REVIEW ON CAMPYLOBACTERIOSIS IN POULTRY: ITS RISK FACTORS AND PUBLIC HEALTH IMPACT IN ETHIOPIA

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SUMMARY: Campylobacter is a one of the major pathogens involved in food-borne illnesses and leading cause of gastrointestinal infections worldwide that colonizing all warm-blooded animals including poultry. The objectives of this review, were to overview the available documents and identify the risk factors of Campylobacteriosis of poultry in Ethiopia and to address its public health consequence. Campylobacters are small gram-negative, non-spore-forming, helical bacteria with a particular `darting' motility, and are catalase and oxidase positive. The transmission can occur through contaminated food (especially poultry meat), water, the environment, and contact with infected animals. It causes fever, abdominal cramps, and diarrhea with blood and leukocytes. In animals, horizontal transmission through ingestions of Campylobacter with contaminated water, feed, soil and fomites and cause enteritis, abortions are the usual route. The bacterial isolation and identification of *Campylobacter* is considered the gold standard for disease identification. Erythromycin and Ciprofloxacin are the drugs of choice for the control of *Campylobacter* spp.in Ethiopia, its highly prevalent ranging from 8-13.7 in human, 9.4-72.7 in food animals and 13% in poultry. High prevalence of zoonotic *Campylobacter* species has been isolated from raw animal products. Therefore, consumption of raw meat, unpasteurized milk and untreated water should be avoided. Implementation of food safety management throughout the food chain requires systems based on well-established principles for effectively control. More surveillance in covering wider areas in collaboration with international organizations and stakeholders is highly recommended.

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1. INTRODUCTION

Campylobacter is one of the major pathogens involved in food-borne illnesses with an estimated 400 million cases per year worldwide and it has been reported that only 500 cells of *C. jejuni* can cause human illness((Hansson *et al.*, 2018) Different enteric pathogens cause gastrointestinal infections in humans such as bacteria, viruses, and parasites. Of the bacterial etiologies, *Campylobacter* is a leading cause of gastrointestinal infections worldwide((Mengelle *et al*., 2013) responsible for 400–500 million cases of diarrhea each year (Gahamanyi *et al*., 2020) and causing more than 37, 000 deaths per year worldwide (WHO, 2015).

The name *Campylobacter* is derived from the Greece ‘campylos’ meaning ‘curved’ and ‘baktron ‘ meaning ‘rod’(Jilo *et al*., 2021). *Campylobacters* are small gram-negative, non-spore-forming, helical bacteria with a particular `darting' motility, and are catalase and oxidase positive (Chitra et al., 2017). They commonly have a single polar unsheathed flagellum at one or both ends (Hassan *et al*., 2019). Currently, the genus has 39 species and 16 subspecies(Zenebe *et al*., 2020) from this at least a dozen of *Campylobacter* species has been associated with human((Sheppard and Maiden, 2015). The transmission of *Campylobacter* from animal reservoirs to humans can occur through multiple routes, including contaminated food (especially poultry meat) and water, the environment, and contact with infected animals. Children may be exposed to *Campylobacter* species directly or indirectly through exposure to animal feces(Dai *et al*., 2020). *Campylobacter jejuni* (*C. jejuni*) and *Campylobacter coli* (*C. coli*) are the predominant cause of human campylobacteriosis and are responsible for approximately 95% of all infections(Casalino *et al*., 2022). The usual route

of Campylobacter transmission in animals is horizontal transmission through ingestions of Campylobacter with contaminated water, feed, soil and fomites(Jilo *et al*., 2021).

The gastrointestinal tracts of domesticated and wild animals are thought to be a natural campylobacter reservoir. As a result, the bacteria are regularly isolated from a variety of animal species, including rodents, pets, domesticated animals, poultry, cattle, pigs, and sheep. However, according to (Chlebicz and Śliżewska, 2018), the chicken reservoir is thought to be the source of between 50% and 80% of the strains that infect people. Early colonization of the bacterium in many chickens occurs without obvious disease or related clinical symptoms. Some studies have reported that challenged chicks may exhibit distention of the jejunum, disseminated hemorrhagic enteritis, and in some cases, focal hepatic necrosis. However, infected flocks seldom exhibit these lesions, increased mortality rates, or decreased feed conversion(Balta *et al*., 2022).Campylobacter species cause enteritis, abortions, and infertility in various species of animals (Sahin *et al*., 2017). In humans, campylobacteriosis could be a self-limiting infection characterized by fever, abdominal cramps, and diarrhea with blood and leukocytes(Mahmood and Al Hakawati, 2014). However, in immunocompromised individuals, the infection can cause life-threatening conditions like Guillain-Barre syndrome (GBS), reactive arthritis(REA), hemolytic uraemic syndrome, meningitis, and abortion((Igwaran and Okoh, 2019).

