

Epidemiology and Public Health Significance of Campylobacteriosis

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Abstract

Emerging food borne pathogens are significant causes of morbidity and mortality both in developing nations as well as developed. *Campylobacter* is well recognized as the leading cause of bacterial food borne diarrheal disease and distributed all over the world. Campylobacteriosis is a collective description for infectious diseases caused by members of the bacterial genus *Campylobacter*. The only form of Campylobacteriosis of major public health importance is *Campylobacter* enteritis due to *C. jejuni* and *C. coli*. Research and control efforts on the disease have been conducted more often in developed countries than developing countries. However, because of the increasing incidence, expanding spectrum of infections, potential of HIV related deaths due to *Campylobacter*, epidemiological data suggest that *Campylobacter* remains a worldwide leading cause of gastrointestinal infections. Improperly prepared meat products, unpasteurized milk as well as non-chlorinated drinking water were shown to be the main sources of Campylobacteriosis. National surveillance programs and international collaborations are needed to address the substantial gaps in the knowledge about the epidemiology of Campylobacteriosis in developing countries. The aim of this review paper is to assess the global and national epidemiology and public health significance of *Campylobacter* with emphasis on the prevention and control options in developing countries following the experience of developed countries.

Keywords: Antimicrobial susceptibility • *Campylobacter* Spp. • Control measures • Epidemiology • Food borne pathogens • Public health

Abbreviations: AIDS: Acquired Immune Deficiency Syndrome; BGOSHU: Bruce-Grey-Owen Sound Health Unit; BoD: Burden of Disease; *C. coli*: *Campylobacter coli*; *C. jejuni*: *Campylobacter jejuni*; CCDA: Charcoal Cefoperazone Deoxycholate; CDC: Centre for Disease Control; CDT: Cytotoxic Distending Toxin; DALY: Disability Adjusted Life Year; DNA: Deoxyribonucleic Acid; ECDC: European Centre for Disease Prevention and Control; EFSA: European Food Safety Authority; EU: European Union; FDA: Food and Drug Administration; FSA: Food Safety Authority; FSAI: Food Safety Authority of Ireland; FSANZ: Food Standards, Australia New Zealand; GBS: Guillain-Barre Syndrome; HACCP: Hazard Analysis and Critical Control Points; HGT: Horizontal Gene Transfer; HIV: Human Immuno Deficiency Virus; HS: Heat-Stable; IBS: Irritable Bowel Syndrome; LMIC: Low and Middle-Income Countries; MFS: Miller Fisher Syndrome; NaCl: Sodium Chloride; NSM: National Standard Methods; Spp.: Species; UK: United Kingdom; USA: United States of America; VNC: Viable Non-Culturable; WHO: World Health Organization

Introduction

Campylobacter is one of the major pathogens involved in food borne illnesses with an estimated 400 million cases per year worldwide [1]. *Campylobacter* infection has been reported to occur more frequently than infections caused by *Salmonella* spp., *Shigella* spp. or *Escherichia coli* O157:H7 [2]. In many countries, the organism is Campylobacteriosis in humans is characterized by watery or bloody diarrhea and abdominal cramps [3].

Campylobacteriosis is a disease caused by species of *Campylobacter*. These infections are a major leading cause of gastrointestinal disease globally. Although gastrointestinal diseases associated with species of *Campylobacter* are rarely fatal, significant proportion of diarrhoeal cases are reported annually, which result in significant burden on health care systems and a major cause of economic loss globally. Another emerging issue is the global increase of *Campylobacter* species resistant to clinically recommended antimicrobials [4].

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The *Campylobacter* bacterial genera contain several species of both public and animal health. Among them *Campylobacter jejuni* and *Campylobacter coli* are the most common cause of gastroenteritis in humans. Children, the elderly and those with weakened immune system (including cancer, HIV/AIDS and transplant patients) being the risk group [5].

Campylobacter spp. is normally carried in the intestinal tracts of many domestic livestock such as poultry, cattle, sheep, pigs, as well as wild animals and birds [6]. Transmission can occur through direct contact with infected animals or from equipment, water or during carcass dressing in a slaughter line [7]. *Campylobacter* contaminated foods as the result of poor sanitation are an important potential source of infection in humans. Food-acquired Campylobacteriosis accounts for up to 74 to 85% of total cases, with poultry being the number one contributing vehicle [8]. Ingestion of undercooked meat is thought to be the main source of Campylobacteriosis in humans. Other important modes of transmission include exposure to faecal material from livestock, contact with animals (particularly ruminants) and recreational swimming [9].

In Ethiopia likewise, a few publications have reported on the occurrence and susceptibility testing of *Campylobacter* strains to antimicrobials on human, foods of animal origin and antimicrobial susceptibility pattern. And a few accessed on the status of on the epidemiology of and public health significances of *Campylobacter* species in both veterinary and public health sectors.

Objective

To asses;

- The epidemiology and public health significance of Campylobacteriosis: Globally, developed and developing countries.
- The public health significance and economic burden of *Campylobacter*.
- The current prevention and control methods against the disease.

Literature Review

General description of *Campylobacter*

Historical emergence: The name *Campylobacter* is derived from the Greece campylos meaning curved and baktron meaning rod. In 1886 Theodor Escherich first described non-culturable spiral shaped bacteria which were observed in the colons of infants who died of a disease he named cholera infantum [10]. Following Theodor Escherich's observations, *Campylobacter* was first identified in the uterine mucus of a pregnant sheep in 1902 by two British veterinarians [11].

Initially campylobacters were referred to as vibrio like organisms until 1963 when Sebald and Veron proposed *Campylobacter* as the genus based on their curved-rod like shape (Figure 1), low DNA base composition, microaerophilic growth requirement, and their non-fermentive metabolism [12].

