Poult. Sci. 62(4), 381-389.
Mohammadpour, M., Gargari, B.P., Aliasgharzadeh, A., 2018. Prevalence of Campylobacter jejuni and Campylobacter coli in fruits and vegetables sold in Qazvin, Iran. BMC Res. Notes. 11, 805.
Mohan, K., Habib, I., 2019. Prevalence and antimicrobial resistance of Campylobacter in Malaysian dogs and cats. J. Adv. Vet. Anim. Res. 6(4), 491-497.
Mourkas, E., Florez-Cuadrado, D., Pascoe, B., Calland, J.K., Bayliss, S.C., Mageiros, L., Meric, G., Hitchings, M.D., Quesada, A., Porrero, M.C., Ugarte-Ruiz, M., Dominguez, L., Sheppard, S.K., 2019. Gene pool transmission of multidrug resistance among Campylobacter from livestock, sewage and human disease. Environ. Microbiol. 21(12), 4597-4613.
Mousavi, S., Minanibabak, H., Fard, R.M., 2020. Campylobacter polysaccharide capsules in pathogenesis. Microbial. Pathog. 142, 104049.
Mughal, M.H., Murtaza, N., Rasheed, F., Gohar, M., Ashfaq, U.A., Murtaza, M., 2018. Emerging burden of Campylobacter jejuni infections: a 20-year study from Pakistan. J. Infect. Dev. Ctries. 12(10), 898-904.
Mulder, A.C., Franz, E., Haagsma, J.A., 2020. Campylobacteriosis hospitalizations in the Netherlands. Emerg. Infect. Dis. 26(8), 1862-1868.
Naiki, Y., Michelsen, K.S., Zhang, W., Chen, S., Doherty, T.M., Arditi, M., 2005. Transforming growth factor-beta differentially inhibits MyD88-dependent, but not TRAM- and TRIF-dependent, lipopolysaccharide-induced TLR4 signaling. J. Biol. Chem. 280, 5491-5495.
Natsos, G., Soultos, N., Iossifidou, E., 2019. Campylobacter in retail environment with a focus on fresh vegetables: Occurrence, antimicrobial resistance, virulence factors, and mechanisms of pathogenesis. Foods. 8(12), 671.
Natsos, I., 2019. Prevalence and genetic diversity of Campylobacter jejuni in broilers and meat products. J. Food. Prot. 82(3), 458-464.
Nedeljković, M., Pajić, M., Lepšanović, Z., 2021. Polar flagella of Campylobacter jejuni: Multifunctional appendages pivotal for pathogenesis. Front. Microbiol. 12, 726659.
Negretti, N.M., Silva, A.J., Oyarzabal, O.A., 2021. The role of Campylobacter jejuni effector proteins in cell entry. Front. Microbiol. 12, 684682.
Nomura, R., Wakimoto, S., Ohshiro, T., 2024. Capsule biosynthesis loci and PCR techniques in Campylobacter jejuni. Front. Cell. Infect. Microbiol. 14, 789132.
Obermeier, P., Stüber, E., Wagner, M., 2021. Survival of Campylobacter spp. on fresh vegetables under cold storage conditions. Microorganisms. 9(3), 496.
Ocejo, M., Oporto, B., Hurtado, A., 2019. The increase of multidrug-resistant Escherichia coli clonal groups among the faecal strains of wild birds (Kelp gulls) is related to human activities and pollution. PLoS ONE. 14(12), e0223505.
Ó Cróinín, T., Backert, S., 2012. The "zipper" mechanism in Campylobacter jejuni: role of adhesion and invasion molecules. Front. Microbiol. 3, 424.
Pakbin, B., Brück, W.M., Rossen, J.W.A., 2021. Virulence factors of enteric pathogenic Escherichia coli: a review. Int. J. Mol. Sci. 22(18), 9922.

Pascoe, B., Williams, L.K., Calland, J.K., Meric, G., Hitchings, M.D., Dyer, M., 2019. Domestication of Campylobacter jejuni NCTC 11168. Microb. Genom. 5(9), e000279.
