Risk Factors for Sporadic Campylobacter Infections: Results of a Case-Control Study in Southeastern Norway

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Received 15 April 1992/Accepted 8 September 1992

In 1989 and 1990, a case-control study designed to identify risk factors for sporadic infections with thermotolerant Campylobacter bacteria was conducted in three counties in southeastern Norway. The investigation was confined to infections which were acquired in Norway. A total of 52 bacteriologically confirmed cases and 103 controls matched by age, sex, and geographic region were interviewed. The following risk factors were found to be independently associated with illness in conditional logistic regression analysis: consumption of sausages at a barbecue (odds ratio [OR] = 7.64; P = 0.005), daily contact with a dog (OR = 4.26; P = 0.024), and eating of poultry which was brought into the house raw (frozen or refrigerated) (OR = 3.20; P = 0.024). The risk associated with consumption of sausages at a barbecue could not be attributed to cross-contamination from poultry products. By univariate analysis, consumption of poultry which was bought raw and frozen was associated with illness (OR = 2.42; P = 0.042), even though freezing substantially reduces the number of viable thermotolerant Campylobacter. When poultry consumption was examined by country of origin, eating of poultry produced in Denmark or Sweden was strongly associated with illness (OR = 13.66; P = 0.014), whereas consumption of poultry produced in Norway was not (OR = 1.33; P = 0.41).

Thermotolerant Campylobacter bacteria (Campylobacter jejuni and Campylobacter coli) have been the focus of growing attention during the past decade because of the increasing frequency with which they have been isolated from human patients, animals, foods, and water (1, 3, 6, 29). The bacteria concerned are now recognized as one of the most important agents of enteritis in the world. In Norway, Campylobacter infections are the cause of considerable morbidity. Following the introduction of laboratory-based national Campylobacter surveillance in 1979, increasing numbers of cases were reported throughout the 1980s (12). In 1988, the reported incidence rate reached 13.13/100,000 persons per year. At least 38% of the cases reported during the first 10 years of surveillance were acquired abroad.

In recent years, interest has been focused on the identification of risk factors and effective control measures. Although much work has been done to identify the environmental and animal reservoirs of Campylobacter in Norway (2, 7, 14, 15, 20–23), the most important risk factors remain to be determined. A variety of vehicles for Campylobacter spp. has been suggested on the basis of case-control studies conducted in Europe and North America (5, 9–11, 16, 18, 19, 24, 26, 27). However, multivariate analysis of risk factors has only rarely been carried out (5, 26).

In 1989, a case-control study designed to identify the risk factors for sporadic Campylobacter infections was launched in the Oslo region, the most urbanized and densely populated area in Norway. The investigation was confined to infections which were acquired in Norway. In this report, we present an analysis of the risk factors associated with Campylobacter infection. The clinical features of illness among study patients will be reported separately (13).

MATERIALS AND METHODS

Identification of cases. The study was conducted during May 1989 through November 1990 in the counties of Oslo, Akershus, and southern Buskerud in southeastern Norway, an area with a combined 1990 census of 1,098,000 (26% of Norway's population). When a bacteriologically verified case of Campylobacter infection was identified at one of the medical microbiological laboratories in the study area, the laboratory contacted the patient’s physician and requested an interview with the patient. If the physician and patient consented, investigators at the National Institute of Public Health contacted the patient by telephone and conducted a brief preliminary interview concerning travel activity and clinical manifestations of the infection. Patients who had traveled abroad during the 2 weeks before the onset of illness were excluded from the study. If stool cultures from more than one member of a household yielded a Campylobacter strain or the case was outbreak related, only the first identified case was enrolled. Campylobacter isolates were forwarded to the Reference Laboratory at the National Institute of Public Health for verification and biotyping by established criteria as outlined previously (22).

Identification of controls. Once enrolled, a case patient’s name was located on the Norsk Folkeregister, a government registry of all Norwegian residents (arranged chronologically by date of birth), which is updated on a quarterly basis. The names and addresses of five sex-matched persons, closest in age to the case and living in the same or an adjacent postal code, were recorded as potential controls. The cases and their controls were rarely more than 2 weeks apart in age. These persons were mailed information about the investigation and were then sequentially contacted by telephone until two agreed to be interviewed. Criteria for exclusion of potential controls were (i) a past history of Campylobacter infection, (ii) diarrhea or abdominal pain with fever in the preceding month, or (iii) travel abroad in the last 2 weeks.

