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Public Health Significance of *Campylobacter jejuni*

Mohamed-Yousif Ibrahim Mohamed[1,2*], Jalila Abu[3], Saleha Abdul-Aziz[2], Zunita Zakaria[2], Abdul Rashid Khan[4], Ihab Habib[1,5,6]

[1]Department of Veterinary Medicine, College of Food and Agriculture, United Arab of Emirates University, Al Ain, United Arab Emirates
[2]Department of Veterinary Pathology and Microbiology, Faculty of Veterinary Medicine, Universiti Putra Malaysia, Serdang, Malaysia
[3]Department of Veterinary Clinical Studies, Faculty of Veterinary Medicine, Universiti Putra Malaysia, Serdang, Malaysia
[4]Department of Public Health and Medicine, Penang Medical College, George Town, Malaysia
[5]High Institute of Public Health, Alexandria University, Alexandria, Egypt
[6]School of Veterinary Medicine, Murdoch University, Perth, Australia
Email: *mohamed-yousif-i@uaeu.ac.ae, *dr.mohamedyousifibrahim@gmail.com

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Abstract

Campylobacter jejuni is a prominent bacterial cause of human gastroenteritis. Campylobacteriosis outbreaks reported were related to the ingestion of the contaminated food. Meat are reported to be frequently infected with *C. jejuni*. It is well recognized that *C. jejuni* is one of the main causes of gastroenteritis in humans, and poultry meat is reported to be the main source. A number of studies in several countries have shown the occurrence of *C. jejuni* in animal farms, slaughterhouses, and meat. This review simply describes the occurrence, spreading, and public health significance of *C. jejuni*.

Keywords

Campylobacter jejuni, Animal Products and Human

1. Introduction

Campylobacter spp. was first observed in veterinary samples in 1913 in the aborted ovine fetus and also in 1918. They were initially classified as *Vibrio fetus* [1]. In 1927, Smith and Orcutt isolated Vibrio-like bacteria and named them, *Vibrio jejuni*. In 1944, Doyle isolated Vibrio from pigs feces and named them, *Vibrio coli*. Similar bacteria isolated from the bovine vagina and semen were classified as *Vibrio bubulus*. Later, in 1963, two researchers known as Sebald and Veron placed *Vibrio fetus* and *V. bubulus* in the *Campylobacter* genus. Veron and Chatelain were pioneers in classifying the organism as microaerophilic organisms a decade later and included four main species in the *Campylobacter* genus: *Campylobacter jejuni*, *Campylobacter coli*, *Campylobacter sputorum* and *Campylobacter fetus* [2]. In 1980, Skirrow and Benjamin were among those who identified *Campylobacter lari* for the first time, by isolating this microbe from gulls, poultry, monkeys, dogs, cats, as well as asymptomatic humans [3]. *Campylobacter* spp. has low DNA based compositions and a non-fermentative metabolism and needs microaerophilic conditions for growth [4].

The name *Campylobacter* is derived from the Greek word "compiles", meaning "curved", and the word "baktron", meaning "rod", which, together, means curved-rod. This gives an indication of the microscopic appearance of the organism. The genus *Campylobacter* comprises 31 species and 13 subspecies, and is grouped within the family Campylobacteraceae [5]. *Campylobacter jejuni* is divided into two subspecies; namely, *jejuni* and *doylei*, the former of which is most common in human cases and the latter has no animal host [6]. Any further reference to *C. jejuni* specifically refers to *C. jejuni* subsp. *jejuni*. *Campylobacter* species are microaerophilic, gram negative bacteria, spirally curved, motile rods with polar flagella, and are intestinal commensals of mammals and birds [7]. They are slow-growing organisms that require selective media containing charcoal and various antibiotics, such as cephalothin, to suppress competing fecal microflora [8].

