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Ambient temperature and age-related notified *Campylobacter* infection in Israel: A 12-year time series study

Alina Rosenberg[a], Miriam Weinberger[b,c], Shlomit Paz[d], Lea Valinsky[e], Vered Agmon[e], Chava Peretz[a,*]

[a] School of Public Health, Epidemiology, Sackler School of Medicine, Tel Aviv University, Ramat-Aviv 61390, Tel Aviv P.O.B 39040, Israel
[b] Infectious Diseases Unit, Assaf Harofeh Medical Center, Zerifin 70300, Israel
[c] Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
[d] Haifa University, Geography, 199 Aba Khoushy Ave. Mount Carmel, Haifa 3498838, Israel
[e] Central Government Laboratories, Israel Ministry of Health, Yakov Eliav St., Givat Shmuel, P.O.B. 34410, Jerusalem 91342, Israel

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ABSTRACT

Background: *Campylobacter* spp. are the leading cause of foodborne infection worldwide, with a seasonal disease peak that might be affected by temperature increase. We studied the relationship between ambient temperature and weekly notified *Campylobacter* spp.infections.

Methods: Data on 29,762 laboratory-confirmed cases of *Campylobacter* infection for the period, January, 1999 to December, 2010 were retrieved from the Ministry of Health registry. To estimate the association between the number of weekly cases of *Campylobacter* infection and the national average temperature at lags 0–3 weeks, firstly, we used GAM models, and secondly two-segment piecewise linear Poisson regressions. The effect of temperature was adjusted for seasonality, long-term trends and holidays.

Results: We found a J-shaped relationship between ambient temperature and notified *Campylobacter* spp. cases. For *C. jejuni* in all ages, the curve below the threshold was constant and the percent increase in cases for 1 °C above a threshold of 27 °C was 15.4% (95%CI: 6.7–24.1%). For ages 3–10 yr and > =26 yr the curve was constant below the threshold and positive above it; the percent increase in cases for 1 °C was 17.7%(95%CI: 6.0–29.4%) and 23.7%(95%CI: 11.6–35.8%), respectively. For ages 0–2 yr the curve was linear with no threshold and the percent increase for 1 °C was 5.1%(95%CI: 2.1–8.1%). For ages 11–25 yr the curve was always constant. Results for *C. coli* were similar.

Conclusion: Our findings indicate that higher temperatures throughout the year affect *Campylobacter* spp. morbidity, especially in younger children. This should be taken into consideration in public education and health system preparedness for temperature increases as a result of climate change.

1. Introduction

Campylobacter species have emerged as leading bacterial causes of gastroenteritis and foodborne infections in developed countries since 1970 (EFSA (European Food Safety Authority), 2017). The annual incidence rates vary between 13/100,000 population in the United States (US), 71/100,000 population in the European Union, and 150/100,000 population in New Zealand (EFSA (European Food Safety Authority), 2017; The Institute of Environmental Science and Research Ltd, 2017; Crim et al., 2015). In Israel, the annual incidence rates of notified *Campylobacter* infections increased from 31 to 91/100,000 population between 1999 and 2010 and mostly affect toddlers younger than 2 years old (Weinberger et al., 2013). The vast majority of human infections are caused by 2 serotypes: *Campylobacter jejuni* and *Campylobacter coli*, which are responsible for 80–90% and 10–20% of infections, respectively (EFSA (European Food Safety Authority), 2017).

Symptoms of gastroenteritis due to *Campylobacter* infection usually persist for 3–4 days but may last for more than 1 week. The usual presentations include diarrhea, fever and abdominal pain. Late but rare complications include Guillain-Barré and hemolytic uremic syndrome. Chronic sequelae are more common and include reactive arthritis and irritable bowel syndrome (Allos et al., 2015; Keithlin et al., 2014). The incubation period in the majority of cases is fewer than 6 days, but may last up to 10 days (Horn and Lake, 2013).

* Corresponding author.
E-mail addresses: alinaros@post.tau.ac.il (A. Rosenberg), miriw@netvision.net.il (M. Weinberger), shlomit@geo.haifa.ac.il (S. Paz), Lea.Valinsky@moh.gov.il (L. Valinsky), vered.agmon@moh.gov.il (V. Agmon), cperetz@post.tau.ac.il (C. Peretz).

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All age groups are affected, but the highest incidence is reported in children under 5 years (EFSA (European Food Safety Authority), 2017; Allos et al., 2015). In Israel the age-specific annual incidence rate during 1999–2010 forms an asymmetric U-shaped curve; with the highest rates in the first and second years of life (363 and 349/100,000, respectively), the lowest rate in the fifth decade of life (13/100,000), and a slight increase that occurs toward the eighth decade of life (26/100,000) (Weinberger et al., 2013).

The incidence of campylobacteriosis varies seasonally and geographically in temperate regions, and tends to be highest during the summer months in several countries (Nylen et al., 2002; Tam et al., 2006) including Israel (Bassal et al., 2016a). The temperature may directly affect the rate of replication of pathogens and their survival in the environment. In the absence of any control measures, increased ambient temperatures may therefore increase bacterial contamination at various points along the food chain. Ambient temperatures may also influence people's behaviour which, in turn, may be translated into more risky patterns of food consumption. For example, higher temperatures may lead to increased consumption of raw foods such as fruits and salads, and higher temperatures may encourage riskier cooking practices such as barbecuing (Kovats et al., 2005; Lake et al., 2009). Finally, in colder countries warmer temperatures may lead to increased outdoor recreational activity, which may make it more likely that people will be exposed to environmental sources of the relevant gastrointestinal pathogens (Lake et al., 2009).