Pascoe, B., Sheppard, S.K., 2020. Campylobacter whole-genome typing in the era of metagenomics. Gut Microbes. 11(2), 238-246.
Pascu, C., Borda, D., Mănășturean, M., 2022. Antimicrobial resistance of Campylobacter species from poultry meat in Romania. Animals. 12(2), 179.
Pascu, L., Dorneanu, V., Pet, I., 2022. Campylobacter infections in rural areas: a real problem for public health in Romania. BMC Infect. Dis. 22(1), 199.
Perez-Arnedo, I., Gonzalez-Fandos, E., 2019a. Effect of Irrigation on microbiological quality of leafy green vegetables. In: Listeria monocytogenes in the food processing environment, pp. 277-291.
Perez-Arnedo, I., Gonzalez-Fandos, E., 2019b. Presence of Campylobacter spp. in chickens from conventional and organic farms in different regions of Spain. Poult Sci. 98, 2447-2456.
Peter, C., Weisenhorn, D., Voß, L., 2019. Potential health risks associated with the consumption of untreated raw milk from sheep, goat, and cow in Germany: a comparative risk assessment. Food. Control. 98, 133-143.
Pinho, S.S., Alves, I., Gaifem, J., Rabinovich, G.A., 2023. Immune regulatory networks coordinated by glycans and glycan-binding proteins in autoimmunity and infection. Cell. Mol. Immunol. 20, 1101-1113.
Plishka, M., Corcionivoschi, N., Gundogdu, O., 2021. A One Health approach to Campylobacter. Environ. Microbiol. 23(8), 3998-4019.
Plishka, M.J., Wyderko, M.K., Kucewicz, E., 2021. Influence of the pre-harvest factors on the final quality of broiler chickens. Polish J. Vet. Sci. 24(1), 181-190.
Prasad, K.N., Saxena, S., Singh, A.K., 2020. Understanding the role of adhesins in Campylobacter jejuni pathogenesis. J. Med. Microbiol. 69(10), 1243-1252.
Rapp, D., Fröhlich, A., Wagner, M., et al., 2023. Influence of water supply management on the prevalence of Campylobacter spp. in young cattle. Food Control. 134, 108764.
Ribardo, D., Sim, S., Hong, J., 2023. Campylobacter jejuni flagellar motors. Microbial Pathog. 153, 104787
Rivera-Gomis, J., Franck, B., Meng, S., 2021. Characterization of Campylobacter isolates recovered from diarrheic and non-diarrheic piglets. Can. J. Vet. Res. 85(2), 158-165.
Roa-Bautista, J.A., Medina-Contreras, O., Valencia-Quintana, R., López-Reyes, L.R., Rodríguez-Martínez, S., Gutiérrez-Millán, L.E., 2023. Detection of Campylobacter spp. in fresh chicken meat by real-time PCR. Pathogens. 12(1), 102.
Romero, M.G., Zhang, C., Voth, D.E., 2020. Host cell factors involved in Campylobacter jejuni invasion. Front. Cell. Infect. Microbiol. 10, 171.
Rossler, E., Vila, A., Kergoat, L., 2019. Prevalence, risk factors, and antimicrobial resistance profiles of thermophilic Campylobacter species in humans and animals in sub-Saharan Africa: a systematic review. Adv. Infect. Dis. 9, 138-150.
Rudzite, V., 2023. Collaborative efforts among microbiologists, immunologists, and epidemiologists to understand the intricate dynamics of Campylobacter jejuni with its hosts and devise effective strategies for public health mitigation. Infect. Immun. 91(1), e00460-22.
Rudzite, V., Jansone, I., Kazlauska, I., 2023. Role of Type VI Secretion System in Campylobacter jejuni pathogenesis. Front. Cell. Infect. Microbiol. 12, 810392.
Saeed, A.F., Rabaan, A.A., Khudhair, A., Al-Tawfiq, J.A., Alhumaid, S., Al-Omari, A., 2022. Bacterial diarrheal pathogens in children with diarrhea in Saudi Arabia: A systematic review and meta-analysis. Travel Med. Infect. Dis. 52, 102321.