Taxonomy: The genus *Campylobacter* has been classified as follows:

Domain: Bacteria

Phylum: Proteobacteria

Class: Epsilonproteobacteria

Order: Campylobacterales

Family: Campylobacteraceae

Genus: *Campylobacter*

Species: *Campylobacter jejuni*; *C. coli*; *C. fetus*

(Source: Vandamme and on, 2001).

Species of *Campylobacter*: *Campylobacter* spp. is gram-negative, non-spore forming bacteria. The genus *Campylobacter* comprises of 17 species and 6 subspecies. The two species most commonly associated with human disease are *C. jejuni* and *C. coli*. Accounts for more than 80% of *Campylobacter*-related human illness, with *C. coli* accounting for up to 18.6% of human illness. *C. fetus* has also been associated with foodborne disease in humans [13].

The emergence of species within the genus *Campylobacter* over the last three decades has indicated their pathogenic clinical importance. *Campylobacter* species have been implicated as aetiological agents for veterinary diseases, such as diarrhoea in cattle, septic abortion in cattle and sheep and more recently as significant clinical pathogens, particularly of human public health concern. *Campylobacter* is a major food and waterborne pathogen where foods of animal origin, particularly poultry, have been identified as significant sources of *Campylobacter* infection [14]. *C. jejuni* and *C. coli* are species of major public health importance of the genus *Campylobacter*.

Morphology: *Campylobacter* species are fastidious, gram negative bacilli that are morphologically spiral or curved. The morphology of *Campylobacter* is comparatively very small, about 0.2 to 0.8 µm wide and 0.5 to 5 µm long [15]. *Campylobacter* species are motile by means of unipolar or bipolar flagellae. When two or more bacterial cells are grouped together, they form an -S or a -V shape of gull-wing. The organisms do not form spores and most are featured with a corkscrew-like motion by means of a single polar unsheathed flagellum at one or both ends of the cell. These thermophilic species of bacteria thrives well at higher body temperatures, ranging from 30 degrees Celsius (°C) to 44°C.

They require longer incubation periods for optimum growth, ranging from 48 hours to 96 hours microaerophilically, depending on the specific species. *Campylobacter* species are non-fermenting organisms due to their incapability to ferment or oxidize common carbohydrate substrates. However, they are oxidase positive and they reduce nitrates. Spirally shaped *Campylobacter* have been reported to transition into coccoid forms when exposed to atmospheric oxygen levels or other environmental stresses. Viable Non-Cultural (VNC) has been used to describe the coccoid transitioned state, and it is suggested to be a dormant state necessary for survival under un-optimal environmental conditions for *Campylobacter* growth [16]. Although *Campylobacter* requires special growth conditions, the bacterium may survive on food or in the environment for a couple of days.

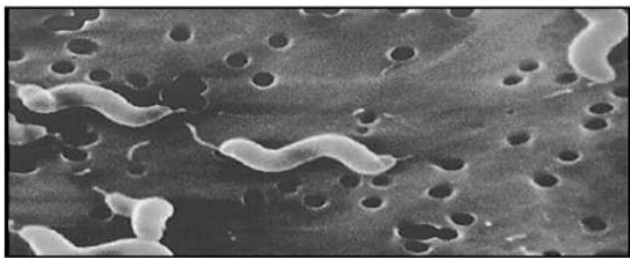


Figure 1. Curved/rod shape and bipolar flagella of *Campylobacter jejuni*; Scanning electron micrograph showing the curved/rod shape and bipolar flagella of *C. jejuni*.

Source: Image adopted from Javid and Ahmed, (2016).

Growth and survival characteristics: *Campylobacter* spp. is fastidious bacteria sensitive to environmental factors like oxygen, drying and heating [17].

The organisms are able to grow at temperatures between 30°C and 44°C, the optimum temperature being 42°C. Since they do not exhibit true thermophily (growth at 55°C or above), they are micro-aerophilic, growing best in an atmosphere with low oxygen tension (5% O₂, 10% CO₂, and 85% N₂).

These characteristics reduce the ability of *Campylobacter* spp. to multiply outside of an animal host as well as in food during their processing and storage. Growth does not occur in environments with water activity (aw) lower than 0.987 (sensitive to concentrations of Sodium Chloride (NaCl) greater than 2% w/v), while optimal growth occurs at aw=0.997 (approximately 0.5% w/v NaCl). *Campylobacter* spp. is easily inactivated by heat treatments. In pure cultures, *Campylobacter* spp. is normally inactivated by frozen storage at -15°C in as few as 3 days (Table 1).

	Minimum	Optimum	Maximum
Temperature (°C)	32	42-43	45
pH	4.9	6.5-7.5	9.5
Water activity	0.987	0.997	-

(Source: Forsythe, 2000)

Table 1. Limits for growth of *Campylobacter* spp. when other conditions are near optimum.

Virulence and infectivity: *Campylobacter* spp. has four main virulence properties: Motility, adherence, invasion and toxin production. The exact nature of how *Campylobacter* spp. adheres to and invades the intestinal epithelial cells is not fully understood. It is thought that the combination of its spiral shape and flagella leads to rapid motility that enables the organisms to penetrate through the intestinal lining unlike conventional bacteria [18].

Host range: *Campylobacter* organisms have a broad host range inhabiting multiple animal hosts and environmental reservoirs, but are thought to be particularly well adapted for survival in birds. They have been isolated from surface and ground waters, domestic and wild mammals, pet animals, rodents, insects and wild birds. Animals usually carry high bacterial loads, suggesting commensal adaptations of the bacterium to their guts. The most prominent source for human infections is consumption of chicken meat, either directly or through cross-contamination with other food items [19].

