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Campylobacteriosis: A Global Threat

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Abstract

Campylobacter species account for most cases of human gastrointestinal infections worldwide. In humans, *Campylobacter* bacteria cause illness called campylobacteriosis. It is a common problem in the developing and industrialized world in human population. *Campylobacter* species extensive research in many developed countries yielded over 7500 peer reviewed articles. In humans, most frequently isolated species had been *Campylobacter jejuni*, followed by *Campylobactercoli* (5-18.6 % of all Campylobacter cases), *Campylobacterlari*, and lastly Campylobacter fetus. *C. jejuni* colonizes important food animals besides chicken, which also includes cattle. The spread of the disease is allied to a wide range of livestock which include sheep, pigs, birds and turkeys. The organism has been responsible for diarrhoea in an estimated 400 - 500 million people globally each year. The most important Campylobacter species associated with human infections are *C. jejuni, C. coli, C. lari* and *C. upsaliensis*. *Campylobacter* colonize the lower intestinal tract, including the jejunum, ileum, and colon. The main sources of these microorganisms have been traced in unpasteurized milk, contaminated drinking water, raw or uncooked meat; especially poultry meat and contact with animals.

Keywords: Campylobacteriosis; Gasteritis; *Campylobacter jejuni*; Developing countries; Emerging infections; Climate change

Introduction

Campylobacter cause an illness known as campylobacteriosis is a common infectious problem of the developing and industrialized world. Campylobacteiosis accounts for most of the cases of human gastrointestinal infections worldwide and extensive research on Campylobacter species yielded over 7500 peer reviewed articles [1]. In humans, the most frequent reported species of campylobacter had been *Campylobacter jejuni* (*C.jejuni*), followed by *Campylobacter coli* (*C. coli*), *Campylobacter lari* (*C. lari*), and lastly *Campylobacter fetus* (*C. fetus*). *C. jejuni* colonizes in most of the livestock which include sheep, pigs, turkeys etc [2]. In a closely watched study, differences in risk factors between the two species showed that *C. coli* infection occurs more with drinking bottled water, while *C. jejuni* is more associated with the tendency in eating habits [3]. *Campylobacter* can colonize in most of the warm blooded animals, and poultry. The world's poultry production is colonized by campylobacter species and these bacterial species have also been isolated from different wildlife i.e. birds, wolves, cats, dogs etc [4,5]. Campylobacteriosis has been responsible for diarrhea in an estimated 400 - 500 million people globally each year and has been identified as zoonotic infection associated with asymptomatic illnesses [6,7]. Annual financial costs for the management of campylobacteriosis in the US has also swelled up to 1.2 - 4 billion [8]. *Campylobacter* is small, 0.2-5.0 μm long by 0.2-0.9 μm wide spirally curved, gram's negative, motile bacteria. The genus *Campylobacter* comprises of 21 species of which *C. jejuni* and 12 species of C. coli have been associated with the diseases in over 95% of human's infections [9,10].

Transmission of Campylobacter

In last 35 years, world have witnessed emergence of numerous new pathogens that have spread quickly in the communities along with new indications [11,12]. Among them, *Campylobacter* is one, besides, *Legionella*, *E. coli*, Rotavirus and Norovirus. Together they are now one of the leading causes of morbidity in humans. Among *campylobacter* species, *C. jejuni*, *C. coli*, and *C. lari* are associated with human infection [13] and *C. upsaliensis*. It is usually sporadic, but some outbreaks may occur. *Campylobacter* colonize the lower intestinal tract, including the jejunum, ileum, and colon. In contrast to other enteropathogenic bacteria, *Campylobacter* possess relatively few virulent factors, and host factors are important in determining the severity of clinical signs that develop. *Campylobacter* can invade intestinal epithelial cells and produce cytolethal distending toxin, which causes cell cycle arrest and apoptosis. Moreover it is believed that in children, the number of *C. jejuni* responsible for the illness is even lower than in adults [14].