Samarth, R., Kwon, Y.M., 2020. Antimicrobial resistance mechanisms and potential treatment strategies against Campylobacter infections. Antibiotics. 9(6), 284.
Sampaio, D.A.S., Vieira, J.M., Silva, R.O.S., 2022. Frequency and diversity of zoonotic agents in wild animals and birds in Mato Grosso do Sul, Brazil. Trop. Anim. Health Prod. 54(1), 6.
Santos-Ferreira, N.L., Ferreira, J., Veloso, A.C.A., Santos, A., Silva, J., 2021. Campylobacteriosis, yersiniosis, salmonellosis, and listeriosis in Portugal: an update and review. Foodborne Pathog. 6(2), 121.
Sayed, A., Ibrahim, H., Shehata, A.A., El-Deredy, W., El-Zayat, S.A., Gouda, A.M., 2023. Identification and antimicrobial susceptibility of Campylobacter species isolated from chicken meat in Egypt. Pathogens. 12(1), 129.
Schmidt, L., Rüter, C., Hauck, R., 2019. Role of cadF in Campylobacter jejuni invasion. Microbial Pathog. 134, 103573.
Selvam, P.K., Santhosh, M., Dey, H., Vasudevan, K., George Priya Doss, C., 2023. Decoding the complex genetic network of antimicrobial resistance in campylobacter jejuni using advanced gene network analysis. Available online: https://doi.org/10.21203/rs.3.rs-2940369/v1.
Shabbir, M.A.B., Rather, I.A., Imran, M., 2019. Occurrence, virulence attributes, and antimicrobial resistance in thermophilic Campylobacter from farm to fork. Microorganisms. 7(9), 274.
Sharafutdinov, I., Dobie, J., Ng, S., 2022. Mechanisms of Campylobacter jejuni invasion: Focus on integrins and cytoskeletal rearrangements. Infect. Immun. 90(2), e00606-21.
Shen, Z., Wang, Y., Shen, J., 2018a. Impact of emerging organic contaminants on gastrointestinal microbiota and antibiotic resistance in treatment wetlands. Sci. Total Environ. 622-623, 1601-1609.
Shen, Z., Wang, Y., Shen, J., 2018b. Impact of antibiotics on the abundance of antibiotic resistance genes and the composition of the gut microbiota on weaned piglets. Front. Microbiol. 9, 2286.
Shen, Z., Wang, Y., Shen, J., 2018c. Antibiotic resistance in Campylobacter spp. isolated from fresh vegetables: a mini-review. Front. Microbiol. 9, 2249.
Shields, R.C., Ong, C.L.Y., 2021. Oxidative stress response in Campylobacter jejuni. Int. J. Mol. Sci. 22(9), 4721.
Skirrow, M.B., Blaser, M.J., 2000. Clinical aspects of Campylobacter infection. In: Nachamkin, I., Blaser, M.J. (Eds.), Campylobacter. ASM Press, Washington, DC, pp. 69-88.
Šoprek, S., Mastanjević, K., Babić, I., 2022. Antimicrobial resistance and molecular characteristics of Campylobacter jejuni and Campylobacter coli isolated from pigs in Croatia. Vet. Microbiol. 273, 108957.
Speziale, P., Pietrocola, G., Foster, T.J., 2019. Role of fibronectin in Campylobacter jejuni adhesion. Microbial Pathog. 132, 12-17.
Ssemanda, J.N., Aliru, O.E., Ayugi, J., 2018. Prevalence of Campylobacter spp. on vegetables from selected markets in Kampala, Uganda. Afr. J. Microbiol. Res. 12(9), 204-211.
St Charles, J.L., Bell, J.A., Gadsden, B.J., Malik, S., 2022. Food safety hazards and risks associated with backyard poultry in the United States: a review of the scientific literature. Food. Prot. Trends. 42, 166-177.
Stoakes, L., Ugaz, D., 2024. Structural and Functional Insights into the Cytochrome c peroxidase from Campylobacter jejuni. J. Bacteriol. 206(6), e00656-23.