Interviews. All cases and controls were interviewed in
person, using a structured questionnaire, by technicians from the National Institute of Public Health or the Norwegian College of Veterinary Medicine who were trained as interviewers. A parent or guardian was interviewed if the patient was under 15 years of age. Each interview covered demographic and clinical information and specific exposures including food consumption, contact with animals, kitchen hygiene, and medications. Patients were questioned about exposures in the 2 weeks before the onset of their Campylobacter illness. In order to reduce recall bias, controls were asked about the 2-week period before the interview. If patients could not specify an illness onset date, they were questioned about the 2-week period before the stool sample which yielded Campylobacter was submitted.

Statistical analyses. Univariate analyses of dichotomous variables were performed by using the procedure for matched data sets (25) in the computer program Epi Info (Centers for Disease Control, Atlanta, Ga.). Conditional logistic regression was implemented for univariate analysis of continuous variables and for multivariate analyses (25) by using the computer program Egret (Statistics and Epidemiology Research Corporation, Seattle, Wash.). All reported P values are two-tailed.

RESULTS

Description of cases and controls. During May 1989 through November 1990, a total of 59 patients satisfying the criteria of a case were identified. One patient declined to be interviewed. Of 121 potential controls contacted, 3 refused to be interviewed and 1 was excluded because of a recent diarrheal illness. The remaining 117 individuals satisfied the criteria of a control. During the interview, six case patients and two controls reported a recent history of recurrent diarrhea. Since we could not determine whether this condition was a risk factor or merely reflected a prolonged Campylobacter infection, these persons were excluded from the analyses. Consequently, 52 cases and 103 matched controls were included in the final data set; 1 case was matched with 3 controls and two cases were matched with 1 control each, while the remaining 49 cases were each matched with 2 control subjects. During the study period, 156 patients with bacteriologically confirmed cases of Campylobacter infection but with no reported history of traveling abroad before the onset of illness were recorded from the study area by the national surveillance system. Thus, 37.2% of eligible cases were enrolled. Study enrollees were similar to cases recorded by surveillance with respect to age and sex distribution and county of residence. The mean age of the 52 case patients was 24.8 years (median, 29 years; range, 1 to 66 years). Twenty-six (50.0%) case patients were female. Viable bacterial isolates from 38 (73.1%) of the 52 case patients were available. Of these, 32 were C. jejuni biotype 1 and 6 were C. jejuni biotype 2.

Univariate analysis of risk factors. Results of the univariate analysis of risk factors are given in Table 1 and are described below.

(i) Poultry consumption. Case patients were significantly more likely than their controls to have eaten poultry of any kind (odds ratio [OR] = 2.69; P = 0.013). Eating of poultry which was precooked at the stage of retail sale or bought at a restaurant was not a statistically significant risk factor. In contrast, consumption of poultry which was brought into the house in a raw form was strongly associated with illness (OR = 2.99; P = 0.008). Among raw poultry items, frozen poultry was a significant risk factor (OR = 2.42; P = 0.042). Only seven cases and five controls had consumed poultry which was bought raw and refrigerated. This exposure was associated with an increased risk, but it did not reach statistical significance (OR = 2.90; P = 0.070). Among poultry products, significant differences between cases and controls were detected only for consumption of broiler chickens (OR = 1.96; P = 0.046). Fewer than five cases and controls had eaten hens, turkeys, marinated poultry, or minced poultry products. When poultry consumption was examined according to the country of origin, eating of poultry produced in Sweden or Denmark showed the highest OR of all variables investigated (OR = 13.66; P = 0.014), whereas eating of poultry produced in Norway was not statistically significantly associated with illness. More cases than controls had prepared raw poultry in the kitchen (OR = 9.55; P = 0.004).

However, since almost everyone who had prepared raw poultry also ate it, we were unable to determine whether this factor was independently associated with illness. The number of cases and controls who consumed raw or undercooked poultry was small, and the effect did not reach statistical significance. However, there was a trend for persons to this exposure to have an increased risk for campylobacteriosis (OR = 6.00; P = 0.12).

(ii) Contact with animals. Contact with an animal was defined as handling or touching the animal or its excreta. Daily contact with a dog was strongly associated with illness (OR = 5.04; P = 0.002), whereas daily contact with a cat was only marginally so (OR = 2.41; P = 0.064). Any contact with a dog was also associated with illness (OR = 2.92; 95% confidence interval [CI] = 1.25 to 6.82; P = 0.014). Among children aged 0 to 5 years, daily contact with a dog showed an OR of 2.67 (CI = 0.58 to 13.32; P = 0.38) compared with an OR of 9.50 (CI = 1.98 to 45.6; P = 0.02) in the remaining age groups, indicating that young children were not at an increased risk. Among people with reported contacts with dogs or cats, there was no significant difference between cases and controls in the ownership of pets with diarrhea; only 1 of 31 cases and 3 of 43 controls reported such exposure. Feeding the pet raw meat scraps was not associated with illness. More cases than controls had been in contact with wild-living birds or with cows. However, no statistically significant differences were detected. Illness was not associated with contact with poultry, caged birds, pigs, sheep, or horses.

