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Risk factors for campylobacter infection in infants and young children: a matched case-control study

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SUMMARY

Campylobacter infection has one of the highest rates of all the notifiable diseases in Australia, with a peak in children aged 0–35 months. A matched case-control study was conducted to investigate risk factors for campylobacter infection for children in this age group. Eighty-one cases and 144 controls were enrolled in the study that was conducted between 24 January 1996 and 21 January 1997. The following risk factors were found to be independently associated with illness: ownership of pet puppies (adjusted odds ratio [OR] 16·58, 95% confidence interval [CI] 3·73–73·65) and pet chickens (OR 11·80, CI 1·37–101·75), and consumption of mayonnaise (OR 4·13, CI 1·61–10·59). We propose that children aged less than 3 years are at risk of campylobacter infection if residing in a household which has puppies or chickens as pets.

INTRODUCTION

In Australia, there are over 10000 notifications of campylobacter infection each year, and campylobacteriosis consistently has one of the highest annual rates of all notifiable diseases (1998 notification rate = 108·3 cases per 100000 population) [1]. This high notification rate for campylobacter infection also occurs in other western countries, along with a seasonal trend of higher notifications in summer, a slightly higher notification rate for males compared to females, and a bimodal age distribution with a major peak in the 0–4 year age group [2].

The majority of cases of campylobacter infection are sporadic, with outbreaks less common. Most of the outbreaks have been linked to the consumption of raw milk or contaminated water [2]. A number of case-control studies have investigated sporadic cases, and have identified the following general risk factors: handling raw poultry [3]; consumption of chicken [3–6], and in particular undercooked chicken [6–9]; consumption of raw milk [7], or milk from bottles with bird-pecked tops [5]; consumption of untreated water [7, 8, 10]; contact with dogs or puppies [4, 5, 7] and cats or kittens [6, 8], and in particular pets with diarrhoea [10, 11]; and travel abroad [5, 7].

When we reviewed local campylobacter notification data in a previous study, we found significantly higher rates of notification for the 0–2 year age group, and in particular for those children aged 12–23 months. In addition, for the factors geographic distribution and socioeconomic status, trends observed in other age groups were not observed for the 0–4 years age group [12]. This suggests that factors which influence notification rates in the general community may not have the same influence for infants and young children.

Risk factors associated with campylobacter infection in infants and young children have been investigated in a limited number of studies. We have located only two published analytic studies and both were conducted in developing countries. These studies found that exposure to live chickens within the household or the keeping of fowl [13, 14] and contaminated drinking water [13] were factors associated with illness. However, controls in both studies were selected from hospital patients with campylobacter-negative diarrhoeal stools, rather than

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healthy community controls, and in one study [13] more than half the cases were co-infected with other known faecal pathogens.

This paper describes a matched case-control study conducted in Queensland, Australia, to investigate risk factors for sporadic campylobacter infection in infants and young children (aged 0–2 years).

METHODS

Study design

A matched case-control study was conducted in the predominantly urban Brisbane Southside and South Coast areas of Queensland (1996 estimated resident population, 1·1 million) and data were collected over a 12 month period between 24 January 1996 and 21 January 1997. Sporadic cases of camplyobacter infection in infants and young children were identified through the routine notification of diseases by pathology laboratories, with a network of general practitioners and hospitals providing earlier referral of possible cases. Control subjects were healthy volunteers obtained through community-based Child Health Clinics in the study area. Personal interviews were conducted by a single project officer, and due to the age of the study subjects, these were with a parent or guardian. A standard questionnaire was used to obtain information on the child's exposures in the 7 days prior to illness or interview (for controls).

Cases

A case was defined as a child aged 0–35 months with a positive stool result (for *Campylobacter jejuni* or *C. coli*) and the following symptoms: diarrhoea (two or more loose stools in 24 h), plus one or more of abdominal pain, fever, malaise or vomiting. The cases had to reside in the study area and the stool sample indicate no other enteric pathogens. Cases were excluded if: the case was part of an outbreak (two or more associated cases), another member of the household or a close contact had been diagnosed with campylobacter infection in the 2 months prior to the cases' illness, if the case was a known carrier, or if matching controls could not be located. Cases were also excluded if not interviewed within 1 month of onset of illness.