Campylobacteriosis is normally a self-limiting disease, but in some cases complications may occur, such as GuillainBarr´e (GB) syndrome - a post infectious polyneuropathy, reactive arthritis (1 - 5% of *Campylobacter* infected patients) with the mortality

of 2-7% and Fisher syndrome that can also lead to paralysis as a result of autoimmune damage in 0.01 - 0.03% of *Campylobacter* enteritis patients [15,16]. Furthermore, it can also trigger an acute respiratory (22-53%) or gastrointestinal (6-26%) infections. Although *Campylobacteriosis* is quite well considered and accepted as foodborne pathogen but it is also transmitted through contact with colonized animals, contaminated environments by animal waste or poor hygiene. Cross contamination during food manufacturing is considered as an important transmission route [17,18]. *C. coli* and *C. Jejuni* species have the tendency to be both human and zoonotic pathogens and these microorganisms have been traced in unpasteurized milk, contaminated drinking water, raw or uncooked meat; especially poultry meat along with contact with animals [19].

Campylobacteriosis Prevalence in the Developed World

North America

United States of America: The incidence of reported Campylobacter disease in industrialized countries, like United States, has risen steadily over the past 2 decades with most reported cases being sporadic. In 2013 from five Campylobacter out breaks, mostly outbreaks were associated with raw milk consumption [20]. Moreover, presence of active food borne surveillance system estimates that one out of 30 cases were reported. In March, 2013 CDC reported 14% rise in the incidence of food-borne infections caused by *C. jejuni*. The data from FoodNet→(2009) indicates that the number of infections by *Campylobacter* has reached a total of 6,033, or 13 per 100,000 people and it is reported that up to 39% of dogs are carriers of *Campylobacter*. Interestingly, campylobacter has also been isolated from free living American crows. If the data from 2013 is compared with 2010-2012, clearly indicates that the incidence for Salmonella decreased, but there is a considerable increase in *Campylobacteosis* [21]. From 2009-2013, an average of about 105 cases of Campylobacter infection has been reported each year from Alaskawith increase of roughly 50% in recent years compared to older data in the region [22].

Canada

In Canadianterritories, the cases of Campylobacteriosis have been mostly sporadic. Investigations into causative agent lead to identification of improper domestic food preparation. In Ontario (Walkerton, ONT) 2,500 people got sick with *Campylobacter* gastroenteritis due to cross contaminated of a supply with the thermophilic *Campylobacter* species (*C. jejuni, C. coliand C. lari*) [23].

South America

Small, community-based study in Guatemala suggests that *Campylobacter* is acommon cause of diarrhea in children. In Peru, *C. coli* and *C. jejuni* were isolated in highnumbers in both cases and controls,from the urban community [24].

European Countries

In European countries, human *Campylobacter* infections incidence has continued to increase since last sixyears and is considered as the most common reported zoonotic disease since 2009. The disease has a clear seasonal trend [25]. In all Eurpean Union (EU) countries the prevalence and incidence of Campylobacteriosis has a large variation. In 2011, total of 11 waterborne outbreaks had been documented with *Campylobacter* and other species in the regionwith an estimated increase of 2.2% cases compared to 2010. Austrian surveillance program on zoonotic bacteria fromfarm animals has revealed as high as 59% *Campylobacterspecies* positivity in broiler flocks during 2002-2007 [26]. Campylobacter species has been recognized as important pathogens since last 20 years and considered as the most common reported bacterial cause of acute gastroenteritis [27, 28].

In a large study on 33967 infections, from 2000-2006, in Scotland showed that rural children are at greater risk to *Campylobacter* infection [29]. The survey on *Campylobacter* infections has shown steady increase in cases since surveillance program began in 1977. In 1999, there has been >60,000 cases with an incidence rate of 103.7 per 100,000. Today incidence of Campylobacteriosis has risen to be 9.3 per 1000 person per years (2008-2009). The financial cost of *Campylobacter* infection to the nation has been estimated as £314.00 million (1994-95 prices). It is estimated that 20 - 40% of sporadic disease might result from eating chicken. In an interesting survey, *Campylobacter* has been identified in 637 ready to eat pies and 55 other cooked meat products [28]. Italy shows a statistically significant increasing trend since 2008. It has been further estimated that the incidence of true cases are586 per year (per 100,000 inhabitants/years [30]. Number of animal studies has shown the presence of *Campylobacter* species in Italian peninsula. A survey has demonstratedthe presence of *C. jejuni* in stray cats with a prevalence of 16.8%, in Southern Italy [31].