(iii) Eating at barbecues. More cases than controls had eaten meat of any kind at a barbecue (OR = 3.94; P < 0.001). Two types of meat were significantly associated with illness: grilled pork (OR = 3.32; P = 0.007) and grilled sausages (OR = 8.57; P = 0.002). There were no significant differences between cases and controls for consumption of grilled beef, grilled mutton or lamb, or grilled poultry. However, only two cases and no controls had eaten at a barbecue where poultry was served. Illness was not associated with eating of grilled meat which was raw, rare, or "red at the bone." Variables concerning the consumption of grilled meats were coded into the following three levels: none, one, and two or more meals where grilled meats were consumed.

(iv) Other risk factors. Although not statistically significantly, drinking of undisinfected water was associated with a slightly increased risk for campylobacteriosis (OR = 1.75; P = 0.12). Nine of the 26 ill persons who had drunk raw water before illness had done so directly from a lake, pond, stream, or brook. This exposure was associated with an increased risk, but it did not reach statistical significance (OR = 2.13; CI = 0.78 to 5.84; P = 0.14). Likewise, a tendency toward increased risk of illness was detected for consumption of
### TABLE 1. Univariate analysis of selected risk factors for campylobacteriosis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No. (%)</th>
<th>OR</th>
<th>CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (n = 52)</td>
<td>Controls (n = 103)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poultry consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bought raw, refrigerated</td>
<td>7/51 (13.7)</td>
<td>5/101 (5.0)</td>
<td>2.90</td>
<td>0.92-9.15</td>
</tr>
<tr>
<td>Bought raw, frozen</td>
<td>17/51 (33.3)</td>
<td>18/101 (17.8)</td>
<td>2.42</td>
<td>1.03-5.67</td>
</tr>
<tr>
<td>Bought raw, refrigerated and frozen</td>
<td>22/51 (43.1)</td>
<td>22/101 (21.8)</td>
<td>2.99</td>
<td>1.33-6.75</td>
</tr>
<tr>
<td>Any poultry, refrigerated, frozen, and precooked</td>
<td>35/51 (68.6)</td>
<td>47/101 (46.5)</td>
<td>2.69</td>
<td>1.23-5.87</td>
</tr>
<tr>
<td>Broiler chickens</td>
<td>28/52 (53.8)</td>
<td>37/103 (35.9)</td>
<td>1.96</td>
<td>1.01-3.79</td>
</tr>
<tr>
<td>Produced in Norway</td>
<td>25/52 (48.1)</td>
<td>43/103 (41.7)</td>
<td>1.33</td>
<td>0.67-2.63</td>
</tr>
<tr>
<td>Produced in Denmark or Sweden</td>
<td>10/51 (19.6)</td>
<td>5/101 (5.0)</td>
<td>13.66</td>
<td>1.70-110.1</td>
</tr>
<tr>
<td>Prepared raw poultry</td>
<td>10/50 (20.0)</td>
<td>2/99 (2.0)</td>
<td>9.55</td>
<td>2.09-43.69</td>
</tr>
<tr>
<td>Undercooked poultry</td>
<td>3/48 (6.3)</td>
<td>1/95 (1.1)</td>
<td>6.00</td>
<td>0.62-57.7</td>
</tr>
<tr>
<td>Contact with animals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dog, daily contact</td>
<td>34/50 (68.0)</td>
<td>11/101 (10.9)</td>
<td>5.04</td>
<td>1.81-14.02</td>
</tr>
<tr>
<td>Cat, daily contact</td>
<td>10/49 (20.4)</td>
<td>8/96 (8.3)</td>
<td>2.41</td>
<td>0.95-6.13</td>
</tr>
<tr>
<td>Cow</td>
<td>3/52 (5.8)</td>
<td>1/103 (1.0)</td>
<td>NC</td>
<td>NC</td>
</tr>
<tr>
<td>Wild-living bird</td>
<td>4/51 (7.8)</td>
<td>3/101 (3.0)</td>
<td>3.35</td>
<td>0.59-18.88</td>
</tr>
<tr>
<td>Eating at barbecues</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grilled pork</td>
<td>3.32</td>
<td>1.38-7.95</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Grilled sausage</td>
<td>8.57</td>
<td>2.26-32.51</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>Any grilled meat</td>
<td>3.94</td>
<td>1.86-8.36</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Other factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undisinfected water</td>
<td>26/51 (51.0)</td>
<td>38/101 (37.6)</td>
<td>1.75</td>
<td>0.87-3.50</td>
</tr>
<tr>
<td>Salted cold cuts</td>
<td>44/51 (86.3)</td>
<td>76/101 (75.2)</td>
<td>2.10</td>
<td>0.81-5.41</td>
</tr>
<tr>
<td>Homemade minced meat</td>
<td>4/51 (7.8)</td>
<td>2/99 (2.0)</td>
<td>6.61</td>
<td>0.72-60.86</td>
</tr>
<tr>
<td>Beef tartar</td>
<td>3/52 (5.8)</td>
<td>0/103 (0.0)</td>
<td>NC</td>
<td>NC</td>
</tr>
<tr>
<td>Unpasteurized milk</td>
<td>2/52 (3.8)</td>
<td>0/103 (0.0)</td>
<td>NC</td>
<td>NC</td>
</tr>
</tbody>
</table>

