Salmonella infections in Norway: descriptive epidemiology and a case-control study

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SUMMARY

The epidemiological progression of human salmonellosis in Norway is parallel to trends noted elsewhere in Europe. During the past two decades, the number of reported cases has increased steadily, with a special sharp rise in the early 1980s due to the emergence of Salmonella enteritidis, followed by a levelling off in recent years. However, in contrast to the situation in most other European countries, about 90% of the cases from whom a travel history is available, have acquired their infection abroad. The incidence of indigenous salmonella infections as well as the prevalence of the microorganism in the domestic food chain, are both comparatively low. In 1993-4, a national case-control study of sporadic indigenous salmonella infections was conducted to identify preventable risk factors and guide preventive efforts. Ninety-four case patients and 226 matched population controls were enrolled. The study failed to demonstrate any statistically significant association between salmonellosis and consumption of domestically produced red meat, poultry or eggs. The only factor which remained independently associated with an increased risk in conditional logistic regression analysis, was consumption of poultry purchased abroad during holiday visits to neighbouring countries. A separate analysis of Salmonella typhimurium infections incriminated food from catering establishments and foreign travel among household members, in addition to imported poultry.

INTRODUCTION

Non-typhoid Salmonella spp. continue to figure prominently in many national epidemiological registries as the leading cause of bacterial foodborne infections, although thermophilic campylobacters have surpassed salmonella in several countries [1–4]. The widespread distribution of salmonella in the natural environment and its prevalence in the global food chain raise legitimate concern about the economic and public health consequences attributable to this pathogen. Over the past couple of decades the incidence of foodborne salmonellosis has increased considerably in the industrialized world and has reached epidemic proportions in several countries [3, 5]. The increase is the result of a combination of factors, including (i) more intensive farming and increased industrialization of all stages of food production, (ii) changes in food handling practices, eating habits and the storage, distribution, and preparation of food, and (iii) more centralized food production and more international trade in food [6–8]. These changes have brought with them new problems in food hygiene and have greatly facilitated transboundary dissemination of salmonella as well as other foodborne pathogens [7].

The risk factors for human salmonellosis are likely to vary appreciably across national boundaries in accordance with cultural patterns, climatic factors, husbandry and agricultural practices, and implementation of control and preventive measures. In Norway,
a restrictive policy regarding the import of fresh meat, live animals and feed has been pursued and the production systems applied to animal husbandry are less intense than in most other industrialized countries [9]. In 1993 a national case-control study of sporadic, indigenous salmonella infection was initiated to identify preventable risk factors and provide a scientific basis for a specific control and prevention strategy. This article describes the epidemiological succession of non-typhoid salmonellosis in Norway and presents the environmental risk factors identified by the case-control study.

MATERIALS AND METHODS

Descriptive epidemiology

The data presented in this communication are based on 22 years’ reporting of human salmonellosis, from the beginning of its surveillance in 1975 to 1996. During this period epidemiological surveillance of salmonellosis in Norway has been undertaken by the National Notification System for Communicable Diseases at the National Institute of Public Health (NIPH) [10]. The notification system receives individual notifications of all culture-confirmed cases diagnosed on the basis of routinely cultured stool specimens from patients with acute enteritis at the medical microbiological laboratories throughout the country. For each reported case, epidemiological, bacteriological and clinical information is entered into a computer database. The bacteriological information is adjusted according to results from the National Salmonella Reference Laboratory at the NIPH, which performs serological typing and biochemical characterization of all salmonella isolates using standard methods [11]. Whereas the bacteriological media and isolation procedures have varied among the diagnostic laboratories over time, reporting procedures have not differed for the 22 years of study, except in 1995 and 1996 when more complete information on the patients’ travel history prior to onset of illness was requested from the physicians who submitted the positive stool samples.

Case-control study

Cases and controls

The study was conducted from April 1993 to October 1994. We defined a case as a patient with acute enteritis who: (i) had a culture-confirmed infection with salmonella (excluding S. typhi and S. paratyphi), (iii) were diagnosed at one of the medical micro-

biological laboratories in Norway during the study period, and (iii) had not travelled abroad in the 2 weeks before the onset of illness. Whenever a routinely submitted clinical stool specimen yielded salmonella, laboratory personnel contacted the patient’s physician who was prompted to mail a structured questionnaire to the patient. The questionnaire was accompanied by a standard letter in which the patient (or a parent for persons under the age of 15 years) was encouraged to answer the questions and return the completed questionnaire to investigators at the NIPH. If stool specimens from more than one member of a household yielded salmonella or the case was part of a recognized outbreak, only the first identified case was enrolled. All bacterial isolates were verified and serotyped at the National Salmonella Reference Laboratory at the NIPH.