In Ethiopia, a few studies have indicated that campylobacteriosis is common in human and domestic animals. In chickens, studies on the prevalence of *Campylobacter* have revealed a range of 13% ((Zenebe et al., 2020) to 86.6 %(Abamecha *et al*., 2015b)**.** In addition the isolation rates of these bacteria in children range from 8%(Tafa *et al*., 2014) to 50 %(Chen *et al*., 2021).The bacterial isolation and identification of *Campylobacter* is considered the gold standard for disease identification; however, it is tedious and laborious due to the complex nature of *Campylobacter(*Ghoneim *et al., 2020)*. Furthermore, differentiation between species through conventional bacteriology is difficult, as very few biochemical characteristics differ among species((Frasao *et al*., 2017). As a result, molecular-based assays, such as polymerase chain reaction(PCR) and sequencing, can enable easy, rapid, and specific detection and epidemiological applications(Barakat *et al*., 2020). While most cases of *Campylobacter* enteritis are self-limiting, in situations where antibiotic therapy is indicated either erythromycin or ciprofloxacin are the drugs of choice(Wieczorek and Osek, 2013). However, there is an escalating number of *Campylobacter* isolates resistant to these drugs due to the misuse of antimicrobials in animals and humans(de Mesquita Souza Saraiva *et al*., 2022).
The objectives of this seminar paper is to review the available documents and examine risk factors of Campylobacteriosis in poultry, to address the public health consequence, and highlight suggested control strategies

2. LITERATURE REVIEW

2.1. Etiology

The genus *Campylobacter* has a place within the phylum *Proteobacteria*, the class *Epsilonproteobacteria*, the order *Campylobacterales* and the family *Campylobacteraceae*. The genus *Campylobacter* taxonomy is in continues variation from its origin because of the re-classification of certain spp. into different genera or the discovery of new spp(Ammar et al., 2021). Currently, 39 Campylobacter species are recognized(Zhong *et al*., 2022), but this number is anticipated to rise over because of advancements in diagnostic methods and genomic analyses(Djennad *et al*., 2019).Twelve spp. of the genus *Campylobacter* are viewed as pathogenic bacteria such as *C. lari*, *C. curvus*, *C. coli*, *C. concisus*, *C. fetus*, *C. upsaliensis* and *C. jejuni.* Disease caused by *Campylobacter* might cause gastroenteritis; but, *C. jejuni* has additionally been incriminated in systemic infections(Parker *et al*., 2022). *C. coli* and *C. jejuni* subspp. *jejuni* are commonly related to human campylobacteriosis representing up to 90% of the outbreaks and sporadic campylobacteriosis cases(García-Sánchez *et al*., 2018).

Additionally, *C. jejuni* consists of 2 sub spp.; *C. jejuni* subsp *Doylei* and *C. jejuni* subsp *jejuni*. However, the *C. jejuni* subsp *doylei* pathogenic role is unknown yet, but it was detected in blood samples of infected children(Ammar *et al*., 2021). These two sub spp. varies biochemically and they can be differentiated by polymerase chain reactions (PCR) on the basis of the nitrate reductase (*nap*) locus (*nap*A and *nap*B genes), where *C. jejuni* subsp *Doylei* strains contained *nap*A deletions of 2761 bp(Ammar *et al*., 2021). C. *jejuni* sub spp. *jejuni* will hereafter be referred to as C. *jejuni*. A system for typing *Campylobacter* spp. depending on the heat-stable lipopolysaccharide (LPS) O-antigenic components has differentiated *C. coli*, *C. lari* and *C. jejuni* into 60 serotypes, although another typing system dependent on heat-labile antigen has detected 100 serotypes of these bacteria(Ammar *et al*., 2021).

Moreover, Miller and Parker reported that *C. lari*, *C. upsaliensis*, *C. jejuni* and *C. coli* are related genetically and are referred to as the thermotolerant campylobacters, due to their growth at 42◦C. These four *Campylobacter* spp.

considered the principle spp. of public health and clinical significance. The remaining spp. of the genus *Campylobacter* form 3 general groups: (1) spp. that have not been associated with human disease and are not detected in water or food (eg, *C. canadensis* and *C. insulaenigrae*) (2) spp. that have been incriminated with children and human diseases (eg, *C. showae*, *C. rectus*, *C. curvus* and *C. concisus*) and (3) spp. that have been associated with disease in livestock animals and infrequently causes human illness (e.g. *C. sputorum*, *C. fetus* and *C. hyointestinalis*) ((Igwaran and Okoh, 2019). Among the genus *Campylobacter*, *C. iguaniorum*, *C. corcagiensis*, *C. troglodytis*, *C. volucris*, *C. avium*, *C. canadenses*, *C. subantarcticus* and *C. cuniculorum* are the only spp. that didn't cause animals or human diseases yet(Ammar *et al*., 2021).