Controls

An attempt was made to match two controls with each case. Subjects were matched by age (± three months), sex and general geographical location (postcode) of the case's residence. If more than two controls met the matching criteria, the two controls with dates of birth closest to the case were selected. Controls were excluded if: they had suffered diarrhoea in the 14 days prior to interview, reported a past history of campylobacter infection, or were otherwise immuno-compromised. If repeated attempts failed to contact one of the selected controls, or if after initial screening the control did not meet the inclusion criteria, the next most eligible control was selected for interview. Interviews were conducted as soon as possible after the corresponding case interview, with all controls interviewed within 1 month of the corresponding case interview.

Questionnaire

The questionnaire was developed through involvement of focus groups of mothers with young children, and piloted prior to use in the study. Information was obtained on the following potential risk factors: contact with other persons including children; interstate or overseas travel; water exposures; animal exposures, including type of animals, and description of contact/interaction; food preparation, including food hygiene and food handling practices; food consumption, including types of foods and formulas; and parental awareness of health promotion and education initiatives.

Sample size

A matched design and a case-control ratio of 1:2 was selected as the most appropriate strategy in order to maximise the study power. To detect an association with a matched odds ratio of 2·0 at the 5% significance level with 80% power (assuming 20% exposure level among controls), a sample size of 126 cases and 252 controls was required [15].

Analysis

Case-control sets were included for analysis provided that at least one control was matched for each case. Epi Info Version 6·02 [16] was used to calculate crude matched odds ratios (OR) with 95% confidence intervals (CI) and two-tailed *P*-values to estimate the association between various potential risk factors and campylobacter illness. Following the univariate analysis, Epi Info 2000 [17] was used to calculate adjusted odds ratios by backward stepwise logistic regression of risk factors with a P-value $\leqslant 0{\cdot}25$.

RESULTS

During the study period, 110 cases were referred to this Unit and 571 children registered as possible controls. Of the 110 cases, 104 agreed to participate in the study and were interviewed. After applying the exclusion criteria, 81 cases were included in the analysis. Eighty percent of the cases were interviewed within 7 days of the investigators receiving notification, and 96·3% were interviewed within 14 days. Following completion of the study, a review of the state-wide notifiable diseases system revealed that 63% of all eligible notified cases were included in the study. From the total number of controls registered, 144 were included in the study, with 18 cases matched to 1 control, and 63 cases matched to 2 controls.

The demographic characteristics of the cases and controls are shown in Table 1. Slightly more males than females were enrolled in the study, with the majority of subject's aged 12 months or older. The main symptoms reported by the cases were diarrhoea (98·8%), bloody diarrhoea (40·7%), and vomiting (39·5%).

Table 1. *Demographic characteristics of subjects*

	Cases (%)	Controls (%)
Sex		
Male	44 (54)	78 (54)
Female	37 (46)	66 (46)
Age		
0–11 months	15 (19)	31 (22)
12–23 months	36 (44)	55 (38)
24–35 months	30 (37)	58 (40)
Total	81	144

Univariate analysis of risk factors

One hundred and sixty variables were included in the initial analysis. Potential risk factors for campylobacter illness (i.e. those with a matched odds ratio > l) are shown in Table 2. In regard to animal exposure, ownership of a pet (OR 2·04, CI 1·8–4·13), ownership of pet chickens (i.e. chickens either free-ranging or in a coup and kept for non-commercial egg production) (OR 11·00, CI 1·21–473·06), and ownership of a pet puppy (OR 16·75, CI 3·76–141·66) were significantly associated with illness. The keeping of guinea-pigs was not associated with illness, as was exposure to two or more pet cats. Exposure to animals that had diarrhoea and access of the child to areas in which the pets roamed were also not associated with illness.

Consumption of mayonnaise was the only food item significantly associated with illness (OR 3·87, CI 1·48–11·21). Other foods with a moderately increased risk of illness were softcheese, raw eggs, mutton and bottle fed milk, but these were not statistically significant. In regard to food handling practices, inappropriate hand washing and food thawing, and inadequate cleaning of utensils were non-significantly associated with illness. Insufficient data were obtained on bottle feeding practices and preparation practices for baby food (from cans or jars), and as such, no conclusions could be made about these exposures.