Once enrolled, the case was matched by age, sex, and geographic area with five potential control persons selected from Norsk Folkeregister, a government registry of all Norwegian residents which is updated quarterly. Matching was obtained by selecting persons in the registry who were closest in age to the case and lived in the same or an adjacent municipality. This approach ensured that the cases and their controls were rarely more than 2 weeks apart in age. The questionnaire and a letter of introduction were subsequently mailed to the potential controls (or their parents for those younger than 15 years). If no eligible controls completed and returned the questionnaire, additional control persons were identified and contacted until at least one has been enrolled for each case. Criteria for exclusion were: a past history of salmonella infection, diarrhoea or abdominal pain with fever in the preceding month, or travel abroad in the last 2 weeks.

Questionnaire

The questionnaire sought information on personal and demographic data, travel history, and exposure to potential risk factors including: consumption of 44 individual food items comprising fresh shell eggs, egg products, poultry, beef, pork, mutton, game and minced meat products; eating homemade meat or fish items; eating outside of the home, eating meat purchased abroad; consumption of raw, rare or undercooked meat; drinking untreated water; contact with wild-living birds; and foreign travel among household members. Exposure frequencies were recorded for each risk factor variable (e.g. number of meals eaten or number of times exposed). Precise information on
drinking water quality was provided by local food control authorities.

Case patients were questioned about exposure in the 2-week period before onset of their illness. The median interval between illness onset and completion of the questionnaire was 25 days (range, 5–286; mean, 36 days). To facilitate recall of food consumption and reduce recall bias, controls were questioned about the 2-week period before they received the questionnaire. A median of 14 days elapsed between the dates when the cases and their controls completed the questionnaire (range, 3–160; mean, 24 days).

Statistical analyses

All risk factor variables were analyzed in dichotomous as well as in continuous format. Univariate analysis of dichotomous variables was performed by using the procedure for matched data sets in the computer program Epi Info (version 5.01a; Centers for Disease Control and Prevention, Atlanta, GA). Conditional logistic regression was implemented for univariate analysis of continuous variables and for multivariate analysis by using the computer program Egret (version 0.26.94; Statistics and Epidemiology Research Corporation, Seattle, WA). The results are reported as matched odds ratios (ORs) with 95% confidence intervals (CIs) and two-tailed P-values. Adjusted estimates of population attributable fractions based on the logistic regression model were calculated as suggested by Coughlin and colleagues [12] by using the multivariable adjustment procedure for matched data provided by Bruzzi and colleagues [13].

The analysis of food consumption was first performed for each of the 44 individual food items listed in the questionnaire. Food items with the same constituent were then aggregated into broader categories. Such aggregate variables were generated for egg, poultry, beef, pork, mutton and minced meat products.

RESULTS

Descriptive epidemiology

During the 22-year period from 1975 to 1996, a total of 17 441 culture-confirmed cases of salmonella infection (excluding S. typhi and S. paratyphi) were recorded among the 44 million Norwegians (1996 census) (Fig. 1). Fewer than 400 cases were reported annually in the first 7 years of surveillance, but the number increased steadily from the early 1980s and reached a maximum of 1583 cases in 1987 (incidence rate, 36.8 per 100 000 population). A decline was noted in the early 1990s followed by renewed increase in subsequent years. The elevated numbers of cases reported in 1976, 1982, and 1987 are attributable to the occurrence of three nationwide outbreaks those years. In 1976 an outbreak of S. heidelberg infection of unknown origin, which involved about 70 confirmed cases, occurred. In 1982 an outbreak caused by imported black pepper contaminated with S. oranienburg resulted in 126 culture-confirmed cases [14]. The outbreak in 1987 which precipitated 349 reported cases of S. typhimurium infection, incriminated contaminated chocolate bars produced by a Norwegian company [15].

Since 1984 S. enteritidis has become the most common serovar reported, except from 1987 when it was surpassed by S. typhimurium due to the outbreak that year (Fig. 1). While S. typhimurium predominated in earlier years, S. enteritidis have increased substantially from a low level in 1975–82 to a peak incidence in 1994 when 769 cases were reported (incidence rate, 17.9 per 100 000 population). No increase of similar magnitude has been observed for any other serovar. Over the period 1988–96, the percentage of cases attributable to S. enteritidis ranged from 46.8–57.2% each year (annual average, 51.4%), compared with 12.6–26.7% for S. typhimurium (annual average, 18.2%).

Since 1982 information on the patients’ travel history prior to onset of illness has been recorded (Fig. 2). In 1982 through 1996, 88.4% of the cases from whom a travel history was available, reportedly developed symptoms abroad or shortly (1–3 days) after their return home (range, 64.7–97.4%; median 92.8%). These patients were defined as imported cases. When the outbreak year of 1987 was excluded, the proportion of cases acquired abroad amounted to 91.2% (range, 85.6–97.4; median, 93.0%). The overall decline in salmonella cases noted in the early 1990s was due to a parallel decline in imported cases (Fig. 2), which coincided with a period of economic depression when the number of air charter passengers to foreign countries was reduced.