Transmission

Campylobacter spp. is transmitted to humans via the faecal-oral route, predominantly through the consumption of contaminated food or water or direct contact with infected animals. They are often present in the intestines of domestic and wild animals, such as cattle, sheep, poultry, dogs, wild birds and rodents, and are shed in the faeces of these animals.

Mostly human Campylobacteriosis are associated with handling of raw poultry, undercooked contaminated meat, cross contamination of raw and cooked foods and poor hygiene.

Campylobacter spp. present on raw meats may contaminate work areas and the hands of kitchen staff before being transferred to ready to eat foods or causing self-infection. External packaging material of raw meat (raw chicken, game fowl, lamb and beef) has been reported

to be a vehicle of cross-contamination of *Campylobacter* spp. in retail premises and consumer homes. This uncommon type of transmission can occur when personal hygiene is poor. Humans act as vectors transferring the organism into poultry production area with contaminated clothing and foot wear.

Occurrence in foods

Poultry meat is generally recognised as a primary source of *Campylobacter* infection in humans. The reported incidence of *Campylobacter* spp. on raw meat products from other food animal species tends to be lower than those reported for poultry. Using population genetics approaches, Wilson, et al. confirmed that the vast majority (97%) of sporadic *Campylobacter* infections in the UK could be attributed to animals farmed for meat and poultry. Chicken and cattle were the principal sources of *C. jejuni* pathogenic to humans, with wild animal and environmental sources responsible for the remaining 3% of human disease.

In an Australian baseline survey carried out during 2007-2008 on the incidence and concentration of *Campylobacter* and *Salmonella* in raw chicken, 84.3% of post-processing carcass rinse samples (n=1,104) were positive for *Campylobacter* spp. These results were similar to those from a retail baseline microbiological survey carried out in 2005-2006 in South Australia and New South Wales, which found that 90.0% of retail poultry samples (n=859) were contaminated with *Campylobacter* spp.

A retail survey conducted in New Zealand between 2005-2008 found 72.7% of poultry carcasses were contaminated with *C. jejuni* (n=500). Several internationally rare serovars as well as common human clinical serovars were isolated.

A baseline survey carried out in the EU in 2008 revealed that 75.8% of broiler carcasses sampled (n=9,213) were contaminated

with *Campylobacter* spp. The prevalence of *C. jejuni* and *C. coli* were 51.0% and 35.5%, respectively. *Campylobacter* spp. was also commonly detected in live poultry, pigs and cattle.

In the UK, a survey of poultry sold at retail carried out during 2007-2008 indicated that 65.2% of samples tested (n=3,274) were contaminated with *Campylobacter* spp. *C. jejuni* was present in 52.9% of the samples while 47.1% contained *C. coli*.

In a survey of retail food stuffs in Ireland between 2001–2002, *Campylobacter* spp. were found in 49.9% of raw chicken (n=890), 37.5% of raw turkey (n=88), 45.8% of raw duck (n=24), 3.2% of raw beef (n=221), 5.1% of pork (n=197), 11.8% of lamb (n=262), 0.8% of pork pate (n=120), 2.3% of raw oysters (n=129), and 0.9% of fresh mushrooms (n=217) tested. Of the positive samples, 83.4% were contaminated with *C. jejuni* and 16.6% were contaminated with *C. coli*.

Factors influencing Campylobacteriosis epidemiology

Age: Campylobacteriosis is often a pediatric disease especially in developing countries. This is because of multiple reasons; as age increases, level of antibody tends to increase. Higher risk of Campylobacteriosis in young children was also associated with ownership of pet chickens [20].

Season: In developed countries epidemics occur in summer and autumn. Isolation peaks vary from one country to another and also within countries; in contrast, in developing countries, *Campylobacter* enteritis has no seasonal preference. The lack of seasonal preference may be due to lack of extreme temperature variation as well as lack of adequate surveillance for epidemics.

Travel and food trade: Foreign travel is a commonly reported risk factor for Campylobacteriosis. In Sweden, where *Campylobacter* contamination of poultry meat is uncommon, international travel has traditionally accounted for approximately 75% of human *Campylobacter* infections. In the United States, it is estimated that between 20 and 25% of *Campylobacter* infections are acquired during international travel. Campylobacteriosis was the most frequently reported enteric bacterial infection in Austrian tourists returning from Southern Europe and Asia. In England, travel to South Africa was associated with *C. coli* infection. The causal exposures for travel associated infections remain to be determined.

Strain variation: Although a diverse group of strains is associated with Guillain-Barre Syndrome (GBS), the syndrome is strongly linked to a few strains of *C. jejuni* (e.g. heat stable or Penner serotype HS: 19 and HS: 4). *Campylobacter* strains contain sialic acid linkages to lipooligosaccharides resembling sialic acid moieties on the gangliosides of peripheral nerve tissues. Patients with GBS develop antibodies against these gangliosides, resulting in autoimmune targeting of peripheral nerve sites. Complement mediated damage and blockage of neurotransmission are suspected to affect GBS pathogenesis.

Host immunity: Acquired immunity is generally accepted to be an important factor in the epidemiology of Campylobacteriosis. Prior exposure to *Campylobacter* may result in at least partial protective immunity. Since immunity may be strain specific, time limited, and/or inadequate in the presence of large challenge doses, repeated or chronic exposure to a variety of *Campylobacter* strains may be required to produce protective immunity.

In developing countries, healthy children and adults are constantly exposed to *Campylobacter* antigens in the environment. As a consequence, the levels of antibodies tend to be much higher than those in children in the developed world such as in the United States.

