

## Campylobacter Jejuni Infection in Israel: A National Study on Molecular Epidemiology

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### Abstract

Over the past ten years, Israel has experienced an increase in the prevalence of Campylobacter infection, making it one of the industrialised nations with the highest rates, particularly among children under two years old. Using multiple methods, this study examined the molecular epidemiology of Campylobacter jejuni in Israel over a decade MLST (locus sequence typing) in conjunction with demographic data. Select veterinary isolates (74) and representative clinical isolates from a sizable national repository were subjected to MLST. Using Poisson modelling, the distribution of age groups, ethnicity, and clinical source among different genotypes was assessed. The 512 isolates under study were given 126 different sequence types (STs), which were organised into 21 clonal complexes (CCs). Most human, chicken, and bovine STs grouped together among the top CCs. Since 2006, only three dominant STs have been identified. Patients carrying the most common CCs were similarly dispersed among densely populated areas. Patients with CC353 (relative rate (RR) 14.2, 95% CI 1.03-3.9, adjusted p value) and CC42 infections had more blood isolates than those with CC257. Different age groups and ethnicities were distributed among the top CCs.

**Keywords:** Campylobacter infections; Campylobacter jejuni; Humans; Epidemiology

### Introduction

Infections with campylobacter pose a serious threat to global public health. The WHO-established Foodborne Disease Burden Epidemiology Reference Group (FERG) named Campylobacter as the most common foodborne bacterial infection in 2010, accounting for about 96,000,000 illnesses and 21,000 fatalities globally. The most prevalent zoonotic disease in the EU is campylobacteriosis, which is also a major contributor to foodborne illnesses and gastroenteritis in the majority of developed nations. Despite national control measures, the incidence of infection has been rising in several European nations [1]. *C. jejuni* is responsible for 80-90% and *C. coli* for 10-20% of Campylobacter infections. It is common for wild animals and birds as well as food-producing animals including chickens, cattle, sheep, and swine to have their digestive tracts colonised with Campylobacter. Humans communicate. It is thought to be a significant reservoir and source of infection, accounting for 50 to 80 percent of disease burden in many nations. Consuming raw milk and unpasteurized dairy products, as well as direct contact with food and domestic animals, are other well-documented ways to get sick. Fresh fruit and water reservoirs, especially private wells, can become polluted with animal or bird faeces and become a source of human sickness. The majority of research on the genetic diversity of Campylobacter isolates collected from clinical samples, animal and environmental sources in various geographic locations, as well as yearly and seasonal trends, uses multilocus sequence typing (MLST). Additionally, MLST-based investigations are utilised to connect the Campylobacter reservoir in wild animals, poultry, and other food sources [2].

By using source attribution techniques, to human ailments. There aren't many studies connecting particular genotypes to the demographics of affected patients or to extra intestinal sources of infection. Laboratory-confirmed. The annual incidence of campylobacter has increased significantly in Israel over the past ten years, reaching 91/100,000 in 2010 and 101/100,000 in 2013, with *C. jejuni* accounting for 78% of cases [3]. These claimed incidence rates are some of the highest in industrialised nations. In Israel, the incidence of infection among young children is the highest, with a rate

of 356/100,000, 26.7 times greater than the rate among those aged 30 to 50. Although poultry intake has been suggested as a potential source, the cause of the sudden rise in the prevalence of campylobacteriosis in Israel is still unknown [4].

### Method

#### Source of Isolates

In Israel, campylobacteriosis is an illness that must be reported. Passively submitted Campylobacter human isolates from microbiology laboratories around the nation are monitored by the National Campylobacter Reference Laboratory at the Israeli Ministry of Health in Jerusalem. Standard techniques are used to phenotypically identify isolates [5]. In the national strain repository, every tenth stool isolate and all blood isolates are kept in glycerol broth at 80C. The National Campylobacter Reference Laboratory identified 42,251 patient-specific *C. jejuni* clinical isolates over the course of the investigation 42,017 from stool and 234 from blood, of which 6406 were kept 213 from stool and 193 from blood. 45 typical ISO-lates were chosen for each research year and subjected to MLST-based typing for the study's purposes [6]. Blood isolates were favoredly chosen to boost the blood source sample's representativeness. Patients' identification numbers were used to access information from the Israeli Ministry of Health records, including age, sex, nationality, and residential address. The National Campylobacter Reference Laboratory received 74 isolates from food and animal sources between 2008 and 2015; these isolates were also examined. The Israeli Veterinary Institutes, Beit Dagan, Israel, collected the majority

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of these isolates from cow and chicken rectal swabs from various places around the nation and submitted them in 2008 as part of a survey. The remaining chicken isolates date back to 2012 and are the results of veterinary examinations of farms and fresh poultry products from across the nation [7].

