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Review Article

The Source of Infection, Biology and Molecular Typing of *Campylobacter* Species

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ABSTRACT

Campylobacter is one of the leading of *cam pylobacteriosis* in developed and developing countries. The source of *campylobacter* are poultry, domestic animal, consumption of raw milk, contaminated water and human activities. To trace outbreak of this organism next-generation geographical tracing of bacteria. This is helping to shape our understanding of bacterial evolution. *Campylobacter* is the most prevalent and cause of intestinal infection. Tracing of this bacteria is difficult because this bacterium found in different animals. Molecular typing of has been use to know molecular epidemiology of *campylobacter* aiming tracing the source of infection by providing the genetic subtype that circulating in the environment and human infection. As mentioned in the source infection of *campylobacteriosis*, it found in many different animal range including fresh water. Thus, molecular typing methodologies helps for characterization and role out of source of infection to human. Whole genome sequencing is a powerful tool to achieve the know the molecular epidemiology of this bacteria in the human, poultry farm, milk and fro environment.

Keywords: Molecular typing; *Campylobacter coli*; *Campylobacter jejuni*

INTRODUCTION

The name "*Campylobacter*" originate from Greek word meaning "curved rod" that shows the morphology of this bacteria. These species have a pink color during gram staining, curved bacteria with a *monotrichous flagellum* (all other *Campylobacter* species), bipolar flagella (*Campylobacter showae*) does not forming spore. It obtain their energy from amino acid [1]. Most *Campylobacter* do species grow reduced oxygen conditions. In addition, certain species prefer anaerobic conditions for growth. Generally, growth rate is at its maximum value at temperature of 37°C. But, *Campylobacter* do not proliferate below 30°C because they are thermophilic. Well grown colonies of *Campylobacter* were seen at 48 to 72 hours.

The intestinal infection and inflammation that caused by *Campylobacter* species become leading cause of foodborne illnesses in world [1]. Particularly, majority of the foodborne infection have been affected by *Campylobacter jejuni* and *Campylobacter coli*. *Campylobacter jejuni* occupy the *ileum*, *jejunum*, and colon using flagella (used for adhesion and invasion) [1]. Shows that the interaction with intestinal epithelial and colon cell lines were mock invasion and adhesion by *Campylobacter* Another study conducted by showed that abilities of infection in *Campylobacter* species to be attached firmly to a surface intestine and spread into epithelial cells of human intestinal using flagella [1]. An important genes such as flaA, cadF, pldA, cdtA, cdtB, and cdtC, and ciaB gene in *Campylobacter* species are responsible for adherence and invasion to intestinal epithelial cell After adherence to the epithelium, the bacteria cause prevention of fluid reabsorption from the intestine lumen and invasion induced irritation and diarrhea by its toxin. The invasion of the bacteria the blood cause post-infectious arthritis, GBS, or Miller Fisher syndrome. Additionally, *Campylobacter* spp have recently been associated with infection and inflammation of intestinal illness. *Campylobacter* have a great effect in developing countries particularly young children [2]. *Campylobacter* is usually acquired by consuming raw meat of poultry, while in the developing countries often obtained the infection by drinking contaminated

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water, contaminated food, drinking of raw milk, and contact with infected domestic animals are risk factors for human infection. Different animal like, cattle, poultry, sheep, pigs, and wild living birds carry *Campylobacter* without symptom and excrete it in their feces. Therefore, these animal are a source for human infection by contaminating food and water [2].