2.1.1. Morphology and biochemical properties

Campylobacter spp. are non-spore forming and Gram-negative bacteria. They can be spiral, curved or sometimes can be seen straight rods, with size ranging from 0.2 μm to 0.8 μm wide and 0.5 μm to 5 μm long. *Campylobacte*r may appear as a spiral, S, V, or comma-shaped forms and can also be found in short or occasionally long chains. First Campylobacter cells begin to age, and then they become coccoid in shape((Bouki, 2010) The cells are highly motile by a kind of single or occasionally multiple flagella at one ends. Rapid movement, darting motility of comma-shaped cells can be seen by a phase contrast microscope. Campylobacter does not utilize carbohydrates and usually obtain energy from amino acids. Typical biochemical reactions create the reduction of fumarate to succinate, acetoin, indole production and negative methyl red. Most species of the *Campylobacter* reduce nitrate and positive in oxidase but only *C. jejuni* is hippurate positive. *C. jejuni* is quite sensitive to drying and storage at room temperature, but at refrigeration temperatures and appropriate humidity(Ebrahim, 2006).

2.2.2. Survival and growth characteristics

Campylobacter spp. can grow best from 37°C to 42°C and in low oxygen or microaerophilic environment, such as an atmosphere of 10% CO2 ; 5% O2 and 85% N2 ((Harrison et al., 2022). Campylobacter is sensitive to freezing and drying (Hellgren *et al*., 2019).The death rate of Campylobacter is dependent on temperature. They die more rapidly on a dry surface at room temperature than at refrigeration conditions((Hagos et al., 2019). They can survive at refrigeration temperatures (4°C) and in meat stored frozen (at -18°C to -22°C) for several weeks(Sansalone *et al.*, 2010) and in general survive better at cooling temperatures((Pokhrel *et al*., 2022).C. jejuni and C. coli are sensitive to NaCl concentrations of 2% and above with, 0.5% NaCI thought to be optimum for their growth. Campylobacter spp. will not survive below 4.9 and above 9.0 PH and grows optimally at pH 6.5-7.5((Hagos et al., 2019). Campylobacter spp. shown as a viable but nonculturable state when exposed to unfavorable environments, such as elevated temperature, low nutrient availability, freezing ((Pokhrel *et al*., 2022). The nature of this coccoid form is uncertain. Campylobacter jejuni is adapting aerobic condition due to an ability to produce (Table 1) (Frirdich *et al.*, 2019).

Table 1: Growth characteristics of thermophilic Campylobacter species

Characteristics	**Minimum**	**Optimum**	**Maximum**
Temperature	30	42-43	45
PH	4.9	6.5-7	9
NaCl	0.5	1.5	-
Water activity	>0.987	0.997	-
Atmosphere	-	5%O2+10% CO2	-

Source: ((Foods, 1996)(ICMSF, 1996).

2.3. Risk Factors

All warm-blooded animals, including humans, are colonized by campylobacteriosis, which is ubiquitous throughout the world(Umaraw *et al*., 2017). *Campylobacte*r species are a part of the gut flora in many domestic and wild animals.

Warm-blooded farm animals such as poultry, pigs, cattle and sheep are major reservoirs and source infection for human being. *Campylobacter* have also been found among wild birds, wild animals and even in non-vertebrate vectors such as flies. The majority of human infections are caused by *C. jejuni* (80-90%) and C. coli (5- 10%). *C. jejuni* is the most prevalent *Campylobacte*r found in most animals, with the exception for pigs for which *C. coli* (Pratt, 2008). There is quite epidemiological difference between low, middle and high income countries which likely arise from differences in diagnostic techniques, biocontrol protocols, food practices, nutritional status, environmental hygiene, climatic condition and the abundance of natural reservoirs(Hlashwayo *et al*., 2020).

In low and middle income countries, Campylobacter infections are hyperendemic among young children aged less than 2 years with up to 2 episodes per child and commonly asymptomatic in both children and adults(Hlashwayo *et al*., 2020). In high income countries, asymptomatic Campylobacter infections are unusual but the average number of Campylobacter infections is less than one per lifetime(Pascoe et al., 2020). Campylobacter infection is usually more prevalent to children suggesting that early life exposure might elicit the development of protective immunity however subsequent asymptomatic shedding are observed(Jilo *et al*., 2021).

Poultry is a leading source of food-related Campylobacter species to humans responsible for outbreaks are consumption of poultry products(Heredia and García, 2018). Huge amount of *Campylobacters* are excreted in poultry feaces and contamination during slaughter contaminate the surrounding environment as the crop of poultry is an important niche for Campylobacter species. Once colonized, chickens remain colonized until they are slaughtered and thus, chicken feces are also a potential source of transmission to the environment or humans when poultry manure is used as a fertilizer (Jilo *et al*., 2021).Thus, abundance of poultry farms in a given area is one of the epidemiological determinants of campylobacter infections due to soil, water, dust, air and fomites contaminations(Wang *et al*., 2023). Campylobacter infection is often endemic in areas with untreated drinking-water, poor sanitation and close contact with animals and environmental sources (Galanis *et al*., 2014). Poultry production in a free range system has a much greater risk of infection compared to conventional production and increased the difficulties in control((Hu *et al.*, 2017). Direct contact with farm animals and consumptions of raw farm animal products play a significant role in epidemiology of campylobacteriosis. Unpasteurized milk source from dairy cattle has also been implicated in a number of campylobacteriosis outbreaks (Bianchini *et al*., 2014).