Global epidemiology of Campylobacteriosis

Campylobacter infections in animals from different countries: *Campylobacter* spp. is carried in the intestines of many wild and domestic animals, particularly avian species including poultry. Intestinal colonization in most of these animals results in a commensal relationship thereby producing carriers. Some studies have however associated *Campylobacter* infections in wild animals with disease manifestations.

Several research reports showed that *Campylobacter* spp. were associated with disease outbreaks in a variety of semi-wild and wild animals, with negative impacts on their health, productivity and welfare. It is suggested that horizontal transmission plays a major role in the spread of *C. jejuni* within and between poultry flocks. Probable sources of infection include colonized birds, contaminated faces, feed, litter, water, equipment and transport vehicles, or even wild birds and insects.

Certain *Campylobacter* species, e.g. *C. fetus* and *C. jejuni*, are important reproductive tract pathogens in farm animals (leading to abortion and/or infertility issues). Other species, such as *C. helveticus* can cause periodontal diseases. However, the majority of species are implicated in acute enteritis.

Human Campylobacteriosis in different countries: *Campylobacter* is a zoonotic pathogen and is the main cause of human bacterial gastroenteritis in the world.

In Europe, it is estimated that there are approximately 9 million cases of human Campylobacteriosis per year. Since 2005, in the EU, *Campylobacter* has been the most commonly reported gastrointestinal bacterial pathogen in humans. Compared to previous years, in 2009, the number of reported and confirmed human Campylobacteriosis cases in the EU increased by 4%. This rise also reflected an overall increase in the Campylobacteriosis notification rate in Europe. Campylobacteriosis is a commonly reported zoonosis in the European Union (EU) and a commonly notified bacterial gastrointestinal disease in Germany. The annual number of notified Campylobacteriosis cases has increased in many European countries in recent years relative to other enteric pathogens such as Salmonella.

In the United States of America (USA), *Campylobacter* infection is the second commonest cause of bacterial enteritis after salmonellosis, with 2.4 million cases estimated to occur yearly.

In New Zealand has, until recently, ranked first in the world for human Campylobacteriosis notification rates. *A. jejuni* has accounted for 24% to 34% of human Campylobacteriosis cases in New Zealand. It is a geno type strongly associated with poultry, particularly in those living in urban areas.

In 2004 the incidence of Campylobacteriosis in Canada increased to 9345 cases per 100,000. Similarly, the incidence of reported human cases of Campylobacteriosis in Northern European countries ranged

from 60 to 90 cases per 100,000, (it has been estimated to be substantially increasing in the last 20 years) a substantial increase over the previous 20 years.

In the United Kingdom in 1998, there were 58,059 laboratory confirmed cases in England and Wales whereas, during 2000 there were 1,388,772 cases of food borne infection acquired in England and Wales of which *Campylobacter* accounted for 359,466 of these cases. There were 171,174 presentations to general practice due to *Campylobacter* infection, 16,946 hospital admissions (accounting for 62,701 hospital bed-days) and 86 deaths.

In Denmark, the incidence of disease remained relatively unchanged from 1980 to 1990 (475 cases) and then from 1992 to 1999 there was a three-fold increase (1,676) in incidence risk. In the case of Germany reported cases of *Campylobacteriosis* in 2003 were 58 per 100,000 and this increased to 79 per 100,000 in 2009. The incidence of *Campylobacter* infection in Australia increased steadily from 1991 through to 2001. From 2001 to 2005 the incidence was relatively stable at 113 cases per 100,000 head of population (approximately 15,000 cases per year).

Stafford, et al. commented that *Campylobacter* is likely to be underreported estimating that there are around 223,000 *Campylobacter* infections occurring annually.

In 2015, a total of 229213 human *Campylobacteriosis* cases were reported by the EU member states, with an incidence of 65.5 per 100 000 inhabitants. As this number only includes confirmed cases, the true annual number of cases is much higher, estimated at nine million in the EU alone.

Human *Campylobacteriosis* in developing countries: The incidence of *Campylobacteriosis* in developing countries estimates of disease frequency in the general population have been shown to be approximately 90 per 100,000 with varying orders of magnitude. Recovery rates of bacteria decrease with the age of the patient.

Campylobacter surveillance in developing countries is not what it should be as compared to developed countries; a situation that compromises incidence values for cases of *Campylobacteriosis* for a population (Figure 2).

In Africa, it is estimated that 3.552 million children of less than five years of age die each year, with diarrhoea accounting for 11% of these deaths. Compiled data from published literature has indicated research gaps existing in developing countries for *Campylobacter*. For instance in Africa, there are few collected published data reports on cases of *Campylobacteriosis* in Kenya and Malawi, as well as Tanzania, and South Africa (Figure 3).

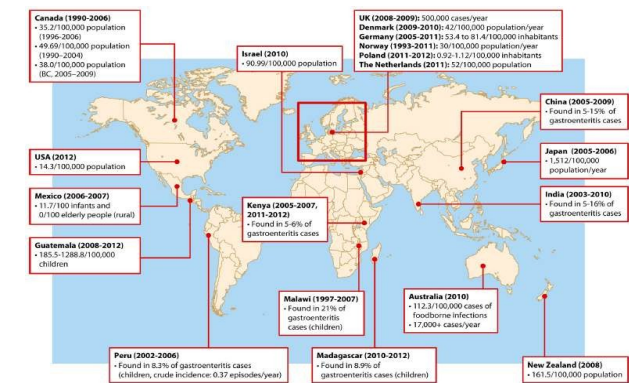


Figure 2. Incidence and prevalence data of *Campylobacteriosis*.