Of the other exposures recorded, travel had an elevated (but non-significant) OR and eating of soil by the child was not associated with illness. However, child contact with other children in nappies (OR 0·44, CI 0·20–0·89) and attending a childcare centre (OR 0·37, CI 0·17–0·83) were significantly associated with a decrease in risk of illness. Insufficient data were obtained on child exposure to persons with an illness, particularly a gastric illness, and as such, no conclusions could be made about these exposures.

Multivariate analysis of risk factors

Of the nine risk factors included in the initial logistic regression model, a significant independent association with illness was found for the following three risk factors: ownership of pet chickens (adjusted OR 11·80), ownership of a puppy (adjusted OR 16·58), and consumption of mayonnaise (adjusted OR 4·13) (refer to Table 3).

DISCUSSION

This study identified three independent risk factors (exposure to puppies, pet chickens and mayonnaise) for campylobacter infection in children aged less than 3 years. Contact with puppies has been previously reported as being associated with campylobacter illness, however, this appears to be the first report of an association with pet chickens in a developed country. Some of the general risk factors identified in previous case-control studies (e.g. consumption of untreated water, raw milk and undercooked chicken, handling raw poultry, and travel) were not found in this study to be associated with campylobacter illness in infants and young children. This may be explained

Table 2. *Univariate analysis of selected risk factors for campylobacter illness* (*matched OR > 1*)

Risk factors	No. Cases ($n = 81$)	Controls ($n = 144$)	Matched odds ratio	95% CI	*P*-value
Pet exposure					
Ownership of a pet	59/81	83/144	2·04	1·08–4·13	0·03
Ownership of more than one pet	35/59	37/83	1·67	0·72–4·23	0·26
Ownership of more than two pets	18/59	17/83	1·44	0·61–3·49	0·46
Bird	11/81	12/144	1·63	0·62–4·61	0·35
Cat	19/81	32/144	1·09	0·54–2·18	0·91
Chickens	6/81	1/144	11·00	1·21–473·06	0·03
Dog	38/81	57/144	1·39	0·75–2·59	0·39
Kitten (cat aged less than 6 months)	3/81	3/144	1·67	0·21–12·17	0·89
Puppy (dog aged less than 6 months)	18/81	3/144	16·75	3·76–141·66	< 0·001
More than two pet dogs	10/81	7/144	2·57	0·85–9·00	0·10
Never hand washing after pet contact (never *vs*. always)	16/36	18/64	1·91	0·47–8·78	0·48
Food handling					
Never hand washing before eating (never *vs*. always)	10/40	10/68	2·63	0·57–16·26	0·28
Food thawing procedure (room temperature *vs*. refrigeration or microwave)	31/76	50/141	1·25	0·63–2·47	0·59
Never wash utensils between use with raw and cooked foods (never *vs*. always)	2/70	3/133	2·00	0·14–27·59	0·86
Food consumption					
Softcheese	8/77	6/143	2·31	0·70–8·19	0·19
Ice-cream	43/77	73/142	1·11	0·59–2·07	0·84
Mayonnaise	17/76	11/142	3·87	1·48–11·21	0·003
Custard	33/77	54/143	1·17	0·63–2·17	0·69
Raw eggs	3/77	1/143	5·50	0·40–275·6	0·30
Microwaved eggs	9/77	10/143	1·61	0·52–5·06	0·48
Ham	36/76	57/143	1·40	0·73–2·70	0·35
Chicken (at home)	39/63	77/120	1·02	0·47–2·27	0·90
Pate	3/77	4/143	1·22	0·18–7·40	0·89
Pork	15/75	22/143	1·46	0·59–3·46	0·49
Bacon	28/77	43/143	1·32	0·68–2·55	0·46
Mutton	25/76	29/143	1·87	0·98–3·81	0·06
Mince	46/76	81/143	1·16	0·60–2·29	0·75
Salads	31/77	60/143	1·03	0·53–2·00	0·72
Raw vegetables	23/77	34/143	1·41	0·69–2·88	0·39
Milk	20/72	36/139	1·07	0·37–3·09	0·94
Milk (bottle fed only)	16/49	11/84	3·29	0·71–19·81	0·16
Other exposures					
Travel – intra/interstate, overseas	5/81	2/144	3·80	0·67–44·68	0·15
Unreticulated water supply	7/81	10/144	1·29	0·41–3·77	0·80
Use of animal manure or processed fertilisers in garden	5/71	9/143	1·33	0·30–5·36	0·92
Child access to areas of fertilizer use	12/70	18/144	1·67	0·60–4·28	0·41
Use of dynamic lifter	7/71	14/144	1·00	0·33–2·80	0·81

by the age of the cases enrolled in our study and a possible lack of study power.