Wild animals are potential reservoirs of Campylobacter species(((Andrzejewska *et al*., 2013). Among all the host species studied, wild birds are most likely to carry Campylobacter species. Some species of wild birds are observed as carrier but their role in Campylobacter transmission to human is not determined yet(Olvera-Ramírez *et al*., 2023). In general, age, farming system, sanitary measures in farms, immunodeficiency, exotic breed, food contamination, animal contact, international travel, and abundance of reservoir hosts are main determinant factors(Jilo *et al.*, 2021).

2.3.1. Host range

Numerous species are vulnerable to or act as reservoirs for Campylobacter spp., and wild birds are recognized to be natural hosts. Among the vast variety of different bird species, members of the family of gulls, cranes, raptors, corvids, waterfowl, and passerines are known to harbor *C. jejuni*. Gulls, corvids, raptors, and passerines can be found foraging in the surrounding of poultry farms, whereas members of waterfowl and cranes as migratory birds help to disperse the bacteria and may contribute to spread and the introduction to poultry flocks((Olvera-Ramírez *et al*., 2023).*Campylobacter*, are detected in every possible poultry production farm. Within the group of Campylobacter spp., *C. jejuni, C. coli* and *C. lari* are found in chicken where *C. jejuni* is the most common in both layers and broilers (Schets *et al*., 2017). Once *Campylobacter* introduced into a flock, the prevalence reaches up to 100% (Sibanda et al., 2018). *C. coli*, found more often in turkey than in chicken, although predominantly appearing in pigs, it can occur in turkeys with a prevalence of almost 50% (Hagos *et al*., 2019). Other domesticated animals are known to harbor Campylobacter spp. as well such as livestock including sheep, cattle, goat and pig but also cats and dogs. As already mentioned, pigs are harboring predominantly *C. coli*, whereas sheep and cattle are regarded as important reservoirs for *C. jejuni* (Due to its high prevalence and persistence in the environment and natural animal hosts, control or exclusion of Campylobacter from poultry and poultry flocks is very difficult (Hagos *et al*., 2019).

2.3.2. Source infection and transmission

Campylobacter is transmitted from animal reservoirs to people in a number of ways, including contaminated water, food (particularly poultry meat), the environment, and contact with infected animals, Children may be exposed to *Campylobacter* species directly or indirectly through exposure to animal feces(Chlebicz and Śliżewska, 2018). *Campylobacter jejuni* (*C. jejuni*) and *Campylobacter coli* (*C. coli*) are the predominant cause of human

campylobacteriosis and are responsible for approximately 95% of all infections(Kittl *et al*., 2013). *Campylobacter* are mainly transmitted to humans via handling and eating raw or undercooked meat, especially poultry(Facciolà *et al*., 2017). Consumption unpasteurized milk, contaminated water and food, person to-person transmissions through fecal-oral or fomites are also potential source of transmission for *Campylobacter* infections (Kaakoush *et al*., 2015). The usual route of *Campylobacter* transmission in animals is horizontal transmission through ingestions of Campylobacter with contaminated water, feed, soil and fomites(Libera *et al*., 2022). Vertical transmission from an infected bird to its offspring prior to shell formation is rare, although "pseudo vertical transmission" from parent flocks to their chickens via fecal contamination of shells can occur(Kaakoush *et al*., 2015).

2.4. Pathogenesis

Campylobacter infections do not always result in sickness. The quantity of organisms that make it to the small intestine, the virulence of the infecting strain, and the specific host immunity to the pathogen consumed all appear to be crucial determinants, but not all of them are well understood (Janssen *et al*., 2008). Campylobacter establishes infection, in the small intestine and later in the colon, and cause diarrheal illnesses with many of the appearances of naturally acquired infection. Diarrhea can be either watery or bloody, this kind of sign indicating that the extents of intestinal inflammation vary among individuals. It has been shown that this is in part correlated to differences in properties of the infecting strain. Limited evidence suggests that different Campylobacter strains can harbor different virulence traits (Hagos *et al*., 2019).

Colonization of human intestine with Campylobacter jejuni results in the expression of several putative virulence factors, yet the mechanisms of pathogenesis are unclear((Hofreuter *et al*., 2006). Colonization may be influenced by the expression of lipopolysaccharides (LPS) on the bacterial cell surface. A mutation in the gale gene involved in the synthesis of LPS reduced the ability of *C. jejuni* to adhere and invade INT 407 cells, suggesting that LPS is a virulence factor for *C. jejuni* infection, although the *C. jejuni* was still able to colonize chickens(Levin, 2007).