Microaerophilic bacteria require oxygen for growth, but at lower levels than regular atmospheric air, and, as such, *Campylobacter* species grow best at 5% - 10% oxygen and 10% carbon dioxide [9]. *Campylobacter jejuni* and *C. coli* are thermotolerant, growing best at 42˚C, while other *Campylobacter* species, such as *C. fetus*, are not [10]. Hence, a typical stool culture at 42˚C on media containing cephalothin for the recovery of *C. jejuni* and *C. coli* from cases of human diarrhea may not be optimal for the growth of other species, such as *C. fetus* or *C. upsaliensis*, which, occasionally, cause human illness.

2. Prevalence in Humans

2.1. Source and Modes of Transmission to Humans

Campylobacter jejuni can be transmitted from infected animals or animal products to humans, animals, and the environment [11] [12]. The sources of *C. jejuni* infections to humans are sometimes unclear. Nonetheless, in recent decades, many studies have implicated poultry products as the primary source of *C. jejuni* to humans [13] [14] [15]. In the UK, a comparison of geographically and temporally matched wild ducks and domestic ducks showed that they had different *C. jejuni* populations in terms of the diversity of genotypes; furthermore, a high level of *C. jejuni* isolates from domestic ducks for which the molecular characterization was done were commonly associated with campylobacteriois in humans [16]. According to Silva *et al.* [17], *Campylobacter jejuni* isolates from humans are similar to the strains from poultry, which suggests that these animals are the main sources of *C. jejuni* in Brazil.

After a survey, wild animals were reported to be the main source of such bacteria in residential areas, villages, and animal farms [18], especially wild birds [19] [20]. The wild birds are suggested to be a vehicle for the introduction of *C. jejuni* to the village environment, residential areas, human houses (backyard) and animal farms. In other cases, pets were implicated as a source of *C. jejuni*, particularly kittens or puppies with *C. jejuni* diarrhea [21] [22]. In Italy, the risk of campylobacterioses of pet origin in dog owners is increasing, and the evidence from molecular characterization showed that the correlation between the strains was the cause of the disease in humans and their pets [23]. In Malaysia, animals harboring *C. jejuni* consistently shed the bacteria through feces, spreading within and among animal species and humans in Malay villages [24].

Campylobacter jejuni can be transmitted to humans directly or indirectly, directly could occur in individuals who have occupations in which there is direct contact with animals or animal products on the farm. A good illustration of some professionals would be veterinarians, farmers, butchers, slaughterhouse workers, and poultry processors [11]. Although several routes of infection from animal to human have been reported, so far, water, milk, and meat are suggested as being the most prevailing routes of the infection.