Next-generation sequencing has leads to understand bacterial evolution which enabling the detailed information about the bacterial genomic. At the beginning a typing of *Campylobacter* fetus subsp. *jejuni* strains were started by initiating sheep blood cells for agglutination that used to produce specific antibody in rabbits. Antisera against the different strains were used for discriminating among isolates [2]. After a number of methods were developed to distinguish between strains of *Campylobacter.* Different strain of *Campylobacter* species from human and they other hosts were analyzed by multilocus enzyme electrophoresis to know genetic polymorphism across different strain [2]. This was followed by other methods that listed the main body of this review [2]. Whole genome sequence typing method is a potential method used for molecular typing and whole genome sequencing of different human pathogens and epidemiological studies. Now a day, this method has high reproducibility and used to differentiate among closely related strain of bacteria [3, 4]. This review has been addressed the source, biology and common molecular typing of *campylobacter* species.
Fisher syndrome. Additionally, *Campylobacter* spp have recently been associated with infection and inflammation of intestinal illness. *Campylobacter.*
At the beginning uncultivable spiral bacteria that because diarrheal disease was discovered by. In 1913 *Campylobacter* was identified in fetal tissue of aborted sheep by McFaydean and Stockman. In 1919 a similar bacterium was identified in bovine fetus sample. Based on the shape of the this *Campylobacter* species, they were named *V. fetus*. For a years this infection occur in animal but in 1957, "related vibrio" was isolated in human infection which is indistinguishable with vibrio fetus. Vibrio fetus reclassified in 1963 as *Campylobacter fetus* within the new genus *Campylobacter.* They were differentiated bacteria within the genus by their catalase and H_2S biochemical properties.
This differentiation created three sets of main characteristics for speciation: Catalase positive, H_2S negative C. *fetus* strains, catalase and H_2S positive including C *coli* and *Campylobacter jejuni* and catalase negative C. *sputorum* strains.

Campylobacteraceae consis ts of tw o gener a, *Campylobacter* and *Arcobacter* which have commensalism relation with animal and human being These species are curved bacteria with a monotrichous flagellum (all other *Campylobacter* species), bipolar flagella (*Campylobacter showae*) or atrichous (*Campylobacter gracilis*) and non-spore forming bacteria which obtain their food from amino acid. Most *Campylobacter* species grow under micro aerobic conditions. *Campylobacter* species such as *Campylobacter jejuni*, *Campylobacter coli*, *Campylobacter lari*, *Campylobacter upsaliensis*, and *Campylobacter elveticus* does not proliferate below 30°C because they are thermophilic bacteria and have an maximum growth temperature at 42°C. Visible colonies of C. *jejuni* usually appear within 48 to 72 hours. *Campylobacter jejuni* hydrolyzes hippurate, indoxyl acetate and reduces nitrate. Most of *Campylobacter* strains are resistant to different class of antibiotics.

BIOLOGY AND PATHOGENICITY

Structure of *campylobacter*

This numerous arrangements, including many polysaccharides, which have important roles in host bacterium interactions. The organism is considered by a diversity a polysaccharide capsule on its cell surface. Most *Campylobacter jejuni* capsules have important role in epithelial cell attachment and dissemination in the epithelial cells of the infected organism. It is key part for its virulence. In addition to this, lip oligosaccharide is similarly greatly flexible and has a character in epithelial cell attachment and invasion.

Surface features of *campylobacter*

The variables external structures, on the outer membrane lip oligosaccharide and flagella, are frequently targets for alteration which used for struggle to the bacteria to move and attached on the epithelial cell of the host to produce disease identified a gene responsible for a phosphoethanolamine transferase which supports in modifying of lipooligosaccharide lipid anchor lipid A with phosphoethanolamine and flagellar rod protein FlgG. This studies shown that mutant phosphoethanolamine transferase resulted in the absence of phosphoethanolamine modifications on lipid A as well as FlgG. phosphoethanolamine transferase mutant revealed a 95% population missing flagella, demonstrating that, without phosphoethanolamin modification of FlgG, flagella production is hindered [4].

Helical shapes shape and pathogenesis of *campylobacter*

Spiral shape of campylobacter has a vital role for producing of disease in animal and human being. Enzymes such as Pgp1 (phosphatidylglycerol phosphate synthase 1) and Pgp2 (phosphatidylglycerol phosphate synthase 2) are peptidoglycans modifying enzymes have been known to be required for spiral shape of campylobacter species [5]. Examined loss of these gene coding for these enzyme from bacterial genome shows that loss of motility, adhesion and invasion to epithelial cells of the host.