Flagella are an important determinant in virulence since the colonization of intestinal tracts does not occur with non-motile mutants of *C. jejuni*. After immigration of the intestine, clinical disease may occur. Based on clinical sign start in patients, there are two mechanisms by which Campylobacter can bring disease were cause: (A) bacterial invasion and replication within the intestinal mucosa accompanied by an inflammatory response resulting in blood containing, inflammatory diarrhea(Hagos *et al*., 2019) and (B) adherence of Campylobacter to the intestine and the production of toxins, resulting in secretory diarrhea, All strains of *C. jejuni* produce Cytolethal distending Toxin (CDT), a nuclease that results in cell cycle arrest and host DNA damage. Separately *C. jejuni* invasion of the mucosa or CDT alone triggers baso-lateral IL-8 release from the epithelium. In-vitro data suggest that C. jejuni can stay alive within macrophages/monocytes for several days, which may allow for some localized bacterial distribution. The pro-inflammatory cytokine IL-8 triggers an influx of PMNs from the lamina-propria, which prevents additional spread of *C. jejuni*. The resulting focal necrosis of the epithelium could result from the local inflammatory response and host cell death caused by CDT(Mahendran, 2016).

2.5. Clinical Signs

2.5.1. In poultry and other animal

Campylobacter species reside in the gut of domesticated warm-blooded animals and birds as part of the intestinal microbiota(Kaakoush *et al*., 2014). Chickens colonized with *Campylobacter* species generally do not exhibit clinical disease. Many chickens are colonized with the bacteria early in life with no associated clinical signs or pathology. Some studies have reported that challenged chicks may exhibit distention of the jejunum, disseminated hemorrhagic enteritis, and in some cases, focal hepatic necrosis. However, infected flocks seldom exhibit these lesions, increased mortality rates, or decreased feed conversion (Hafez and Shehata, 2021).

2.5.2. Public Health Importance of Campylobacteriosis

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((Whitehouse et al., 2018). Campylobacter* may cause mild or severe diarrhea, bloody diarrhea, nausea, and stomach pain, often with fever((Same and Tamma, 2018). 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 (Same and Tamma, 2018).

Extra-intestinal infection and chronic sequelae of infection occur in smaller proportion of patients .Bacteremia has been noted in less than 1% of patients with *C. jejuni* infection. Meningitis and endocarditis are rare manifestation of *C. jejuni* infection. There have been infrequent reports of *C. jejuni* infections manifested as septic abortion, acute cholecystitis, pancreatitis, and cystitis(Hagos *et al.*, 2019). *Campylobacters* have also been linked to some autoimmune diseases such as Reactive Arthritis (RA) and Guillain-Barrè Syndrome (GBS). These two major late onset complications of *Campylobacter* are estimated at one case per 2000 infections(Myintzaw *et al*., 2023). *Campylobacter* infection is recognized as the most commonly identified antecedent event in GBS (40-60% of all cases), also known as post-infective polyneuropathy. The main lesions are acute inflammatory demyelinating polyradiculo-neuropathy that results in a flaccid paralysis(Hailemariam, 2014). Reactive arthritis occurs in approximately 1% of patients with *Campylobacter* enteritis(Nachamkin, 2002).

2.6 Diagnosis

2.6.1Culture and Isolation

According to ((Hagos *et al*., 2019)Campylobacteriosis can be diagnosis by direct examination of feces and isolation of the organisms confirmed by culture of the organism. Campylobacter species require a micro aerobic atmosphere containing about 5% oxygen, 10% carbon dioxide, and 85% nitrogen. The conventional method for isolating the common enteric Campylobacter species (C. jejuni and C. coli) from feaces is primary plating on selective media and incubation at 42 °C for 48 to 72 hours in a micro aerobic atmosphere with commercially available anaerobic jars. Selective media blood based, or blood-free charcoal-based, and contain one or more antibiotics, can be used. Suspect colonies should be screened with oxidase test, wet mount preparation under dark-field or phase-contrast microscope, and Gram stain. Isolation of Campylobacter spp using enrichment culture is time consuming and complex((El Baaboua *et al.*, 2022). Reducing the time taken to confirm the presence or absence of Campylobacter spp rapid techniques such as real-time PCR can detect campylobacters from complex samples but blood in enrichment culture can inhibit the PCR reaction, if applied directly to enriched samples(Chon *et al*., 2021).

2.6.2 Identification

Identification of Campylobacter species requires tests including morphological appearance, biochemical reactions, growth temperature, tolerance tests and antibiotic sensitivity to cephalothin and nalidixic acid. Polymerase chain reaction (PCR) can be applied in the diagnosis of campylobacteriosis, using either species-specific or multiplex reactions based on ribosomal 16S gene sequences, and microarray-based identification tests, have been developed((Natsos *et al.*, 2019)

2.7. Treatments

In poultry many cases of *campylobacteriosis* are self-limiting and require only supportive therapy. Antibiotics may be useful for some cases of enteritis, especially those that are severe. Macrolides and fluoroquinolones are commonly prescribed for *campylobacteriosis* however, resistance to these and other antibiotics also occurs. Treatment of healthy animals is not recommended for several reasons: there is a high likelihood of re-exposure and there is no evidence that treatment is effective(Deckert, 2012).