Source: Eextracted from literature published from studies conducted in developed and developing countries. Image adopted from Kaakoush, et al.

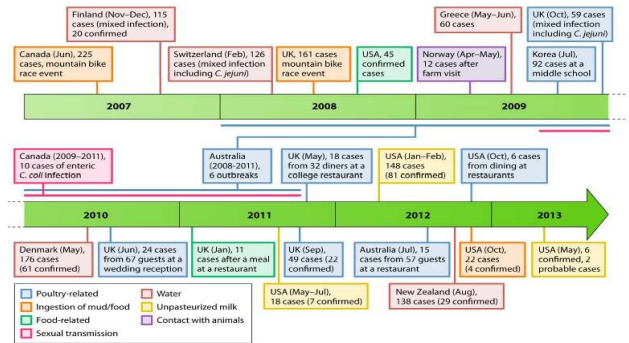


Figure 3. Timeline of published *Campylobacteriosis* outbreaks since 2007.

(Source: Castrodale and Gerlach, 2013; Longenberger and Palumbo, 2013; Wensley and Coole L. 2013; Parry and Fearnley, 2012; Merritt and Combs B, 2011; Inns and Foster, 2010; Yu JH and Kim NY, 2010).

Current status of *Campylobacter* in Ethiopia

Several studies have reported *Campylobacter* infections in humans in developing countries. According to Tadesse, et al. *Campylobacter* species that are most commonly associated with human illness are *C. jejuni* and *C. coli*. The authors further point out that *C. jejuni* is responsible for up to 90% of the cases of human infections, whereas *C. coli* is responsible for the majority of the remaining human case (Tables 2 and 3).

Prevalence	Sample orgin	Study area	Reference
39%	Feces of sheep	Jimma	Kassa and gebre-selassie
10.60%	Feces of sheep	Debre Birhan	Chanyalew and Asrat
13.10%	Sheep carcasses	Addis Ababa	Seble hailemariam
9.30%	Chicken, beef, sheep, goat and pork meat	Addis Ababa and Debre Zeit	Lemma and daniel
10.10%	Sheep and goat carcasses	Debre-Zeit	Tefera and daniel

Table 2. Some Prevalence of *Campylobacteriosis* in different areas of Ethiopia in different sample type.

Sample type	Abattoir	Butchers' shop	Supermarket	Total
Beef	9/138 (6.5)	4/69 (5.8)	1/20 (5.0)	14/227 (6.2)
Mutton	11/93 (11.8)	1/10 (10.0)	0/11 (0)	12/114 (10.5)
Goat	6/67 (9.0)	1/11 (9.0)	0/14 (0)	7/92 (7.6)
Pork	3/30 (10.0)	-	1/17 (5.9)	4/47 (8.5)
Chicken	8/30 (26.7)	-	13/60 (21.7)	13/60 (21.7)
Total	37/358	6/90 (6.7)	7/92 (7.6)	50/540 (9.3)

Table 3. Prevalence of *Campylobacter* in food of animal source, Addis Ababa.

Symptoms and clinical characteristics of Campylobacteriosis

In humans: The clinical feature of *Campylobacter* enteritis in humans caused by *C. jejuni* and *C. coli* are indistinguishable from each other and from acute bacterial diarrhea caused by other pathogens like *Salmonella* enteritis. *Campylobacter* may cause mild or severe diarrhea, bloody diarrhea, nausea, and stomach pain, often with fever.

Abdominal pain can persist for up to 7 days and recurrence of symptoms can occur. The illness may start with cramping abdomen, diarrhea, fever, chills, headache, myalgia and occasionally delirium, with typical more intense long lasting abdominal pain and occasionally blood or mucous in the stool.

In food or farm animals: *Campylobacter* spp. resides in the gut of domesticated warm-blooded animals and birds as part of the intestinal microbiota. *Campylobacter* species cause enteritis, abortions, and infertility in various species of animals. The role of *C. jejuni* as primary pathogen in farm animals is uncertain.

In general: Symptoms of Campylobacteriosis include diarrhoea (sometimes bloody), nausea, abdominal pain, fever, muscle pain, headache, and vomiting. The incubation period before onset of disease is usually 2–5 days, with illness generally lasting for 2-10 days. The unique feature of the disease is the severity of abdominal pain which may become continuous and sufficiently intense to mimic acute appendicitis. As a consequence of *C. jejuni* infection a small number of individuals develop a secondary condition such as reactive arthritis or Guillain-Barre syndrome, in which a harmful immune response of the body attacks part of the peripheral nervous system leading to symptoms of muscle weakness or paralysis.

Clinically, *Campylobacter* infections are indistinguishable from acute gastrointestinal infections caused by other bacterial pathogens. Upon infection with *C. jejuni* and/or *C. coli*, susceptible subjects generally experience (after one to seven days) acute abdominal pain, often accompanied by fever, nausea and or vomiting, as well as general malaise.

Progression of symptoms is accompanied by either loose or watery profuse diarrhoea, which may contain mucous or blood. In developing countries, infection with *C. jejuni* and closely related organisms is less severe, without bloody diarrhoea, fever or fecal leukocytes. The disease is usually limited to a period of five to eight days, but may continue longer and bacterial shedding often persists after clinical symptoms have ended.

Pathogenesis

Meats, particularly of poultry origin, raw milk, and untreated water are well documented sources of human *Campylobacter* infections. Approximately 50%-70% of all *Campylobacter* infections are attributed to chicken consumption; which is not surprising in light of the frequency with which poultry products are consumed as well as the nearly universal contamination of chicken carcasses with *Campylobacter* during slaughter processes.