Scandinavian Countries

In a telephonic survey it was found that in almost 4000 interviews, 61% have been affected in a Campylobacteriosis out breaking Denmark [32]. Water samples obtained from the community water works contained *C. jejunisero* type HS:2. In 1999, a legislation has been adopted to reduce the spread and distribution of *campylobacter* species in contaminated poultry by freezing to reduce bacterial counts before being supplied to customers. This simple solution resulted in 72% reduction in campylobacteriosis in following year [10]. Iceland comparable mitigation strategies have been adopted by Norway and Denmark to control the cross contamination and spread of campylobacteriosis. In Sweden, a study on *Campylobacter* infections has found association of *Campylobacter* incidence to average water pipe length per person and ruminant density. In the same study negative association was also reported between the percentage of population receiving water from a public water supply [33,10].

Campylobacteriosis Prevalence in The Developing World

The incidence of *Campylobacter* in the developing world has been high, as these countries lack sophisticated surveillance systems in line seen in many developed countries making an assessment of

true incidence very difficult [34,35]. Even with the development of improved modalities, the true burden of campylobacteriosis especially in children has seriously been underestimated with recent reports of association between *Campylobacter* infection with malnutrition. One study showed an alarming high rate of infection of 60,000 per 100,000children <5 years of age [36]. Poultry specifically has accounted for 50%-70% infection with an increase during summers due to undercooked meat from outdoor cooking facilities [35].

African Countries

Numerous studies have reported that in South Africa, diarrheas by *Campylobacter* has been clinically less severe than other developing countries. In a relatively large study in Malawi, *Campylobacter* species had been detected in 415/1,941 (21%) of diarrhea children. Species identification accounted for 85% being *C. jejuni*. Importantly median age of these children was 11 months. In Botswana, estimates from the prevalence data indicates that *Campylobacter* diarrheal infection of hospitalized <5 year children has range as low as 1.5%. In Mozambique it is, 1.7%, 9% in Uganda, 11% in The Central African Republic. Highest rate has been found in Tanzania where it is 18%. Where as, 3.3% in Djibouti and 0.8% in Guinea-Bissau. These low rates may be due to their socioeconomic status but still needs further evaluation [36]. In Africa, from 1993 to 2011, five studies had been conducted to assess the extent of colonizationof chickens and ducks in Tanzania. All studies found to be positivelyassociated to *Campylobacter*; and specifically to *C. jejuni* followed by *C. coli*. Two of these studies also looked at seasonalvariation on human infections and did not found any difference. Previousstudy conducted in the Congo, had reported high prevalence of *Campylobacter* during the wet season [37].

Middle East

Campylobacter infection ranked among the top three etiological agents of bacterial enteritis in the region. In Jeddah, Saudi Arabia, *Campylobacter* infection has the second in prevalence to Salmonella with 69% cases being due to *C. jejuniand* 31% due to *C. coli*. In Kuwait, *Campylobacter* ranked third after *Salmonella* and Enterotoxigenic *E. coli* [38]. In Israel, campylobacteriosis is a reportable disease and microbiology laboratories of thecountrysubmithuman isolates from all sources to the National *Campylobacter* reference Laboratory working under Ministry of Health. Recently a sharp increase in the incidence of *Campylobacter* species infection was noted with rates tripling withinjust 12 years. These infections have been mostly among children <2 years of age. During that period, most (>99%) infections were *C. jejuni* followed by *C. coliand* remaining <1% have been identified as *C. fetus*, *C. upsaliensis*, *C. lari* and some unidentified cultures [39].