2.2. Meat

According to molecular characterization studies for the *C. jejuni* strains, the occurrence of high interrelatedness among *C. jejuni* genotypes detected in beef, mutton, pork and especially poultry meat, with that of human infection, indicate that meat could play as a vehicle for transfer *C. jejuni* from farms to human [17]-[26]. Raw retail meats in developed countries are one of the main sources of *C. jejuni*, and, recently, there has been a significant relationship between handling meat and eating raw meat or undercooked meat and campylobacteriosis in humans [27]. However, the prevalence of *C. jejuni* is markedly different in different types of meat. According to a study in two Australian states by Walker *et al.* [28], there is a prevalence of *Campylobacter* in beef in the state (A) (10%) and the state (B) (21%), while pork in the state (A and B) was 13% and 48% and lamb in the state (A and B) was 30% and 54% respectively. In Poland, the occurrence of *C. jejuni* in retail chicken (46.6%), beef (66.7%), and pork (68.6%); however, *Campylobacter coli* was the highest isolate in turkey meat (71.2%) [29]. In Greece, the proportion of *C. jejuni* positive samples was high for retail lamb that was sampled in the areas closest to consumer purchase and handling [30]. Remarkably, the prevalence of *C. jejuni* in chicken meat of Estonian origin was lower compared to that of other EU countries, however higher than that formerly reported by the EFSA [31]. While in the United States, there is strong epidemiological evidence for the transmission of *C. jejuni* from the meat of ruminants to humans, which suggests that *C. jejuni* is a significant threat to public health [32]. *Campylobacter jejuni* has the capability of proliferating in ruminant slaughterhouses and contaminating the products and equipment [33]. So far, several reports have recognized the epidemiological evidence for the zoonotic transmission of *C. jejuni* strains from beef to humans [34] [35], and a few reports have implicated ruminants as sources of campylobacteriosis in humans. According to a study conducted in Japan and Thailand, the isolation rates of *C. jejuni* and *C. coli* isolated from broiler chicken meat was high at 60.7% out of 164 samples in Japan, with *C. jejuni* identified at 93.8%; whereas, in Thailand, the prevalence rate of *Campylobacter* spp. was lower at 13.3%; *C. jejuni* were determined at 42% [36]. More than 20 areas in China identified a low rate of *C. jejuni* in raw broiler meat between 2007 and 2010, ranging from 0.29% to 2.28% [37]. According to a report in modern broiler meat treating plants in Malaysia, 61% of the broiler carcasses were found to be contaminated with *Campylobacter* spp., and *C. jejuni* was identified at 70.9% [38]. In the Middle East several studies implicates chicken meat as source of *C. jejuni*. According to Ghaffoori [39], in Iraq, the occurrence of *C. jejuni* in chicken carcasses was as high as 60%. In Saudi Arabia, *Campylobacter* spp. was detected at 5% in retail unwashed eggshells that were sampled from retail at Al-Taif city [40]. In Tunisia, Jribi *et al.* [41] detected *Campylobacter* spp. from turkey meat samples at 23.7%. According to surveyed in Assiut city, Egypt, *Campylobacter coli* was frequently isolated from chicken carcasses at 46.7% [42]. Due to the growing number of campylobacteriosis in humans, and the implication of meat as a source of *C. jejuni* infection, further comparable studies related to the spread of *C. jejuni* in farms and the mechanism of *C. jejuni* in infiltration into the food chain are needed.

From this review, caution should be taken in abattoirs and raw retail meat markets when handling the meat using mesh gloves [43]. Even though from a care viewpoint some mesh gloves are beneficial, it has been reported that using these gloves contributes significantly to the spreading of *C. jejuni* and other pathogens over the carcass [30], as it has been reported that numerous mesh gloves were contaminated with pathogens. Similarly, the risk of spreading such organisms over other equipment, such as chutes, plastic cutting boards, and tables that could transfer *C. jejuni* to the meat is high [44]. Further, improved surveillance tools in the meat production chain are necessary for the control of *C. jejuni* in humans, as *C. jejuni* can survive for hours on moist surfaces, gloves, and hands [43].

2.3. Milk

Unpasteurized milk constitutes one of the main sources of transmission of *C. jejuni* to humans in developed countries [45]. In the United Kingdom, the partial failure of milk pasteurization is paving the way for the transmission of *C. jejuni* from cattle to humans [46]. Other studies suggested that dairy products might play an important role in the transmission of *C. jejuni* from dairy farms to humans [47] [48]. According to Heuvelink *et al.* [49], in the Netherlands, twenty-two out of a group of 34 children who visited a dairy farm exhibited diarrheal illness of *C. jejuni*, and drinking raw milk was highly correlated with the disease; in addition, 30% of dairy cattle tested positive for *C. jejuni*. In California, unpasteurized raw milk has been associated with about 80% of *C. jejuni* infection outbreaks [50]. However, *C. jejuni* infection has been associated with unpasteurized milk in multiple states.

Before processing the milk it could be contaminated through milk production as well as the handling procedures. Yuen and Alam [51] examined the raw milk hygiene among smallholder dairy farmers in the Tawau area Sabah, Malaysia. They found that suitable hygiene treatment was able to decrease the bacterial amount to an acceptable level in all periods of the study. Hence, to achieve an acceptable microbial level for raw milk, it is important to reduce the period before processing the raw milk, and freezing the raw milk should occur immediately after milking.