Cross contamination in the kitchen from contaminated meat to items that will not be cooked is considered a major pathway for transmission. The infectious dose ranges from 500-800 organisms which can be carried in approximately one drop of chicken juice.

Person to person transmission, which occurs through the faecal oral route, is uncommon. Human exposure from reservoirs has been linked to multiple pathways which include: Food, particularly poultry; the environment; and direct animal contact (Figure 4).

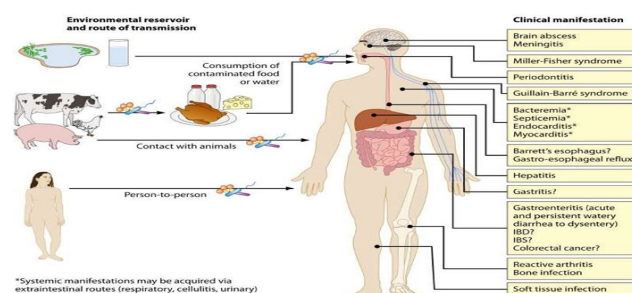


Figure 4. Pathogenesis of *Campylobacter* infection: And the associated clinical manifestations.

Source: Image adopted from Kaakoush, et al. (2015).

Mechanisms by which *Campylobacter* species are virulent still remain largely undetermined. A possible reason contributing to this stagnancy is the lack of pathogenesis similarity between *Campylobacter* species and other enteric pathogens. Advances in medical model technologies aided in unraveling mechanisms by which *Campylobacter* causes infection (Figure 4).

According to Dastia, et al. as well as Croinin and Backert, flagella-mediated motility, bacterial adherence to intestinal mucosa, invasive capability, and the ability to produce toxins (particularly Cytotoxin Distending Toxin (CDT), an important virulence factor for *Campylobacter*) have been identified as virulence. Flagella are required for the colonization of small intestine, followed by the migration to the target organ, which is the colon.

Invasion, which results in cellular inflammation, has been reported to result from the production of cytotoxins, which compromises the absorptive capacity of the intestines. The ability of *C. jejuni* or *C. coli* to reach the intestinal tract is, in part, due to resistance to gastric acids and also to bile salts. Disease severity may depend on the virulence of the strain, as well as on the host's immune condition.

Public health and economic significance

Campylobacter species have received considerable attention in recent years as a major cause of bacterial enteritis in man. *Campylobacter* enteritis is recognized as an important source of diarrheal illness worldwide. The pathogen is also an important causative agent of traveler diarrhea accompanied by predisposing debilitating factors such as pregnancy, premature birth, chronic alcoholism, neoplasia and cardiovascular disease.

Campylobacteriosis affects all age groups; however, infections are recognized with increasing frequencies in infants, children, aged individuals, and immune compromised persons. According to the Centre for Disease Control (CDC) report, *Campylobacter* infections accounted for approximately one-third of laboratory confirmed food borne illness that occurred globally in food net surveillance areas. A serious consequence of diarrheal diseases in human is called Guillain Barre Syndrome (GBS) which is characterized by polyneuritis of the peripheral nerves that may lead to either short term or lengthy paralysis. GBS, a demyelinating disorder resulting in acute neuromuscular paralysis, is serious sequelae of *Campylobacter* infection.

Campylobacteriosis cause severe economic losses both in the public health and food industry sector. Campylobacteriosis has an enormous economic impact in terms of treatment costs, loss of production, and

human welfare. In livestock, particularly sheep and cattle, *Campylobacter* species are the cause of important economic losses associated with infertility problems and abortion.

Campylobacteriosis represents a substantial burden to public health in developed countries. It has been estimated that 2.4 million cases of *Campylobacter* enteritis occur annually in the United States of America accounting for 5% to 7% of all human gastroenteritis cases.

It has been estimated that nearly 1% of the US population suffer from Campylobacteriosis per year and these infections result in around 13,000 hospitalizations and 124 deaths each year. In Canada in 2000 more than 2,300 people became infected with *Campylobacter* in Walkerton Ontario following a heavy rainfall event that resulted in bacteriological contamination of the town's water supply.

This infection has major economic repercussions on human health care. Indeed there are direct illness costs such as health consultations, laboratory diagnosis, medical treatment or hospitalization and indirect costs such as loss of work productivity due to sickness, product recalls and legal costs (international consultative group on food irradiation, 2009). In the EU the cost of Campylobacteriosis to public health systems is estimated to be about €2.4 billion per year. The most recent data published by the FSA, indicate that the cost of human Campylobacteriosis in the UK is around £900 million per year, which alone represents more than half of the cost for all food borne infections in the country (£1.5 billion).

The burden and the cost of illness, in the country indicated that cost of illness were direct health care costs (e.g. doctors consultations, hospitalization, rehabilitation), direct non-health care costs (e.g. travel costs of patients, co-payments by patients) and indirect non-health care costs (productivity losses).

According to the Centre for Disease Control (CDC) report, *Campylobacter* infections accounted for approximately one-third of laboratory confirmed food borne illness that occurred globally in food net surveillance areas.

Reported incidence of Campylobacteriosis: The true incidence of gastroenteritis due to *Campylobacter* spp. is poorly known, particularly in LMIC; studies in high income countries have estimated the annual incidence at between 4.4 and 9.3 per 1000 population. Generally, developing countries do not have national surveillance programs for Campylobacteriosis; therefore, incidence values in terms of number of cases for a population do not exist. Most estimates of incidence in developing countries are from laboratory based surveillance of pathogens responsible for diarrhea. *Campylobacter* isolation rates in developing countries range from 5 to 20% (Table 4).