* Values are number of cases/total number of subjects. Denominators exclude persons with missing values on the risk factors.
* NC, not calculable.
* Variables were categorized into the following three levels: none, one, and two or more meals with grilled meats.

salted cold cuts (OR = 2.10; P = 0.13). More cases than controls had consumed unpasteurized milk, beef tartar, or foods made from homemade minced meat. However, the number of individuals exposed to these factors was small.

No significant differences between cases and controls were detected when the following exposures were analyzed: consumption of beef, pork, mutton or lamb, elk, reindeer, fish, shellfish, forced or minced meat including sausages and hamburgers, cooked cold cuts, egg or egg products, prepared salads, potato salad, raw vegetables, milk or milk products including ice cream, cream-filled cakes, and soft cheese. Except for raw minced meat and undercooked poultry, no more cases than controls ate raw, rare, or undercooked meat or fish products. Cases and controls did not differ significantly with regard to kitchen hygiene parameters like cleaning of hands, chopping boards, knives, or the countertop with soap and water during meat preparation and the use of separate cutting surfaces for raw meats. Illness was not associated with the preparation of raw red meat; eating of poultry or red meat heated in a microwave oven; eating at a restaurant, hotel, street kitchen, or hot dog stand; attending or working in a kindergarten or a day-care center; visiting a farm or zoo; eating soil, sand, or snow; or taking an overnight trip within Norway. Cases were no more likely than controls to report a recent history of anemia, liver disease, or nongastrointestinal medical conditions. They were also similar with respect to the recent use of antimicrobial agents, antacids, or iron supplements and to the use of regular medications.

**Multivariate analysis of risk factors.** Conditional linear logistic regression analysis was performed to determine which variables were independently associated with illness. Risk factors were included in multivariate analysis if they (i) reached the 0.1 level of significance or less, (ii) were potential confounders, or (iii) were of theoretical interest regardless of their level of significance. Some variables which were statistically significant in the univariate analysis were not placed in the model since the number of persons exposed was too small to be modeled. No significant interactions among the variables included in the analysis were detected. The following variables were all found to be independent risk factors when placed simultaneously in the model: consumption of sausages at a barbecue (OR = 7.64; CI = 1.83 to 31.89; P = 0.005), daily contact with a dog (OR = 4.26; CI = 1.21 to 15.01; P = 0.024), and eating of poultry which was brought into the house in raw form (frozen or refrigerated) (OR = 3.20; CI = 1.17 to 8.76; P = 0.024).

**DISCUSSION**

Although several case-control studies of *Campylobacter* infection have been carried out (5, 9-11, 16, 18, 19, 24, 26, 27), only a few studies have tested the relative importance of multiple risk factors identified in the univariate analysis. In
the present investigation, poultry consumption was found to be independently associated with campylobacteriosis. No previously published investigation has addressed the question of whether the risk associated with poultry products varies according to the country of origin. Although foreign poultry is not sold at retail outlets in Norway, some people buy poultry products on weekend trips to Denmark or Sweden. In our study, the risk from eating of poultry was largely accounted for by consumption of poultry produced in Denmark or Sweden, while eating of poultry produced in Norway was not significantly associated with illness. This finding is supported by a recent study which found a comparatively low prevalence of campylobacters in Norwegian broiler chicken flocks (15). Transport at high ambient temperature cannot account for the risk of infection associated with poultry purchased in Denmark or Sweden, because, unlike salmonellae, campylobacters tend to die out rather than multiply at room temperature (6, 29).