2.4. Water

From surveys, zoonotic bacteria or parasites traced to the contamination of surface water through feces originating from wildlife or domestic animals are considered to be a significant source of pathogens to which people could be exposed by drinking water or water recreation [52] [53]. According to Galanis *et al.* [54], in Canada, the correlation between *C. jejuni* infection in sporadic human and drinking water suggested that water is a probable source for *C. jejuni*. Another study reported that a high level of *Campylobacterlary* and *C. jejuni* was isolated from the Qu'Appelle River watershed in Canada, which is an essential source of irrigation water for plant producers in Southern Saskatchewan [55]. However, a recent study conducted in Canada by Kovanen *et al.* [27], found that the molecular characterization of *C. jejuni* strains isolated from swimming water do not show any relationship with outbreaks in domestic human *C. jejuni* infections in the same area; so far, most of the human *C. jejuni* strains were traced back to chickens. Moreover, *Campylobacter jejuni* have been isolated from surface water in some countries in Europe [27]-[54]. Thus, more molecular characterization studies for the *C. jejuni* strains should be conducted to reassess the role of surface water as a reservoir of *C. jejuni* in the *C. jejuni* epidemiology in Europe.

2.5. Occurrence in Humans

In recent decades, a number of species have been added to the curved-rod-shaped bacteria cases of gastroenteritis in humans, such as *Arcobacter butzleri*, *A. cryaerophilus*, *Helicobacter bilis*, and *H. canis* [56] [57]. However, *C. jejuni* is still the most commonly reported cause of gastroenteritis in developed countries [17] [18]. In addition, campylobacteriosis is regarded as a fundamental health concern in several European countries during the summer [27]-[58]. Exposure to the disease is probably more common in the developing world. However, children could be immunized in the first 3 years of their lives, as well as adults between 20 and 25 years of age [11]. There is a high threat of infection to those individuals whose profession exposes them to animals on the farms or animal products, such as veterinarians, farmers, poultry processors, slaughterhouse workers, and butchers [15].

Jore *et al*. [58] reported the trends of campylobacteriosis in humans and broilers in six European countries—Sweden, Denmark, Norway, Iceland, Finland, and the Netherlands for the period 1997-2007. They found that the occurrence of campylobacteriosis in humans and the occurrence of *C. jejuni* colonization in broiler flocks showed a concordant seasonality for all the countries, which indicated a significant relationship between the occurrence in humans and broilers in a given month and the average temperature of the same month. Other studies reported similar outcomes that seasonal influences could play a role in the occurrence of *C. jejuni* infection in humans [59] [60]. According to the findings of the study in Denmark by Boysen *et al*. [61], there was a slight reduction from 2005 to 2008 in the human risk level from Danish-produced poultry meat, and a reduction from 2005 to 2010 in the risk level from imported chilled poultry meat. This decrease in the level of risk coincides with the control measures implemented to reduce *C. jejuni* in imported chilled poultry and Danish meat. The human risk level of *C. jejuni* infection from Danish frozen poultry meat increased recently, but remained lower compared to that from chilled poultry meat. Overall, the relative risk from poultry meat available for consumption in Denmark increased from 2001 to 2005. However, after that, the risk reduced to a level near to the period 2001-2002. Campylobacteriosis has been confirmed to be the main foodborne disease in Germany; therefore, public health concern has in-creased [62]. According to Schielke *et al*. [62], in Germany, from 2001 to 2010, more than 588,000 cases of campylobacteriosis were reported. Furthermore, the campylobacteriosis outbreaks reported were related to the ingestion of fresh red meat. Also, in the UK, many of the recent gastroenteritis outbreaks were caused by the handling of red meat products due to *C. jejuni* or Salmonella. In Iceland, there was a reducing trend for *C. jejuni* infection in humans from 1999 to 2007, despite the *C. jejuni* trend in poultry being stable from 2001 to 2004 and falling thereafter [58]. In Norway, human *C. jejuni* infection showed a stable increase. However, Norwegian broilers showed a decreased incidence of *C. jejuni* from 2001 until 2004, albeit remaining steady thereafter. There was no important decrease or increase concerning the occurrence in humans [62].