Without using antibiotics, most people recover from a *Campylobacter* infection. As long as the diarrhea persists, patients should increase their fluid intake. Some persons who have severe illnesses or are at high risk for developing infection may require antibiotic therapy. These individuals include those who are 65 years of age or older, pregnant women, and those who have compromised immune systems, such as those who have AIDS, blood disorders, or are undergoing chemotherapy. If individuals have compromised immune systems or exhibit severe symptoms, the CDC has advised initiating treatment regimens for *Campylobacter*. Fluoroquinolones and macrolides are often recommended medications, with macrolides favoured due to their low resistance rate((Rehman, 2022). The prognosis for *Campylobacter* enteritis is often very good, and treatment is not necessary when these organisms are isolated from feces. For two to seven weeks following sickness, feces remain positive in the absence of chemotherapy (Granato *et al.*, 2010).

2.8 Prevention and Control

The complex epidemiology of *Campylobacter*, a multi-tiered approach to control is needed, taking into consideration the different reservoirs, pathways, exposures, and risk factors((Endtz, 2020). 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(Jacxsens *et al.*, 2011).

2.8.1. 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(Organization, 2001). 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(Hazards, 2011). In field studies, poultry flocks that drank chlorinated water had lower intestinal colonization rates than poultry that drank unchlorinated water(Sahin *et al*., 2002). 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(Hailemariam, 2014).

2.8.1. In 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 (Hazards, 2011). 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(Williams *et al*., 2020). In studies of chickens and turkeys at slaughter, bacterial counts increased by approximately 10- to 100-fold during defeathering and reached the highest level after evisceration. However, bacterial counts on carcasses decline during other slaughter and processing steps such as: Forced-air chilling of swine carcasses caused a 100-fold reduction in carcass contamination. In turkey plants, scalding reduced carcass counts to near or below detectable levels(Hailemariam, 2014).Adding sodium chloride or trisodium phosphate to the chiller water in the presence of an electrical current reduced *C. jejuni* contamination of chiller water by 2log10 units. Use of chlorinated sprays and maintenance of clean working surfaces resulted in a 10- to 100-fold decrease in carcass contamination. In another study, lactic acid spraying of swine carcasses reduced counts by at least 50% to often undetectable levels((Ben Braïek and Smaoui, 2021). A radiation dose of 2.5 KG reduced *C. jejuni* levels on retail poultry by 10 log10 units. However, some consumers report that the color and texture of chicken fillets are altered by irradiation. Competitive exclusion products have also been proposed to reduce broiler colonization. Various products containing defined poultry isolates of *C. jejuni*, Lactobacillus, and undefined cultures are reported to reduce colonization under experimental conditions. Diet may also alter intestinal carbohydrates that affect the colonization potential of *Campylobacters (Awad* et al., *2014)*.

2.8.3. 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(Hailemariam, 2014). 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(Hailemariam, 2014).

2.9. Public Health Aspect of Campylobacter

The human *Campylobacter* infection of incredible public health importance is *Campylobacter* gastroenteritis caused mainly by *C. jejuni* and sometimes by *C. coli*. Chickens are distinguished as the principle reservoirs of thermophilic *Campylobacter* spp. Furthermore, chickens are answerable for an expected 80% of *Campylobacter* infection in human. Chickens are believed to be asymptomatic carriers(Ammar *et al*., 2021). *Campylobacter* spp. can colonize large proportion of poultry flocks. An European Union baseline research stated that campylobacter was detected in 75.8%

of broiler carcasses, 71.2% of cecal contents of broiler batches were also contaminated with campylobacter ((Prendergast *et al*., 2022) and there was a 61.3% prevalence rate of *Campylobacter* in samples of chicken skin at the retail level, 18.6% of which had *Campylobacter* counts more than 1000 CFU/g(Gölz *et al*., 2018).

Despite, campylobacteriosis severity rate is low (0.03%), the quantity of human *Campylobacter* infection cases is elevated. Interestingly, human *Campylobacter* infection is the third most common reason of mortality between the foodborne microorganisms and death can occurs in immunocompromised patients suffering from liver diseases, cancer and acquired immunodeficiency syndrome (AIDS)((Lund and O'Brien, 2011). *Campylobacteriosis* are mainly self-limiting and sporadic. Gastroenteritis caused by *Campylobacter* is distinguished by high body temperature, vomiting, weight loss, abdominal pain/cramps, headache and acute watery and sometimes bloody diarrhea(Todd, 2014).