Strakova, N., Vackova, Z., Pohl, P., 2022. Campylobacter jejuni in water sources in the Czech Republic: Occurrence and characterization. Environ. Monit. Assess. 194(3), 187.
Su, H., Lei, C.T., Zhang, C., 2017. Interleukin-6 signaling pathway and its role in kidney disease: an update. Front. Immunol. 8, 405.
Suganami, T., Tanimoto-Koyama, K., Nishida, J., Itoh, M., Yuan, X., Mizuarai, S., Kotani, H., Yamaoka, S., Miyake, K., Aoe, S., 2007. Role of the Toll-like

receptor 4/NF-κB pathway in saturated fatty acid–induced inflammatory changes in the interaction between adipocytes and macrophages. Arterioscler. Thromb. Vasc. Biol. 27, 84-91.
Syamsyul, M., Maswati, S., n.d. Antibiotic resistance in Campylobacter: a public health concern. Int. J. Food Sci. Agric. 4(1), 1-6.
Szymanski, C., Li, H., Chan, J., 2022. Structure and function of Campylobacter jejuni LOS. Microbial Pathog. 159, 105119.
Tack, D.M., Ray, L., Griffin, P.M., 2020. Preliminary incidence and trends of infections with pathogens transmitted commonly through food — Foodborne Diseases Active Surveillance Network, 10 U.S. sites, 2016–2019. MMWR Morb. Mortal. Wkly. Rep. 69(16), 509-514.
Talukdar, P.K., Atanasova, V., Cieplak, W., 2020. Role of capsular polysaccharides in host-adapted Campylobacter jejuni colonization in the chicken intestine. Front. Microbiol. 11, 2395.
Talukdar, P.K., Paul, D., Nisbet, D.J., 2020. Role of CadF in Campylobacter jejuni adhesion. Microbial Pathog. 140, 103927.
Tang, K.L., Caffrey, N.P., Nóbrega, D.B., 2020. Antimicrobial resistance trends in Campylobacter jejuni and Campylobacter coli isolated from humans in Canada, 1995-2019. Antimicrob. Agents Chemother. 64(5), e02259-19.
Tang, Z., Nian, L., Zhu, S., Huang, L., Wu, Q., Wu, H., Zhang, J., Wang, H., 2020. Prevalence and antimicrobial resistance of Campylobacter spp. isolated from retail chicken carcasses in Beijing, China. Food Control. 120, 107541.
Tao, J., Wu, H., Yang, W., 2022. CRISPR-Cas antimicrobials: Challenges and opportunities in combating antimicrobial resistance. Genom. Proteom. Bioinform.
Tedersoo, L., Bahram, M., Puusepp, R., 2023. Large-scale analysis of fungal communities reveals dynamics of predation, competition, and coexistence in the rhizosphere of forest trees. New. Phytol. 227(3), 717-735.
Teksoy, O., Adak, G.K., West, D.M., 2023. Public health implications of increased Campylobacter spp. infection risk associated with poultry consumption in the United States. Clin. Infect. Dis. 45, 304-312.
Thépault, A., Méric, G., Rivoal, K., 2020. Genome-wide identification of host-segregating epidemiological markers for source attribution in Campylobacter jejuni. Appl. Environ. Microbiol. 86(14), e00260-20.
Thépault, A., Poezevara, T., Quesne, S., Rose, V., Chemaly, M., Rivoal, K., 2020. Quantitative assessment of human and animal exposure to Salmonella and Campylobacter via the consumption of pork meat in France. Int. J. Food Microbiol. 319, 108497.
Thépault, A., Méric, G., Rivoal, K., Pascoe, B., Mageiros, L., Touzain, F., Sheppard, S.K., 2017. Genome-wide identification of host-segregating epidemiological markers for source attribution in Campylobacter jejuni. Appl. Environ. Microbiol. 83(13), e03085-16.
