Risk factors for sporadic human infection with shiga toxin-producing *Escherichia coli* in South Australia

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Abstract

This paper reports the findings from a preliminary study seeking to identify risk factors for sporadic human infection with shiga toxin-producing *Escherichia coli* (STEC) in South Australia. This phase of the study, conducted between February and September 2002, aimed to make recommendations regarding study methodology, and provided an opportunity to identify any potential risk factors for STEC infections in South Australia. The study design was a prospective age-matched case control study. A case was defined as a person with macroscopic or microscopic evidence of blood in a faecal specimen, and in which a gene associated with the production of shiga toxin (*stx* 1 or 2) was identified. Two community controls per case were randomly selected from the Social Environmental Risk Context Information System database. Eleven cases and 22 controls were enrolled in the pilot phase of the case control study. Cases were more likely than controls to have eaten berries, including strawberries, blueberries, and blackberries, in the 10 days preceding illness (Mantel Haenszel matched OR 11; 95 per cent CI 1.26-96.12). No other exposures were significantly associated with illness. Due to the small number of study participants, the power of the study was insufficient to expect any significant results. National participation will be vital to obtain sufficient cases in a realistic time, however this would necessitate more consistent ascertainment and reporting of STEC disease between the states and territories. *Commun Dis Intell* 2004;28:74–79.

Keywords: Escherichia coli, *foodborne disease, surveillance, case control study*

Introduction

Shiga toxin-producing *Escherichia coli* (STEC) have emerged over recent years as an important cause of gastroenteritis in humans worldwide. Initially acknowledged as a potential foodborne pathogen, the importance of non-food related transmission of STEC is now also being recognised.[1,2] Absolute numbers of infections are low when compared to other enteric pathogens, however the severe and potentially life threatening illness caused by STEC has prompted the need for rapid expansion of knowledge about the organism and the disease it causes.[3]

Outbreaks of STEC in Australia are quite rare, with only three outbreaks being documented prior to 2002.[4,5,6] Due to inconsistencies in ascertainment and reporting practices, STEC disease is likely to be largely under-reported in national surveillance data. Data for Australia suggests a yearly average of 47 cases for the past five years.[7] Internationally, annual incidence rates vary by region and country and appear to be influenced by numerous local factors including seasonality, dietary habits, food management practice, and animal husbandry methods.[3] Globally, incidence rates are almost impossible to interpret due to inconsistencies in surveillance and diagnostic techniques.

Internationally, risk factor information for STEC infection is mostly derived from outbreak investigations and descriptive epidemiological investigations. Studies of common-source outbreaks have identified numerous risk factors for STEC infection, including consumption of ground beef, salami, sliced meats, raw milk, yoghurt, cheese, sprouts, lettuce, and jerky.[4,–11] However, it is not clear what role these or other risk factors play in sporadic disease. A small number of international case control studies have investigated risk factors specifically for sporadic STEC infection.[12,–16] Risk factors identified

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in these studies included; consumption of beef burgers from commercial premises, consumption of sliced meats from caterers, consumption of fish, and recreational or work visits to farms.

To date, no epidemiological studies have been conducted in Australia to identify local risk factors for sporadic STEC disease. We conducted a case control study to investigate risk factors for sporadic human infection with shiga toxin-producing *Escherichia coli* in South Australia. This paper documents the pilot phase of the study that was conducted between February and September 2002. Current practices in South Australia facilitate the detection of STEC. Since 1997, all faecal specimens submitted to laboratories with microscopic or macroscopic evidence of blood have been polymerase chain reaction (PCR) tested for the presence of *stx* genes.

Methods

A prospective age-matched case control study was conducted in South Australia to investigate potential risk factors for STEC infection between February and September 2002. Cases and controls were recruited from the study population defined as the population of South Australia (approximately 1.5 million persons). A case was defined as a person with macroscopic or microscopic evidence of blood in a faecal specimen, and from which the genes associated with the production of shiga toxin (*stx* 1 or 2*)* was identified. The identification of cases in this study was facilitated by the presence of a reporting system, the South Australian Notifiable Diseases Surveillance System (NDSS).

Cases were excluded from the study if they were secondary cases within a household; identified as part of an outbreak; had travelled overseas in the month before onset of illness; or had no residential telephone number. Cases that had a mixed infection, such as cases that were positive for both *Salmonella* and STEC, were also excluded due to difficulties in establishing an accurate onset date for the STEC infection.