Additionally, *Campylobacter* can cause post infectious immune disorders like Guillain Barré syndrome (GBS), which is a nervous system disorder distinguished by an advanced weakness and flabby paralysis in the extremities and it may cause paralysis in the respiratory muscles, reactive arthritis (inflammation of joints) and Miller Fisher syndrome (MFS) which is characterized by coulometer weakness (areflexia and ataxia) and the vision problem (ophthalm{Van den Berg, 2014 #187}oplegia)((Van den Berg *et al.*, 2014). In developing countries, campylobacteriosis is hyperendemic and the *Campylobacter* infection is symptomatic and occurs almost exclusively and repeatedly in young children and infants. Subsequent infections can be asymptomatic, which make the symptomatic infection rare in adults or older children(Ammar *et al*., 2021). Campylobacteriosis is usually sporadic, but there were many reported outbreaks(García-Sánchez *et al*., 2018) stated a *C. fetus* outbreak due to ingestion of products of unripen cheese, which made from contaminated raw sheep's milk. (García-Sánchez et al., 2018) detected an outbreak of *C. jejuni* as a result of drinking contaminated unpasteurized milk.(Heuvelink *et al*., 2009) reported a campylobacteriosis outbreak in 75 school children in Spain. Animals have been also identified as human campylobacteriosis sources due to the appearance of multidrug-resistant *Campylobacter* infections outbreak in several states that is related to the contact with infected puppies in a pet store. This outbreak occurred in 17 states in USA with 23 hospitalizations from 113 reported infected cases(García-Sánchez *et al*., 2018).

Globally, 166 million *Campylobacter* cases per year have been reported, but there is a great difference by the region. In region where surveillance programs for foodborne illness are well settled, the campylobacteriosis yearly rate is high. In New Zealand, 152.9 cases/ 100,000 populations were stated (Ministry for Primary Industries, 2015). This was followed by Australia and Europe where 93.5 (NNDSS, 2016) and 59.8 (European Centre for Disease Prevention and Control, 2016) cases/ 100,000 populations were reported. In USA, 14 cases/ 100,000 populations were stated yearly((Ammar *et al*., 2021); however, in Canada, 23 cases/ 100,000 populations were reported in 2015((Inglis et al., 2021). Interestingly, there is a significant difference in the epidemiology of campylobacteriosis between developed and developing nations. In developing countries, (Ammar *et al*., 2021)*{Ammar, 2021 #196}*. In the developing nations the knowledge about the status of *Campylobacter* infection is obtained from research articles on *Campylobacter* isolation from different specimen(Silva *et al*., 2018).

2.10. Economic Impact of Campylobacter

Campylobacteriosis cause severe economic loses 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 vaccination. In livestock, particularly sheep and cattle, *Campylobacter* species are the cause of important economic losses associated with infertility problems and abortion(Hailemariam, 2014). A study, estimating the disease burden and the cost-of-illness, in Netherland indicated that cost-of-illness has 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), using cost estimates for a year 2000. The results, costs-of-illness were estimated to total 21 million per costs-of-illness year with a 90% confidence interval of between11 million and 36 million per year(Mangen *et al*., 2004).

2.11 .Overall Status of Campylobacters in Ethiopia

2.11.1. In humans and Poultry

In Ethiopia, there are only few reports on the prevalence of Campylobacters isolated from humans and food animals(Kassa *et al*., 2007). However, prevalence ranging from 8-13.7 in human and 9.4-72.7 in food animals have been reported. The first study of human campylobacter prevalence in Ethiopia done in 1992 at diarrheic patients at

Tikur Anbessa hospital reported that prevalence of 13.7 Campylobacters from total of 630 examined patients(Beyene et al., 2008). Similarly, study conducted at Jimma on 430 children who had diarrhoea reported prevalence of Campylobacter 11.6% from stool specimen(Beyene and Haile-Amlak, 2004). A study conducted in urban and rural farm animal in Jimma in 2004 on 485 various food animals (cattle, poultry, pigs and sheep) to isolate Campylobacter species were isolated 192 (39.6%) from fecal specimens. The highest isolation rate was recorded among chickens (68.1%), followed by pigs (50.0%), sheep (38.0%) and cattle (12.7%). Among these 192 Campylobacter species isolated, 135 (70.3%) were identified to be *C. jejuni*, 51 (26.6%) were C. coli and 6 (3.1%) were C. lari (Kassa *et al*., 2007).