### Molecular Identification

The chosen isolates were defrosted and subcultured using conventional culture techniques. An internal multiplex PCR using primers targeting four genes, two specific to *C. jejuni* and two specific to *C. coli*, was used to confirm the species. According to the PubMLST methodology, the seven housekeeping loci of the Campylobacter MLST scheme were amplified. The forward and reverse amplicons were sequenced using BigDye Terminator chemistry at The Center for Genomic Technologies, The Institute of Life Sciences, and The Hebrew University of Jerusalem, Israel [8]. The sequences were examined using the programme BioNumerics v. The public Campylobacter MLST database's allelic profiles, sequence types (STs), and clonal complexes (CCs) were then retrieved. The PubMLST database received fresh alleles and STs.

### Statistical Method

To assess the distribution of age groups, ethnicity, and source of isolation between the five most prominent (top-five) CCs, poisson regression models accounting for over-dispersion were utilised. The percentage of a particular investigated CC among the top five CCs as a whole served as the dependent variable. The specific factor and its interactions with the CC type were the independent variables. The results are presented as relative rate (RR) with 95% CI. The corrected p-value utilised for all studies was determined using the false discovery rate (FDR) approach, which was also employed to account for multi-testing [9].

### Ethical Considerations

438 human isolates (384 from stool and 54 from blood), 65 from food, 24 from rectal swabs, and 9 from bovine isolates were successfully subjected to MLST (from rectal swabs). The source-recommended typing results are displayed. The 512 research isolates were divided into 126 unique STs and 21 CCs, with 62 isolates (12.3%) not belonging to any recognised CC. 26 different STs, including half new STs, were present in the isolates with unassigned CCs. In all, 48 new STs were attributed to 96 isolates (18.8%), of which 76 (79.2%) had new allelic profiles (42 different STs), while the remaining six contained novel alleles. The top new STs were ST6565 (13 isolates), ST6566 (14 isolates), and ST6608 (14 isolates) [10]. A total of 60.0% of all isolates (61.0% among human, 52.3% among poultry, and 66.7% among bovine isolates) were caused by the top five CCs CC21, CC206, CC353, CC257, and CC42. Bovine isolates were detected in three out of the top five CCs, and poultry isolates were prevalent in all top-five CCs. 50.6% of all isolates belonged to the top ten STs.

### Result

The MLST-based molecular epidemiology of *C. jejuni* infections in Israel, a nation with a high incidence of campylobacteriosis, is described for the first time in this paper [11]. The study was based on a sizable collection of *C. jejuni* clinical isolates that were meticulously gathered over a ten-year period. Israeli *C. jejuni* isolates from human, poultry, and bovine sources showed a significant amount of new STs and unique alleles, as well as a broad genotypic diversity. In spite of this, five common CCs were shared by 59.8% of the isolates. Studies from other nations' research support this pattern. The top-five Israeli

CCs appear to be widespread in numerous nations in Europe, North America, and Australia [12]. Some of these CCs, particularly CC21 and CC257, are also dominant genotypes in these nations, suggesting that these subtypes may be better suited to these regions. Only a few of the top ten Israeli STs, namely ST21, ST50, ST572, and ST257, were also widely used in other nations, including Luxemburg, the United Kingdom, and Australia. Clinical isolates clustered with poultry and bovine isolates in the phylogenetic analysis, indicating that they might be potential food sources for human campylobacteriosis in Israel. These are, in fact, Israel's primary suppliers of beef [13].

### Discussion

According to a recent case-control research, Israeli youngsters were more likely to have Campylobacter infection the more chicken dinners they ate the week before the development of clinical symptoms. These findings concur with a number of MLST-based investigations that point to poultry as the primary source of human Campylobacter infections. The discovery of new STs between the years of 2006 and 2007 is one of it is noteworthy that one of them (ST6608) is exclusive to Israel. Between 2006 and 2007, a significant rise in the prevalence of *C. jejuni* and Campylobacter infections in Israel was noted. Within the limits of our small annual sample size, the introduction of new STs may explain some of the increase in the Campylobacter clinical infections around these years.

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