Healthy dogs and puppies have been shown to have campylobacter carriage rates of between 5% and 29% [18, 19] and ownership of a pet puppy has been previously identified as a risk factor [5, 7, 11]. Our study supports this association and confirms that infants and young children are at particular risk of infection. Poor hygiene in this age group and closer than normal contact with pets may partly explain this

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Table 3. *Multivariate analysis of selected risk factors for campylobacter illness*

Risk factor	Adjusted odds ratio	95% CI	*P*-value
Ownership of pet chickens	11·80	1·37–101·75	0·025
Ownership of a puppy	16·58	3·73–73·65	< 0·001
Consumption of mayonnaise	4·13	1·61–10·59	0·003

increased risk. Having a household pet (including a puppy) with diarrhoea has also been described as a risk factor for campylobacter infection [10, 11]. However, in our study only 2 of the 18 case households reported puppies with diarrhoea in the week before onset of illness in the child. Interestingly, 15 of the 18 cases (83%) regularly played in an area of the home in which the puppy also had access.

The association of pet chickens with campylobacter infection in young children has been previously reported, but this has been in developing countries and for situations in which the chickens were allowed access within the home [13, 14]. Also, daily contact with chickens in a farm setting has been recently reported as a risk factor [20]. This source of exposure is biologically plausible, as campylobacters have been shown to be excreted in the faeces of healthy chickens [18, 21] and have been isolated from the feathers of healthy chickens [22]. The route of transmission of infection to young children is probably similar to that for puppies and young children.

The significant association between consumption of mayonnaise and campylobacter illness is difficult to explain in this age group. This association is biologically plausible as one of the ingredients of mayonnaise is raw eggs and healthy chickens are known to excrete campylobacter [21]. However, there have been no reported outbreaks of campylobacter infection associated with contaminated or cracked eggs, or egg products. In addition, studies have shown that *C. jejuni* is rarely isolated from the shell surface or egg contents of chickens faecally excreting this organism [21]. It is most likely that this association occurred through random error or some type of systematic error.

The protective effect shown for children who had contact with other children in nappies and for children who attended a childcare centre was unexpected, as it has been reported that person-to-person transmission of campylobacter is uncommon in adults [23, 24]. Furthermore, immune mechanisms following campylobacter infection are not well understood, however, it has been suggested that lack of immunity in humans may be due to type-restricted protective immunity, poorly immunogenic protective antigens, or short life of the induced antibodies [25]. Random error could also account for these findings.

In this study, ownership of pet puppies and pet chickens, or consumption of mayonnaise could account for 41 (51%) of the 81 cases at most, with significant risk factors for the remaining cases not identified. This suggests there was probably insufficient study power to detect further independent risk factors for campylobacter infection in infants and young children, including the failure to find a significant association between illness and other food and animal exposures, and poor food hygiene and handling practices among respondents.

Alternative explanations for the observed results of this study include random error, selection bias, observation bias and confounding. However, given the magnitude of the associations for exposure to pet chickens or pet puppies and the low probability of these associations occurring if the null hypothesis were true, it is unlikely that these alternative explanations could totally account for the observed results. Selection bias, if any, was considered to be minimal because the methods used to select the cases and controls were not related to any specific exposures, and were completely independent of each other.

Attempts were made to minimize observation bias during the design of this study. This included limiting the recall period to 7 days prior to illness (cases) or interview (controls) and enforcement of the exclusion criteria. In an attempt to reduce interviewer bias, only one trained interviewer was used in this study. However, interviews were not conducted blindly with cases and controls, and as such interviewer bias cannot be excluded as having an influence on our findings. Finally, we suggest that it is unlikely that confounding by unknown risk factors, which were not measured in the study or controlled for during the analysis, would be totally responsible for the magnitude of the observed association with ownership of puppies or chickens.

In conclusion, the evidence presented in this study supports a likely association between campylobacter infection and ownership of pet puppies and pet chickens. Consequently, we propose that children aged less than 3 years are at risk of campylobacter infection if residing in a household which has puppies or chickens as pets.

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