In Brazil, *C. jejuni* has shown to be the main cause of campylobacteriosis in humans, and goats have been considered to be the potential source [63]. Several studies indicated that goats could play a role as a source of human *C. jejuni* infections as well as contamination of the environment [30]-[64]. Further, the occurrence of campylobacteriosis markers in humans, coupled with the high prevalence of *C. jejuni* among crows in California in the USA, suggests that crows shed *C. jejuni* in their feces, which are possibly pathogenic to humans [65].

2.6. Public Health Significance of *C. jejuni* Infection

Currently, *C. jejuni* has been recognized as one of the leading causes of bacterial gastroenteritis in humans worldwide [17]. *Campylobacter jejuni* infection could be severe among people with weak immunity, such as children and old people, and mild in middle aged people who have strong immunity [9]. The symptoms usually begin after 2 to 5 days and consist of headache and fever followed by watery or bloody diarrhea (often foul smelling), abdominal pain, nausea, and sometimes vomiting. In a few cases, the symptoms can be more severe, similar to acute appendicitis. Less commonly reported was septic arthritis and bacteremia. An infective dose is estimated to be about 500 cells, which is a small amount. Usually it does not require antibiotic treatment, but, if required, erythromycin followed by ciprofloxacin are the drugs of choice [66] [67].

According to the European Centre for Disease Prevention and Control (ECDC) and Community Zoonoses Reports of the European Food Safety Authority (EFSA), in the last fifteen years, *C. jejuni* and *C. coli* infections surpassed salmonellosis and yersiniosis in Europe [68]. In the European Union, food safety standards include the microbiological criteria and goals in primary production due to estimate the possible food safety measures to be implemented after the food chain step. Poultry meat constitutes the most dominant source of transmitting campylobacteriosis. According to the ECDC report in 2014, the number of confirmed cases of campylobacteriosis reported in humans was 71.0 cases per 100,000 population, which was an increase compared to the data for 2009 in which there were 45.2 cases per 100,000 population in Europe [68].

In 2015, in the US, the Foodborne Diseases Active Surveillance Network (FoodNet) of the Center for Disease Control and Prevention (CDC) reported that the incidence of campylobacteriosis per 100,000 population in terms of hospitalization and death was 6309 or 12.97%, and 1065 or 11%, respectively [69]. Also in the US, *C. jejuni* has been reported as being the most common pathogen cause of concern to public health followed by *Listeria* and *Salmonella*. In developing countries, it was reported as being more than 30 times higher [43].

In the US and the UK, the level of campylobacteriosis in humans in the last ten years has increased compared to other pathogens, such as *Shigella* and *Salmonella* [68] [69]. Furthermore, serious complications may occur, such as septicemia, meningitis, reactive arthritis, acute cholecystitis, recurrent colitis, Guillain-Barre syndrome, Miller-Fisher syndrome, and Reiter's syndrome [43]. Of these, the molecular mimicry evidence between a *C. jejuni* glycan and the Anti-GM1 IgG antibodies associated with Guillain-Barré syndrome has been clearly confirmed, and is regarded as the source of anti-GM1 IgG antibodies found in Guillain-Barré syndrome patients [70].

According to Australian Government Department of Health in 2018, 32,086 cases were notified in Australia, a crude incidence of 130 cases per 100,000 population [71]. Campylobacteriosis complications can include Guillain-Barré syndrome (30 cases per 100,000 cases of campylobacteriosis) and immune-mediated reactive arthritis (7000 cases per 100,000 cases of campylobacteriosis) [28].

3. Conclusion

Campylobacter jejuni is one of the main agents of gastroenteritis in humans and foods are play as vehicles of this pathogen from farms to humans. In the present review, the detection of *C. jejuni* is frequent in foods of animal origins especially poultry. Further study certainly needs to be done on *C. jejuni* in foods of animal origins and the sources of this pathogen on the food chain from the farms to the markets. To address the question of whether isolates from the poultry are a source of infection for humans, there is a need to characterize the isolates by molecular typing. Surveillance data are also important to evaluate and validate their results. A combined approach is crucial to be able to use and understand these data, and this type of approach involves several sectors: public health and healthcare organizations, animal food production, and distribution.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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