Several epidemiological studies have demonstrated positive associations between temperature and *Campylobacter* spp. infection in England and Wales (Lake et al., 2009) Brisbane, Australia (Bi et al., 2008) and in Alberta and Newfoundland-Labrador in Canada (Fleury et al., 2006), accounting for seasonality using different modeling approaches.

It is not certain whether the results from those studies can be applied to other ecological/meteorological regions, given various population characteristics, eating behaviors, food processing chains, socio-economic status and climate types.

We aim to evaluate the age-related relationship between ambient-temperature and weekly notified *Campylobacter* spp. cases using time-series analysis in Israel, a country with Mediterranean climatic conditions and a high incidence of infection. The majority of the Israeli population reside in regions that have a Mediterranean climate.

2. Materials and methods

2.1. Surveillance data

Campylobacteriosis is a reportable disease in Israel. Microbiology laboratories throughout the country passively submit all isolates of *Campylobacter* spp. to the *Campylobacter* Reference Center, Israeli Ministry of Health, Jerusalem, for confirmation, final identification and further classification. The registry completeness of *Campylobacter* spp. cases is about 90%. Demographic data on 29,762 laboratory-confirmed cases of *Campylobacter* infection among the Jewish population during the period, lst January, 1999 to 31st December 2010 were obtained from the *Campylobacter* Reference Center. During the study period, there were no changes in the reporting practices and no interventions to control the disease. The date of each *Campylobacter* case was the date on which the specimen was submitted for culture in the reporting Microbiology laboratory. The delay between the disease onset and the submission of stool culture for testing is estimated at a median of 5–7 days based on a recent study from Israel (Ziv et al., 2011). Therefore, the reporting date was a reasonable indicator of disease's onset date, with an approximate 1-week delay. In order to achieve maximal homogeneity of the study population, only the Jewish population was included; during the study years, this accounted for 78.8% (1999) to 75.1% (2010) of the total population in Israel. Weekly cases of *Campylobacter* infection for the serotypes *C. jejuni* and *C. coli* and for 4 age groups were calculated for the whole study period (626 weeks).

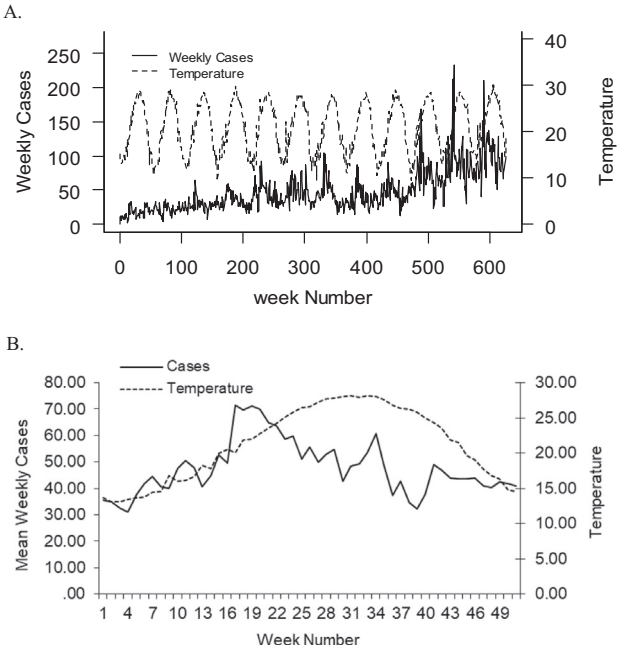

Fig. 1. Patterns of weekly total number of *Campylobacter* infection cases (_____) and weekly mean temperature in °C (————) during the period, 1st January, 1999 to 31 st December, 2010; A) The study weeks in a sequential order (n = 1–626), (B) The study weeks in a year (n = 1–52). Note: the Israeli week is Sunday-Saturday hence the first two observations were omitted.

2.2. Meteorological data

The national temperature and relative humidity series were constructed using daily data from the weather climate station in Ben Gurion Airport (in the center of the country) obtained from the Israeli meteorological office archive. The mean temperature and relative humidity for each week were calculated and the weekly changes in this station represent quite well the changes across the country.

2.3. Statistical methods

We modeled the effect of temperature on the weekly number of cases (dependent variable) in two steps, assuming Poisson distribution with over-dispersion. Models were controlled for the following variables: holidays (number of days per week 1–7; typically, the number of cases are low during holidays and high immediately afterward; week number (1–626, to control for long-term effect); seasonality (Fourier terms, up to the second harmonic, were included). First, to explore the shape of the relationship, we fitted and graphed a Poisson Generalized Additive Model **(**GAM) model with a penalized natural cubic spline of weekly temperature. The degree of smoothness of model terms was estimated as part of the fitting. Smooth terms were represented using penalized regression splines with smoothing parameters selected by Generalized Cross Validation (GCV) or Akaike Information Criterion (AIC) (Kovats et al., 2004). Secondly, in order to quantify the relationship, we fitted a two-segment piecewise linear regression model (Kovats et al., 2004) under which it was assumed that there are different linear effects of temperature until a threshold value is reached, and afterward. The temperature threshold was estimated by maximum likelihood from among thresholds across all integer values of the temperature measure (Muggeo, 2003). Likelihood-profile confidence intervals were calculated from these arrays of likelihood, scaled to allow for over-dispersion. If the threshold temperature was found to be a value lower than the P25 (the 25th percentile) or greater than the P75