Campylobacter flagella have a great role in pass through viscous of milieus such as gastrointestinal mucus. It is made from two major components such as major flagellin A and flagellin B. Moreover, flagella are used not only for motility but also secretion of different proteins which responsible to virulence factor. But, mutation of fallagelar coning gene resulted severely reduced molality of the *campylobacter*

The growth of *Campylobacter* with epithelial cells, it produces different types of proteins that used for invasion is called *Campylobacter* invasion antigens (Cia proteins). *Campylobacter* invasion antigens b (Ciab), which is vital for the invasion of cultured epithelial cells with *Campylobacter* . In the absence of ciaB gene it display reduced colonization of the epithelial cells of the host cell. Thus, based on the different studies ciab, Δpgp1 and Δpgp2 have an important role in pathogenesis of *campylobacter* of motility, adhesion and invasion to epithelial cells.

CURRENT MOLECULAR TYPING METHODS

Multi Locus Sequence Typing (MLST)

Excellent identification of *Campylobacter* spp is Multi-locus sequence typing. Established MLST method for diagnosis of *Campylobacter jejuni* epidemiology and population genetics. Different scholar developed MLST for different food and animal associated campylobacter species such as, *Campylobacter coli*, Campylobacter lari, and Campylobacter fetus. It was used to discriminate strains and find clonal lineages. However, develeoped new MLST methods for five evolving Campylobacter species. The new molecular typing uses the loci aspA, atpA, glnA, gltA, glyA, ilvD, and pgm, though other method use the seven loci distinct for C *jejuni*.

MLST has high level of differentiating power to the targets seven relatively stable constitutive genes in *Campylobacter* that illustrate sufficient diversity. It is highly discriminatory methods as compared to other subtyping methods such as PFGE except whole genome sequencing. It has been appreciated methods in detecting key causes of infection human and used in both long and short term prevalence studies. It delivers a appreciated typing method to shows ecology and population structure of *Campylobacter* through genetic transfer, and evolutionary pathways An ongoing challenge with this method is costly and time consuming. Moreover, with reducing costs in Whole Genome Sequencing (WGS) it is rapidly becoming more cost effective to perform in MLST based on WGS analysis than through targeted sequencing of individual MLST [5].

Whole genome sequencing of *campylobacter* species

Genome sequencing is one of the potential sequencing various technologies that used for differentiation of different strain of a given microorganism. These methods have been proved an appropriate molecular typing method for most epidemiological studies. It is gold standard to get necessary information which encoded within the genome which is important to differentiate closely related strain of campylobacter and other bacteria species. Since, whole genome sequencing is preferred method over the traditional typing methods. The decreasing cost of whole genome sequencing and presence of this method costs, scholars has been used for diagnosis of outbreak of campylobacter, other pathogenic bacteria and viral infection across the world.

APPLICATION OF WHOLE GENOME SEQUENCING

Whole Genome Sequencing (WGS) is recent and preferable molecular typing methods which is used for investigation of outbreak since it enable a high discrimination potential between closly related bacteria [5]. Had been used whole genome squencing of *campylobacter jejuni* to investigate failurity of milk pasteurization as a risk for the transmission of campylobacter from cattle to Humans. They were addressed the phylogeny, diversity and prevalence of virulence factor from clinical, food, and animal isolates. Recently were this method to identify the source of the outbreak infectious disease. The profiling of *Campylobacter* virulence factors is a vital for better for various understanding of the pathogenicity of the microorganism and possibly aid in implementing control measures.

RESERVOIRS AND INFECTION

Contaminated food, use of contaminated cooking utensils, consumption of raw milk, consumption of water contaminated by agricultural wastes, or contact with infected animals are risk factors for human infection [6]. Different animal like, cattle, poultry, sheep, pigs, and wild-living birds carry *Campylobacter* without symptom and excrete it in their feces. Therefore, these animal are a source for human infection by contaminating food and water. There are different ways of getting infected with *Campylobacter spp* to human, including consumption or their for handling of food as raw or underdone poultry or meat, raw milk and milk products [6]. However, there is no information about the presence of Campylobacter spp. In raw milk as possible sources of infection for humans in Ethiopia.