For each case, two controls were randomly selected from the Social Environmental Risk Context Information System (SERCIS). The main role of SERCIS is to conduct health surveys via a computer assisted telephone interview method. Through these surveys SERCIS also recruits participants for other more specific surveys or studies such as case control studies. The reliability of the SERCIS telephone health survey method has been demonstrated.[17,18]

Two controls were matched to each case by five-year age groups, except for those less than 12 months of age who were matched by 6-month age groups (for example, 0–5 months, 7–11 months, 1–4 years, 5–9 years, >65 years etc). The controls were not matched to cases on any other variables. Controls were excluded if they had a history of gastrointestinal illness in the 14-day period prior to the day of interview; reported overseas travel in the month prior to the day of interview; reported another household member with diagnosed STEC disease in the 10-day period before the day of interview; or had *stx* detected in a faecal specimen in the 10-day period before the day of interview.

Information on food and environmental exposures for the 10 days prior to the onset of illness for cases and prior to interview for controls was collected using a questionnaire administered by telephone. One hundred and twelve exposures were selected either because they were previously reported or suspected to be related to STEC infections, because they were food items or sources from which STEC had ever been detected, or they were hypotheses generated in a local case series investigation conducted in South Australia between 1994 and 1997 (Table 1). Details were also collected regarding illness, demography, occupation and household contacts. Data were analysed using Epi Info Version 6.04 software. Mantel Haenszel matched odds ratios were calculated for all dichotomous variables.

Results

In total, there were 11 cases that were enrolled between February and September 2002. The cases were identified from laboratory notifications received by the South Australian Communicable Disease Control Branch that fitted the case definition. Twenty-two age-matched controls were selected from the SERCIS database and enrolled in the study. The median age of the cases was 75 years (age range: 4–90 years) compared with 66.5 years (age range: 2–77 years) for the controls. There was an over representation of females in the control group (59% female) compared with the cases (45% female).

Prevalence of symptoms among the cases varied (Table 2). All cases reported experiencing diarrhoea, with only nine self-reporting that it was visibly bloody. Most cases experienced abdominal pain (n=9), however fewer reported nausea (n=4), vomiting (n=3), headache (n=4), and/or fever (n=4). One case reported constipation prior to diarrhoea onset but subsequent to the onset of other symptoms. One case reported rigors. Five of the 11 cases were hospitalised, and almost all cases sought medical advice from a general practitioner or medical centre (n=10). Three cases reported missing between one and six days of work, recreation time, or childcare.

Table 1. Exposures examined as risk factors for shiga toxin-producing *Escherichia coli* infection, South Australia, 2002

Food exposures	Environmental exposures	Travel exposures
Beef/beefburger/minced beef/roast beef/beef steak/beef shish kebab/shaslicks/beef sausages/silverside/corned beef	Regular attendance at any of the following institutions: Childcare centre Primary school Pre-school Play group Special needs school Hospital Aged care facility	Travel overseas
Sausages		Travel interstate
Lamb		Camping
Pork		
Offal		
Chicken/chicken meat	Occupational exposure to animals	
Turkey/turkey roll	Occupational exposure to raw meat	
Duck	Household member with occupational exposure to animals	
Fish or seafood	Household member with occupational exposure to raw meat	
Salami/mettwurst/cabanossi	Having a household pet	
Jerky	Having a sick household pet	
Devon	Exposure to pet foods: Commercial canned Commercial dry Household leftovers Raw meat Cooked meat	
Ham		
Fruit: Apples/pears/plums/peaches/nectarines/ apricots/strawberries/other berries/ watermelon/rockmelon/honeydew melon		
Fruit salad	Handling of raw red meat fed (either cooked or raw) to household pets	
Vegetables: Lettuce/cabbage/pre-packaged/bagged salad/carrots/spring onion/shallots/radishes/ celery/cucumber/alfalfa sprouts		
Eggs (raw or cooked)	Handling of dried meat strips subsequently fed to pets	
Unpasteurised dairy products	Living in a rural farm or remote property	
Consumption of the following types of water: Tap/municipal water Bore or well water Rain water from above ground tank Rain water from below ground tank Dam water River or stream water	Visiting a farm	
Unpasteurised fruit or vegetable juices	Touching animals	
Handling of any of the following while preparing a meal or snack: Raw meat Raw fish Raw fruit Raw poultry Raw vegetables	Visiting zoos, petting zoos, wildlife parks	
	Attending regional shows/fairs where there were animal displays	
	Contact with fertiliser or compost made from animal faeces	
	Swimming in: Public pool Private pool Paddling pool Spa/jacuzzi River stream Lake Sea Dam	
Involved in the slaughter, cutting up, packaging or wrapping of any raw red meat (not part of work)		
Being given a sample of meat to eat in a butcher, supermarket or food store		
Eating at: Restaurant cafe National hamburger chain National pizza chain National chicken chain Milk bar Bakery School/work canteen Home cooked meal at someone else's house		