In contrast to many other countries, the majority of the poultry products sold at retail outlets in Norway are frozen. It was somewhat surprising to find a significant association between illness and consumption of poultry which was bought frozen in raw form, since frozen storage has been shown to reduce substantially the number of viable campylobacters (1, 28, 29). We are not aware of any published epidemiological investigation which has identified frozen poultry as a risk factor for campylobacteriosis. On the other hand, laboratory studies have suggested that low numbers of campylobacters may survive for several weeks during frozen storage (8, 30). Our results support the suggestion that the presence of even a small number of campylobacters in food may be epidemiologically significant because of the low infective dose of these organisms (1, 29).

We found an association of illness with the preparation of raw poultry in the kitchen, which is in accordance with previous reports (11, 18). However, we were unable to determine whether this factor was independently associated with illness. Although we could not demonstrate any significant difference between cases and controls with regard to kitchen hygiene parameters, it is likely that the risk of eating poultry was, at least partly, due to errors in food handling that led to contamination of cooked poultry or to cross-contamination of other foods. In a case-control study conducted in Seattle, Wash. (27), persons with Campylobacter infections were less thorough than were controls in their cleaning of cutting surfaces and used separate cutting surfaces less often for prepared foods and raw meats.

Our results indicate that living in a household with a dog may significantly increase the risk of Campylobacter infection. Contact with cats or dogs has been identified as a risk factor in a previous case control-study and in several case reports (1, 5, 10, 24). Although daily contact with a cat was not independently associated with illness, the OR in the multivariate analysis was 3.14 (CI = 0.95 to 10.39; \( P = 0.061 \)), suggesting that cats should be considered a potential risk factor. The biological plausibility of cats and dogs as vehicles of transmission has been well established. In a survey conducted in the Oslo region, campylobacters were frequently isolated from asymptomatic and diarrheic dogs and cats (7). Dogs suffering from diarrhea have been cited as a likely cause of Campylobacter infection (1). In accordance with Schmid et al. (26), we did not find any difference between cases and controls in the ownership of dogs or cats with diarrhea. It has been suggested that young children may be more susceptible than people in other age groups to fecal-oral spread from pets (24). Our results, however, did not support this suggestion.

Whereas C. jejuni is the predominant species found in poultry, C. coli is common in pigs (1, 29). Although C. coli has been frequently encountered in Norwegian slaughter pigs (22) and as a surface contaminant of freshly eviscerated carcasses and livers (20), we could not recover a single isolate from retail pork products (17). Accordingly, pork consumption was not identified as a risk factor in the present study. Likewise, there was no significant association with overall consumption of sausages, a group of products containing minced pork, beef, milk, potato flour, water, salt, and seasoning. Interestingly, eating of sausages at a barbecue was strongly associated with illness. In The Netherlands, eating of chicken at a barbecue was determined to be a risk factor (19). However, cross-contamination from poultry could not explain our results, since few people ate poultry at barbecues. Further investigations are needed to examine the presence of campylobacters in sausages and to ascertain whether our observations can be explained by suboptimal hygienic practices, insufficient heat treatment, or non-pork additives in sausages. Indeed, campylobacters have frequently been recovered from minced pork in Sweden (30). Although virtually all sausages are heated to at least 70°C before retail sale, it is conceivable that the high fat content of these products may increase the thermal resistance of campylobacters, analogous to the situation with Salmonella spp. in chocolate (4).

Untreated water has been incriminated as the source of infection in sporadic cases as well as in large outbreaks of Campylobacter infections (1, 10, 26). In our study, consumption of undisinfected water was associated with a slightly increased risk, but it did not reach statistical significance; the OR in the multivariate analysis was 2.42 (CI = 0.94 to 6.23; \( P = 0.068 \)). However, since cases and controls were matched by geographic region, we may have underestimated the importance of water as a risk factor. It is likely that people living in the same area will tend to have the same or similar drinking water supply. Recent studies have shown that surface water sources in southeastern Norway are frequently contaminated with campylobacters (2).

At our present state of knowledge, the following measures are likely to have the greatest impact on the incidence of domestically acquired campylobacteriosis: (i) reinforcement of hygienic practices during contact with dogs, handling and preparation of poultry in the kitchen, and barbecuing; (ii) restricted import of poultry products from foreign countries; and (iii) measures that maintain a low level of contamination with campylobacters in Norwegian poultry flocks.

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