Antibiotic Resistance

Macrolides are considered the first drug of choice in enteritis from *C. jejuni* and *C. coli* while Erythromycin and Ciprofloxacin are the preferred drugs for treatment of human campylobacteriosis. Genera *Campylobacter* is recognized as reservoirs for antimicrobial resistance genes that potentially can be exchanged between other pathogenic and other common bacteria [40]. Since last few decades antibiotics have been in use in animal food production for control, prevent, and treatment of infections that enhance growth. This usage has caused an increase in resistance to multiple antibiotics by members of *Campylobacter* species in food production animals and surrounding environment. The development of antimicrobial resistance in *Campylobacter* species is a serious threat to human health because of its prevalence in general. The worldwide rapid increase in the proportion of *Campylobacter* strains resistant to antimicrobial agents has evolved. *Campylobacter jejuni* and *C. coli* are almost intrinsically resistant to penicillins, cephalosporins (with exception of a few 3rdgenerationcephalosporins), Trimethoprim, Sulfamethoxazole, Rifampicin and Vancomycin.

For patients infected with Campylobacter species, the prognosis occurs in them without specific treatments other thanreplacement of fluids and electrolytes. It is believed that increasing resistance to fluoroquinolones and Erythromycin by *C. jejuni* and *C. coli* might compromise the effectiveness of these treatments. Acquired antimicrobial resistance to macrolides, fluoroquinolones and other antibiotics has given us a challenge in *Campylobacteriosis* control worldwide [41].

This increasing resistance of campylobacter to relevant antibiotics; macrolides and fluoroquinolones has become a serious public health concern in developed as well as the developing world. The adverse effects of an infection with quinolone-resistant *Campylobacter* on severity and extent of infection are the subject of de¬bate [42]. In children suffering from diarrhea in Guatemala; antimicrobial resistance was high, and treatmentregimens in the ambulatory setting were metronidazole and trimethoprimsulfamethoxazole [24]. Korolik et al. [43] reported that human strains collected between 1989-1990and 1994-1995,79-81 strains of *C. jejuni* and 6-8of *C. coli* showed resistance to Erythromycin.

Strategies for Control of CampyloBacteriosis in Climate Change

Warming trend due to the changes in the global climate is affecting in increase of various important infections and on the other hand the extreme weather conditions lead to outbreaks of clusters of different diseases as a surprise. Most studies indicated about a positive association between temperature and enteric infections such as *Salmonella*, *Campylobacter* and Bacillary infections. It is reported that 1°C increase in temperature can increase the risk of severe diarrhea by 5-15% [44]. The food consumption habits due to increase in the cost affected by the climate change also affect food safety protocols (pesticide and chemical residues) resulting in food-borne illness. The increase in cost of food will force more people to shift from expensive but fresh poultry to relatively cheap but frozen chicken that can lead to increase in incidence of Salmonella but on the contrary may lead to less cases of campylobacterosis [45].

One study has reported that minimizing or complete elimination of animal proteins from the diet and proper sanitization of the water supply has been found effective in preventing the infections [46]. The use of antibiotics are no longer recommended

due to high incidence of antibiotic resistant strains which will limit the sensitivity and specificity of the drugs while treating human diseases. However, the use of Pre- and Pro-biotics have been reported to have shown results by some groups and need further evaluation. Interestingly, bacteriocins-producing bacteria (paenibacilluspolymyxma) has shown some interesting results and further researches are required to fully validate these results [47].

Conclusion

More research is required in this field to refine our understanding of the pathophysiology of *Campylobacter* infections in the developed as well as developing countries. The findings of these few studies indicate a need for increased surveillance and *Campylobacter* screening both at the slaughter houses and at the sales levels. Collaborative efforts from veterinary and human medicine targeting different aspects of the infections are need of the hour, to allow for efficient and more effective strategies for prevention and/or control of the disease. Thoroughly washing of hands with soap especially before eating or drinking can avoid hand-to-mouth contact, after handling of a companion animal and it can further help in prevention of transmission of the zoonotic disease.

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