Similarly, another survey done in Addis Ababa and in and around Bishoftu in 2007 on 540 raw meat samples from different food animals isolated Campylobacter species from 50 (9.35%) samples. The highest prevalence was reported in chicken (21.7%) followed by sheep meat (10.5%), pork meat (8.5), goat meat (7.6%) and beef (6.25).Among the 50 isolates of Campylobacter species 78% were *C. jejuni*, 18% and 4% C. coli ((Dadi and Asrat, 2008). A cross-sectional study conducted on apparently healthy sheep and goat slaughtered at a private export abattoir in Bishoftu in 2008 reported 40 (10.1%) prevalence of Campylobacter species out of 398 carcasses examined, of the 40 thermotolerant *Campylobacter* isolates, *C. jejuni* and *C. coli* accounted for 29 (72.5%) and 11 (27.5%), respectively((Woldemariam *et al*., 2009). On other hand, Campylobacter survey on 220 chickens and 210 humans in Bahir Dar in 2008 revealed prevalence of thermophilic Campylobacters of 8% and 72.7% in humans and chickens respectively. In humans, 94.1% of the isolates were C. jejuni and 5.9% were C. coli. C. jejuni was a predominant species of thermophilic Campylobacters(Ewnetu and Mihret, 2010). Study undertaken at Debre Birhan in 2012 on 70 fecal and 310 carcass samples found that 33 (10.6%) with 87.9% *C. jejuni* and 12.1% C. coli from fecal samples whereas, 15 (21.4%) *Campylobacter* isolates were found from 70 carcass samples from which *C. jejuni* and *C. coli* accounted for 93.3 and 6.7% respectively((Chanyalew *et al*., 2013). A cross sectional study conducted on 384 raw bovine meat samples in Addis Ababa in 2013 isolated in 36 (9.4%) *Campylobacter* species that showed that 28 (78%) C. jejuni and C. coli 8 (22%). In, Gambella, Out of 368 fecal samples taken from farm animals, overall prevalence of 56.5% with 83.7% *C. jejuni*, 12.9% C. coli and 3.4% *C. lari* was reported(Abamecha *et al*., 2015a).

2.11.2. In Poultry

Campylobacter is a leading cause of diarrhea in both the developing and the developed world that has become increasingly prevalent. In developing countries, *Campylobacter* isolation rates for foodborne illnesses are between 5% to 20%.There is quite an epidemiological difference between low, middle, and high-income countries which likely arise from differences in diagnostic techniques, biocontrol protocols, food practices, nutritional status, environmental hygiene, climatic condition, and the abundance of natural reservoirs((Jilo *et al*., 2021). In Ethiopia Reports of *Campylobacter*-positive poultry flocks vary widely from 13%(Chala *et al*., 2021) to 86.6% ((Abamecha *et al*., 2015b). The variations of prevalence are seen between regions, seasons, productions system, and flock age. In Bahir Dar, the prevalence was 72.7 %(Ewnetu and Mihret, 2010), whereas in Gondar((Nigatu et al., 2015), Mekele ((Hagos *et al*., 2021) and Bishoftu (Assefa *et al*., 2022) was respectively 28.9, 43.93, and 70% (Table 2).

Table 2:Prevalence of poultry campylobacteriosis in different parts of Ethiopia

Study Area	Sample type	Prevalence	Source
Addias Abeba and Debre zeit	Meat	21.7 %	Dadi and Asrat,2008
Bahir Dar	Feces	72.7 %	Ewnetu and Mihrt, 2010
Nuer zone	Feces	86.6%	Abamecha *et al*.,2015
Gondar	Feces	28.9%	Seleshe Nigatu *et al*., 2015
Mekele	Meat	43.93%	Hagos *et al*., 2021
Bishoftu and Mojo	Cloacal Swab	70%	Assefa *et al*., 2022
Addis Abeba	Cloacal Swab	13%	Chala *et al*., 2021

3. CONCLUSION AND RECOMMENDATIONS

Campylobacteriosis is widespread worldwide colonizing all warm blooded animals including human beings. Human *campylobacteriosis* caused by thermo-tolerant Campylobacter spp. continued to be one of the major commonly reported zoonotic diseases, which results in a serious consequence of diarrheal in human and severe economic losses worldwide. Attempts of studies on *Campylobacter* in Ethiopia are encouraging. In Ethiopia its highly prevalent ranging from 8-13.7 in human, 9.4-86.6 in food animals and 13% in poultry. However, highest prevalence (86.6%) has reported from that of chicken meat. *C. jejuni* and *C. coli* were the predominant species, are recorded. According to the research findings reported from Ethiopia, high prevalence of zoonotic *Campylobacter spp.* have been recovered from both row types of animal product(meat and milk) and fecal samples of different domestic animals (poultry, cattle, sheep, goat, and pig) and human; Although the scientific researches regarding Campylobacter spp. published from the country are few in number, findings have indicated that undercooked meat from food animals mainly that of poultry could provide as the main source of *campylobacteriosis* infection in Ethiopia, through the consumption of undercooked meat. Hence, the concern should focus on breaking the transmission from these sources to human beings. Depending on the above facts the following points are recommended

- Public awareness creation to minimize risk of *campylobacteriosis* in implementation of hygienic practice from slaughterhouse up to the consumers, using chlorinated water in birds ' feed and to perform slaughtering, skinning, and evisceration under asepticm conditions,
- proper handling and cooking meats of animal origin are very important points to be needed. Consumption of raw meat, unpasteurized milk and untreated water should be avoided,
- More surveillance in covering wider areas in collaboration with international organizations and stake holders is highly recommended.
- Further researches should focus on study samples other than meat and economic significance of the diseases.

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