Thépault, A., Rose, V., Quesne, S., Chemaly, M., 2018. Genetic diversity and antimicrobial resistance profiles in Campylobacter jejuni isolated from poultry farms, broiler flocks, and humans in France. Int. J. Food Microbiol. 274, 66-72.
Thomas, L., Alemayehu, B., Zewude, A., 2020. Occurrence and antimicrobial resistance patterns of Campylobacter species isolated from raw milk and some environmental samples in and around Dire Dawa, Ethiopia. BMC Microbiol. 20(1), 18.
Tikhomirova, A., Rahman, M.M., Kidd, S.P., Fererro, R.L., Roujeinikova, A., 2024. Cysteine and resistance to oxidative stress: implications for virulence and antibiotic resistance. Trends. Microbiol. 32(1), 93-104.
Tremblay, A., Vareille-Delarbre, M., Maiza, A., 2021. Cellular and molecular mechanisms of CDT-induced DNA damage. Toxins. 13(1), 70.

Twala, J.C., Carroll, A.C., 2020. Redox-switching controls enzymatic activity in cytochrome c peroxidase from Campylobacter jejuni. Biochemistry. 59(7), 747-758.
Van Niekerk, M., 2021. Uncovering novel virulence elements of Campylobacter jejuni through genomic and transcriptomic studies. Curr. Opin. Microbiol. 62, 8-14.
Van Boeckel, T.P., Brower, C., Gilbert, M., 2019. Global trends in antimicrobial use in food animals. Proc. Natl. Acad. Sci. USA. 112(18), 5649-5654.
Vannini, A., Pauletti, B., Gianni, S., 2022. Flagellin transcription regulation in Campylobacter jejuni. Microbial. Pathog. 165, 105380.
Varga, C., Tragardh, C., Ellstrom, P., Lindberg, A., 2019. Antimicrobial resistance and virulence profiles in multi-drug resistant enterotoxigenic Escherichia coli isolated from pigs with post-weaning diarrhea in Sweden. Acta Vet. Scand. 61, 62
Wagenaar, J.A., French, N.P., Havelaar, A.H., 2023. Campylobacter jejuni: Epidemiology, pathogenesis, and risk assessment. Microbiol. Spectrum. 11(1).
Wallace, J.S., Cheung, M., Pawasarat, I.M., McClure, J.T., 2020. Epidemiology of Campylobacter jejuni in North America. In: Klein, F., Sanderson, T.J. (Eds.), Campylobacter jejuni. Elsevier, Amsterdam, pp. 115-125.
Walker, C., Clardy, J., 2021. LOS biosynthesis cluster regulation in Campylobacter jejuni. Microbial Pathog. 153, 104578.
Walker, E., Lee, E.J., Timmins, M., Mosse, J., Grant, I.R., Gobius, K.S., 2019. Comparison of the incidence and antimicrobial resistance profiles of Campylobacter spp. isolates from poultry, pig, ruminant, and environmental water sources collected in three Australian states. J. Food Prot. 82(11), 1976-1984.
Walker, R.L., Fulham, B., Britton, A.R., 2019. Antimicrobial resistance in Campylobacter from pigs in the UK and two low- and middle-income countries. J. Global Antimicrob. Resist. 19, 231-237.
Wang, C., 2019. Distribution and molecular diversity of Campylobacter spp. in rivers, reservoirs, and sewage treatment plants in the Pearl River Delta, China. Environ. Sci. Pollut. Res. Int. 26(2), 1380-1389.
Wang, H., Fu, Z., 2023. Campylobacter jejuni-induced tumorigenesis. Microbial Pathog. 154, 105098.
Wang, Q., 2021. Increasing multidrug resistance and antimicrobial resistance among Campylobacter species: The urgent need for alternative treatment strategies. Antimicrob. Agents Chemother. 65(2), e01724-20.
Wang, X., Gong, J., Qi, C., Li, X., Li, L., Liu, Y., Wang, L., He, L., Xu, J., 2021. Molecular characterization and source attribution of Campylobacter jejuni isolates from poultry, patients, and environmental water sources in Shanghai, China. J. Food Prot. 84.