WHO region and country	Isolation rate (%)
Africa	
Algeria	17.7
Cameroon	7.7
Ethiopia	13.8

Nigeria	16.5
Tanzania	18
Zimbabwe	9.3
Americas	
Brazil	9.9
Guatemala	12.1

Table 4. Isolation rates of *Campylobacter* from diarrhea specimens: From <5 years old in selected developing countries.

Food born implications of *Campylobacter*: Food acquired Campylobacteriosis accounts for up to 74 to 85% of total cases, with poultry being the number one contributing vehicle. *Campylobacter* contaminated foods the result of poor sanitation are an important potential source of infection in humans. For example, *Campylobacters* were isolated from 40% and 77% of retail poultry meat sold in Bangkok, Thailand, and Nairobi, Kenya, respectively.

The serotypes of the organisms isolated in Thailand were similar to those of organisms isolated from humans. In Mexico city, a survey of ready to eat roasted chickens showed that they were contaminated with *Campylobacters*. In developed countries, risk factors associated with foods include occupational exposure to farm animals, consumption of raw milk or milk products, and unhygienic food preparation practices (Table 5).

Year	No. (fatalities) cases	Food	Country
2008	98	Raw peas	US
2007	68	Cheese	US
2005	79	Chicken salad	Denmark
2005	86	Chicken liver pate	Scotland
2003	81	Custard prepared	Spain
1998	79	Tuna salad	US
1995	78	Cucumber	South Australia

Source: Anne (2012).

Table 5. Selected major food borne outbreaks associated with *Campylobacter* spp. (>50 cases and/or ≥ 1 fatality).

Discussion

Estimates of impact of human Campylobacteriosis in developing countries: The Disability Adjusted Life Year (DALY) is the basic unit used in Burden of Disease (BoD) methodology to quantify the impact of disease on a population. DALYs have been applied in the Dutch population to measure the mean health burden of *Campylobacter* associated illness in the period 1990-1995. The mean estimate was 1,400 DALYs per year; the main determinants of health burden were acute gastroenteritis (440 DALYs), gastroenteritis related mortality (310 DALYs) and residual symptoms of GBS (340 DALYs).

Although data on DALYs due to Campylobacteriosis in developing countries are not available, diarrhea, which is a clinical manifestation of Campylobacteriosis, was one of the top three causes of death and disease in developing countries in 1990. The disease is projected globally to remain one of the top 10 by 2020. (The burden of Campylobacteriosis in developing countries may increase by 2020 because HIV is projected to move up to the 10th position from 28th by 2020). Considering the higher incidence of Campylobacteriosis in developing countries, DALYs for the disease in developing countries will likely be higher than those of the Dutch population.

Diagnosis

The principle encompassing definitive diagnosis of Campylobacteriosis is based on the isolation of *Campylobacter* species from a stool culture (UK standards for microbiology Investigations). However, only a small percentage of individuals suffering from Campylobacteriosis consult for medical care and have their infections culture confirmed. Alternatively, when they do consult, they submit samples for culturing after they have started antibiotic treatment, which may make it even more difficult for a laboratory to grow *Campylobacter*.

Microscopic appearance: Diagnosis can be carried out by direct examination of a stool sample using contrast microscopy or gram's strain. Direct examination provides a rapid presumptive diagnosis that must still be confirmed by stool culture. Observation of darting motility in fresh fecal specimens or of vibrio forms in gram stain provides presumptive diagnosis for *Campylobacter* (UK Standards for microbiology investigations).

Stool culture: Sensitivity of *Campylobacter* species to oxygen and oxidizing radicals has been exploited to develop selective media for isolating *Campylobacter* from clinical specimens. A number of selective agars have been developed, preston, Charchoal Cefoperazone Deoxycholate (CCDA) is one of the selective agars found to be effective

because it permitted high yields of isolated *Campylobacter* strains at 42°C microaerophilically.

Another technique used in conjunction with primary isolation of *Campylobacter* species on selective media is the filtration method. The method is based on the principle that *campylobacters*, particularly *C. jejuni* and *C. coli*, can pass through membrane filters (0.45 µm to 065 µm pore size) with relative ease while other stool flora are constricted during filtration onto the surface of the media. One of the limitations of the culturing method is that *Campylobacter* species are fastidious organisms, taking up to 72 hours to obtain growth, thus isolation methods for these organisms are not commonly used in routine laboratories.

Colonial morphology: On CCDA selective media, culture positive colonies for *Campylobacter* appear either grey/white or creamy grey in colour and moist in appearance. They may appear as a layer of growth over the surface of the selective agar. On blood agar, colonies are translucent and moist in appearance (UK Standards for microbiology investigations).

Prevention and control in the food chain

Overview: *C. jejuni* grows easily if contaminated foods are left out at room temperature; however, the bacterium is sensitive to heat and sterilization methods like pasteurization of milk, cooking meat, and water chlorination. To prevent *Campylobacter* infection, make sure that any poultry products are cooked at 74°C and choose the coolest part of the car for transportation of meat and poultry as well as defrost meat and poultry in the refrigerator and never leave food at room temperature for over two hours, wash hands after contact with pets or farm animals.

The complex epidemiology of *Campylobacter*, a multi-tiered approach to control is needed, taking into consideration the different reservoirs, pathways, exposures, and risk factors. Control of *Campylobacter* spp. throughout the food chain requires implementation of food safety management systems based on well-established principles such as those of the Hazard Analysis Critical Control Point (HACCP) system. That is a structured systematic approach to achieving food safety which involves identifying potential hazards and measures for their control. However, in the interests of control HACCP based principles should be applied by all sectors of the food industry.