The consumption of 'berries' in the 10 days before the onset of illness was associated with STEC infection (Mantel Haenszel matched OR 11.00, 95% CI 1.26–96.12). Six of the 11 cases reported eating strawberries, blackberries, or blueberries. The association between STEC and eating strawberries alone was not significant although the OR was elevated (Mantel Haenszel matched OR 5.00, 95% CI 0.97–25.77). Of the five who reported eating strawberries, two reported obtaining these from supermarkets, while the other three were obtained directly from the farm, of which only one was a commercial berry farm. The case that reported eating blackberries obtained them from his own farm, and the case that reported eating blueberries obtained them from a commercial berry farm.

No other food items were significantly associated with STEC infection. Despite this, there were several that had elevated ORs in the matched analysis (Table 3). No environmental exposures were associated with illness. There was no association with travel interstate, intrastate or camping. Many of the ORs obtained in the matched analysis were undefined because the Mantel Haenszel numerator or denominator was zero. This was not unexpected due to the small numbers of cases and controls available for the study.

Table 2. Case illness profile (N=11)

Symptoms	Number of cases
Diarrhoea	11
Bloody diarrhoea*	9
Nausea	4
Vomiting	3
Abdominal pain	9
Headache	4
Fever	4
Other	2
– constipation – rigors	

* Self reported by cases as blood being visible in faeces.

Discussion

The consumption of berries, including strawberries, blackberries and blueberries, in the exposure period was the only exposure significantly associated with sporadic STEC infection in South Australia. No other food or environmental exposures were significantly associated with STEC infection. Some risk factor exposures did have elevated odds ratios, but their association with illness was not significant. Additionally, due to the small study numbers and zero cell counts, many of the odds ratios were undefined, which restricted the interpretation of the results.

Table 3. Selected food exposure frequencies and matched odds ratios in shiga toxin-producing *Escherichia coli* cases and controls

Exposure	Exposed (cases)	Exposed (controls)	Matched OR	95% CI
Berries (including strawberries, blackberries and blueberries)	6/11	2/22	11.00	1.26–96.12
Strawberries	5/11	2/22	5.00	0.97–25.77
Apricots	3/11	1/22	6.00	0.62–57.68
Plums	4/11	3/22	3.50	0.60–20.45
Pork	4/11	3/22	2.67	0.60–11.92
Chicken	10/11	15/22	3.5	0.45–27.13
Turkey	2/11	1/22	4.00	0.36–44.11
Beef	7/11	19/22	0.40	0.06–2.65
Salami	3/11	1/22	6.00	0.62–57.68
Delicatessen sliced meats	7/11	15/22	0.80	0.16–3.91
Being given a sample of meat to eat in a butcher, supermarket or food store	2/11	1/22	4.00	0.36–44.11
Eating at a national hamburger chain	4/11	3/22	6.00	0.56–64.71
Involved in the slaughter, wrapping, or packaging of large quantities of raw red meat*	4/11	2/22	3.50	0.62–19.89

* If a child, immediately present at the time of slaughter, wrapping, or packaging of large quantities of raw red meat.

The association between sporadic STEC disease and the consumption of berries though unexpected is a possible vehicle of infection. Outbreaks of STEC and other enteric pathogens due to the consumption of fresh produce have been documented illustrating that it is a biologically plausible route of infection.[19,20,21] Implicated raw produce have included radish sprouts, lettuce, alfalfa sprouts, unpasteurised apple juice and apple cider.[5,10,22,23]

This is the first reported study to examine risk factors for sporadic infection with STEC conducted in Australia. Conducted as a pilot over a 6-month period, it was not anticipated that any significant results would be obtained from this study. This was due to the limited number of cases of STEC disease that are notified in South Australia, and the requirement for a large study sample to facilitate the detection of any effect. Additionally, it is likely that any association between a risk factor exposure and illness would be small. Given the resource and time limitations, the study was successful in meeting stated objectives. National participation in this study will be vital to identify more reliably the risk factors for STEC in Australia. It would reduce the time frame for the study due to an increased number of cases available for potential inclusion in the study. National participation would require more consistent ascertainment and reporting of STEC disease between the states and territories. The benefits of a national study would include an increased understanding of risk factors for STEC disease, which would enhance the national capability to facilitate the development of targeted prevention and control strategies.

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