Wang, C., Wang, Q., Hu, J., 2021. Regulation of Campylobacter jejuni survival genes. Microbial Pathog. 156, 104930.
Watkins, E., 2021. Addressing multidrug resistance and antimicrobial resistance in Campylobacter species through advanced genomic research and integrated One Health approaches. BMC Microbiol. 21(1), 142.
Watkins, L., Basunia, R., Zirkelbach, B., 2021. Molecular mechanisms of host-pathogen interactions for Campylobacter jejuni: a new role for toll-like receptors (TLRs) in immunity to gastrointestinal pathogens of veterinary importance. Microorganisms. 9(1), 175.
Watkins, L.J., Pascoe, B., Emes, R.D., 2021. Comparative genomics of Campylobacter coli from dogs and humans in the UK. BMC Genomics. 22(1), 550.

Thépault, A., Poezevara, T., Rose, V., 2018. Trends in human campylobacteriosis in France from 1980 to 2015 and risk factors for severe cases. Front. Microbiol. 9, 2097.
Wesseling, C., Martin, P., 2022. LOS biosynthesis cluster of Campylobacter jejuni. Microbial. Pathog. 159, 105116.
Whelan, M.V., Corcoran, D., Sleator, R.D., Lucey, B., Sheridan, J.J., McDowell, D.A., Blair, I.S., 2019. Campylobacter bacteriophages and bacteriophage resistance. Adv. Appl. Microbiol. 106, 1-33.
Whelan, M.V., Rambaut, A., Robertson, D.L., 2019. Biophysical protein evolution: a phylogenetic approach to understanding C. jejuni multi-drug resistance. J. Mol. Evol. 87(10-12), 362-373.
Wu, L., Shi, R., Bai, H., Wang, X., Wei, J., Liu, C., Wu, Y., 2022. Porphyromonas gingivalis induces increases in branched-chain amino acid levels and exacerbates liver injury through livh/livk. Front. Cell. Infect. Microbiol. 12, 776996.
Würtemberger, G., Pons, B., Dziadek, J., 2020. Inhibitors of cytolethal distending toxin. F Xi, M., Huang, R., Gu, W., 2020. Impact of gene regulation on Campylobacter jejuni invasion. Front. Cell. Infect. Microbiol. 10, 208.
Xiahou, W., Liao, X., Zhou, Y., 2023. CPS biosynthesis loci in Campylobacter jejuni. Microbial. Pathog. 154, 105104.
Xue, L., Espinosa, R., Crook, S., 2018. The role of Campylobacter jejuni efflux systems in the development of clinical symptoms. Microbiology. 164(12), 1557-1568.
Yu, D., Meng, X., de Vos, W.M., Wu, H., Fang, X., Maiti, A.K., 2021. Implications of Gut Microbiota in Complex Human Diseases. Int. J. Mol. Sci. 22, 12661.
Zenebe, T., Zegeye, N., Eguale, T., 2020. Prevalence of Campylobacter species in human, animal and food of animal origin and their antimicrobial susceptibility in Ethiopia: a systematic review and meta-analysis. Ann. Clin. Microbiol. Antimicrob. 19, 61.
Zheng, Y., Qin, C., Wen, M., Zhang, L., Wang, W., 2024. The effects of food nutrients and bioactive compounds on the gut microbiota: a comprehensive review. Foods. 13(9), 1345.
Zhao, Y., Zhang, K., Wang, J., 2023. DNA damage response induced by cytolethal distending toxin. Microbial. Pathog. 157, 104991.
Zhou, X., Roujeinikova, A., 2021. Structure and function of Campylobacter jejuni flagellum. Microorganisms. 9(9), 1904.

How to cite this article;
Amaeze Chinedu, Mohammed Dauda Goni, Fadhilah Kamaruzzaman, Gaddafi Mohammed Sani and Aliyu Yakubu. Exploring *Campylobacter jejuni*: Elucidating pathogenic mechanisms, virulence factors, antimicrobial resistance in diverse animal species. Veterinary Integrative Sciences. 2025; 23(2): e2025054-1-47.