On-farm control: The interventions that have consistently been shown to be effective at pre-harvest are the application of strict biosecurity and good animal husbandry and health measures. Control of *Campylobacter* contamination on the farm may reduce contamination of carcasses, poultry, and red meat products at the retail level. Epidemiologic studies indicate that strict hygiene reduces intestinal carriage in food producing animals. In field studies, poultry flocks that drank chlorinated water had lower intestinal colonization rates than poultry that drank chlorinated water. Recent studies undergone to develop methods such as treatment of chickens with commensal bacteria other than *Campylobacter*, which is called competitive exclusion regimens and flock vaccination.

The abattoir: The post-harvest phase: Good hygienic practices and the application of control measures based on HACCP principles are also critical for successful post-harvest control, and decontamination of the carcass by physical or chemical means.

Bacterial counts on carcasses can increase during slaughter and processing steps. In one study, up to a 1,000-fold increase in bacterial counts on carcasses was reported during transportation to slaughter. Hazard Analysis Critical Control Points (HACCP) studies of the slaughter process show specific areas where contamination occurs.

At home: At home, the consumer is the last link in the food chain and has to deal with residual pathogens in food. The measures required in the kitchen to minimize risk of infection with *Campylobacter* spp. consist of the application of the basic principles of safe food preparation. In addition to awareness of basic measures such as hand washing and separation of ready to eat and raw food, some traditional food preparation practices should be discouraged. For example, the practice of washing dressed poultry carcasses in the kitchen sink is unnecessary and increases the risk of contamination.

Proper and hygienic preparation of food, avoidance or heating of unpasteurized dairy products, avoidance of eating raw meat, travel to underdeveloped countries (hyper endemic *Campylobacter* transmission area), and exposure to animals such as pet animal with diarrhea (particularly puppies and kittens) should be avoided.

Water: Untreated water has been identified as an important source of *Campylobacter* infections in humans. The presence of *Campylobacter* in surface water and shallow wells is likely the result of contamination by wild bird feces, manure run-off from dairy or poultry farms, or human sewage. The chlorination of carcass wash water, an important component of the HACCP programs in processing plants contributed to the decline in human Campylobacteriosis.

Disease surveillance and public awareness: Surveillance of enteric diseases, including Campylobacteriosis, is common in high income countries; it is rarely attempted in other parts of the world. Nevertheless, a well-designed surveillance program for Campylobacteriosis can provide information to inform national decision making by: Determining the relative importance of Campylobacteriosis compared with other enteric infections; showing which animals are the primary reservoirs for infection; and helping to identify the most common pathways of transmission. Educating farmers on improved disease prevention measures and hygiene may lead to a lower prevalence of *Campylobacter*.

Treatment and antimicrobial resistance

Campylobacteriosis is often a self-limiting disease, with symptoms typically disappearing within one to three weeks. For short lived infections, fluid and electrolyte replacement are the cornerstone for treatment. When *Campylobacter* induced enteritis is severe and prolonged, particularly in young and immunosuppressed individuals, antimicrobial therapy is recommended for treatment of patients.

The first-line choice of treatment involves macrolides (erythromycin), followed by fluoroquinolones, where ciprofloxacin is predominantly administered. Other alternative drugs, depending on the severity of Campylobacteriosis, include tetracyclines, chloramphenicol, and serious systemic infections may be treated with aminoglycoside such as gentamicin.

All *Campylobacter* species are inherently resistant to vancomycin, rifampicin, and trimethoprim. In contrast, *Campylobacter* species are generally susceptible to aminoglycosides, chloramphenicol, clindamycin, nitrofurans, and imipenem. In severe cases where antibiotic treatment is mandatory, appropriate and timely treatment is of importance in the light of antibiotic resistance.

Antimicrobial resistance is the inherent or acquired *de novo* mutation or through Horizontal Gene Transfer (HGT) ability of bacteria to subsist in an environment enriched with antimicrobial agent(s). The ability of bacteria to have mechanisms which results in higher inhibitory concentration in comparison to the wild type bacteria describes the definition of antimicrobial resistance in a microbiological and molecular. Mechanisms by which bacteria can achieve antimicrobial resistance include inactivation or modification of the antimicrobial, alteration of antimicrobial target site thereby reducing its binding efficacy, increased efflux or decreased influx of the antimicrobial, as well as gene duplication and amplification.

Conclusion

In our evaluation *Campylobacter* species are the common bacterial pathogens causing gastroenteritis in both human and animals throughout the world. Foods of animal origin could be a potential source of *Campylobacter* spp. with higher isolation rate for *C. jejuni* which is primary cause of human Campylobacteriosis for the public there are currently insufficient epidemiological data to provide an accurate assessment of the burdens of Campylobacteriosis in Africa (including in our country), Asia, and Central and South America. However, it is clear that in many of these regions, where data are available, *Campylobacter* species appear to be endemic in children. It is now well established that poultry, particularly fresh and frozen chicken meat, is a major reservoir of *Campylobacter* species. Other domesticated animals, such as cattle and pigs, and environmental sources, such as contaminated water, also play a vital role in the direct transmission of these organisms to humans.

Based on the above conclusions forwarded the following recommendations:

- Various measures should be put in place to minimize the possibility of fecal material being transferred from the gut or the skin to the animal originated foods.
- Integrated control strategies and regular microbiological testing on the abattoir as well as farms should be implemented.
- Intensive education, training and awareness creation for producers, retailers, and consumers on the proper handling and cooking of food of animal origin.
- Additional research efforts focusing on their growth conditions, methods of detection, and mechanisms of pathogenesis could be understand their global distribution and impact on animal and human health of the diseases.

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