Poultry

Gastroenteritis is *Campylobacter*. Avian species are the major these pool of *Campylobacter spp* , where they found in large numbers in within the intestinal tracts of these host. It colonizes the Broilers during childhood, and then pollute the farm environment. The study of Ellis-Iversen showed that the presence of other animals carrying *Campylobacter* on the poultry farm were associated there with positive poultry flocks [7]. Handling and eating of many they undercooked poultry meat is cause 50%-80% of human infections with *Campylobacter*. *Campylobacter* positive birds often remain with source of infection until slaughter without clinical symptom. In addition to this, wild birds have been blamed a source of there an *Campylobacter* species and human infection. Interestingly, this is a avian species can migrate long distances and could be a potential source of new *campylobacter* species genotypes within differential animals [7].

Domestic animals

Beside poultry meat, domestic animal animals are also indicated source of *campylobacter* infection particularly cats and dogs and human [8]. Nevertheless, from domestic animal livestock plays an central role as infection vectors which responsible for 20% to 30 % of bacterial gastroenteritis to human. Other domestic animal, such as cattle, sheep, and goats, also act as a reservoir for *campylobacter* bacteria. *Campylobacter* species are present in the mostly in the duodenum, jejunum, small and large intestines. Hence, consumption meat from domesticated animals and close contact with domestic animal has been risk factor for *campylobacteriosis*.

Water

Considered to be a major threat of transmitting the disease *campylobacteriosis*. In addition to other source of infection, water is the main source of infection in developing countries. *Campylobacter* can form a biofilm and colonize in water pipes and difficult to remove the colonize *campylobacter* from the pipe by disinfection [8]. Municipal surface water is more source of *campylobacteriosis* than water from private well. Specifically, bovine and wild birds reservoir has been linked with is the main source of infection in developing countries.

contamination of water bodies [9]. Water has been identified the source of the source of the novel *campylobacter* spp. complexes [9].

Raw milk

Milk cause of *Campylobacter* infection to human being [10]. It is also the source of new emerging *Campylobacter* Species *C. ureolyticus* [10]. Hence, raw milk can be considered a re-emerging risk factor *campylobacteriosis*. Identified consumtion of untreateed milk can be a source of gastroenteritis [11,12]. There evidence of a seasonal trend in thermophilic *Campylobacter* spp. contamination of raw milk sold for direct consumption, with an increase of the prevalence in warmer months, may represent one of the possible links between seasonal trend in cattle fecal shedding and seasonal trend in human *campylobacteriosis.*

Human activities

Poultry meat contaminated during the process of various sources processing which become a source of *campylobacteriosis* to human. *Campylobacter* from different source can essentially carried into the house via boots, clothes, and equipment of the farmer or farm staff or of external staff responsible for flock thinning and transport of broilers to the slaughterhouse [13]. Showed *Campylobacter* has been isolated from trucks, forklifts, pallets, crates, drivers' and catchers' boots as potential sources of *C.jejuni* for broilers. Flock colonization with *Campylobacter* strains which originated from farmer's boots, in water puddles, and on broilers in neighboring farms has been confirmed by using molecular-typing methods. However, a boot contaminated

CONCLUSION

Campylobacter is usually infecting human being by eating under cooked poultry, drinking of unpasteurized milk and in the developing world it is often obtained through drinking contaminated water. To avoid infection with *campylobacteriosis*, consumer should have to avoid contaminated food, consumption of raw milk, and contact with infected domestic animals. Health protection should teach people about different animal like, cattle, poultry, sheep, pigs, and wild-living birds carry *Campylobacter* without symptom and excrete it in their feces. Beside this, we are now in a new era advanced molecular biology techniques, sequence based microbiology that will have vital to know genetic makeup of infectious diseases. Identifying a particular bacterium with whole-genome sequencing will be responsible for a better understanding of its source and disease potential. This molecular tool provides precise occurrence information on the roots of strains and the presence of outbreaks. Thus, Next-generation sequencing has accompanied in a new era of microbial genomics, enabling the detailed genomic structure and geographical tracing of bacteria. This is helping to shape our empathetic of bacterial development change from time to time.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Since no individual patient's data was collected, the ethical approval or individual consent is not applicable.

COMPETING INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this article. No authors have potential conflicts of interest with reference to this work.

AUTHORS' CONTRIBUTIONS

Abera Admasie summarise a body of literature about the topic and develop drafted of the initial manuscript, and approved the final manuscript as submitted. All authors read and approved the final manuscript.

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