The percentage of infections related to foreign travel was higher for S. enteritidis than for S. typhimurium. In the 9 years following the 1987 outbreak, 94.5% of the S. enteritidis cases were imported (range, 83.6–93.3%; median, 95.7%), while only 75.0% of the S. typhimurium cases were acquired abroad (range, 62.0–85.7; median, 78.6%) (data not shown). The corresponding figures for all other serovars combined were 90.8% (range, 85.1–96.1%);
Fig. 1. Culture-confirmed human cases of salmonella infections (excluding *S. typhi* and *S. paratyphi*) by year and serovar, Norway 1975–96. A, B, and C indicate prominent outbreaks (see text).

Fig. 2. Culture-confirmed human cases of salmonella infections (excluding *S. typhi* and *S. paratyphi*) by place of infection, Norway 1982–96. Black bars indicate patients who had not travelled abroad prior to onset of their illness (defined as indigenous cases). Hatched bars show patients who developed symptoms abroad or shortly after their return home (defined as imported cases). Missing values are indicated by open bars. The increased numbers of indigenous cases noted in 1987, 1989, 1993 and 1996 are due to outbreaks (see text).

median, 91·6%). The percentage of indigenous *S. enteritidis* cases peaked in 1989 (16·4%) due to an outbreak involving 60 confirmed cases among employees in the oil industry offshore, which was traced to imported poultry products. Likewise, the percentage of indigenous *S. typhimurium* infections increased in 1993 (37·3%) and 1996 (38·0%) when two outbreaks of unknown origin involving approximately 70 and 20 cases, respectively, occurred.

**Case-control study**

Ninety-four case patients and 226 matched controls were enrolled in the study. One case was matched with 5 controls, 9 with 4 controls, 26 with 3 controls, 49 with 2 controls, while the remaining 9 cases were each matched with 1 control subject. The response rate among controls was 69·9%. The median age of the case patients was 25 years (mean, 26; range, <1–84 years). Forty-seven (50·0%) were female. Stool samples from 44 (46·8%) of the case patients yielded *S. typhimurium*, whereas 19 cases (20·2%) were infected with *S. enteritidis*. A total of 19 other *Salmonella* serovars were recovered from the remaining 31 case patients. During the study period, 159 culture-confirmed cases of sporadic salmonella infection with no reported history of travelling abroad before the onset of illness, were recorded by surveil-
Consumption of beef or beef products was associated with a reduced risk of salmonellosis (OR = 0·5, \( P = 0·02 \)). A negative association was also detected for minced and forced meat products, including hamburgers, beef cakes, pork cakes and sausages, but this factor was of marginal significance (OR = 0·4, \( P = 0·06 \)). Enrollees were questioned about consumption of homemade, as opposed to packaged or store bought, meat or fish items. This aggregates food variable which comprised homemade fish cakes, beef cakes, pork cakes and sausages, was associated with a reduced risk (OR = 0·5, \( P = 0·03 \)). There were no significant differences between cases and controls regarding their consumption of raw, rare or undercooked meat products. Likewise, eating outside of the home, at restaurants, hotels, street kitchens or hot dog stands, was not identified as a risk factor.

Many Norwegians visit other Scandinavian countries. Thus, 59·1% of all eligible cases were enrolled. Study enrollees were similar to non-enrollees with respect to age, sex, geographical and serovar distributions.

**Univariate analysis (Table 1)**

Study enrollees were questioned about consumption of fresh shell eggs (including raw, soft boiled, hard boiled, fried and scrambled eggs) and 6 individual egg products. None of these food items was associated with an increased risk of infection. Likewise, no significant risk was detectable for consumption of 10 poultry products, including chicken, hen, turkey, duck or geese items. However, there was a tendency towards a slightly increased risk for this exposure (OR = 1·5, \( P = 0·15 \)). Case patients were no more likely than their controls to report consumption of meat products containing pork, mutton or game.
consumption of poultry purchased abroad was significantly associated with illness (OR = 7.6, \( P < 0.001 \)). Out of the 11 patients who reported such exposure, 6 had eaten poultry which was (illegally) imported from The Netherlands. Consumption of Danish poultry was identified as a risk factor (OR = 11.8, \( P = 0.01 \)). An increased risk was also noted for consumption of Swedish poultry, but statistical significance was not attained (OR = 4.3, \( P = 0.12 \)). More cases than controls had eaten pork, sausages or cold cuts purchased in Denmark or Sweden. While consumption of foreign pork was significantly associated with illness (OR = 3.6, \( P = 0.04 \)), sausages and cold cuts were of marginal significance. The number of persons who had consumed foreign beef, mutton, minced meat or cheese, was too low to enable a meaningful analysis (data not shown).

Drinking undisinfected water did not significantly increase the risk of infection, while contact with wild-living birds or their faeces (e.g. touching dead birds, cleaning a bird table, removing bird droppings) was marginally associated with salmonellosis (OR = 2.7, \( P = 0.08 \)). Cases were no more likely than controls to report foreign travel among other household members in the month prior to onset of illness or to have eaten food from a catering establishment. Four cases but no controls worked offshore in the oil industry where meat produced abroad are legally imported without prior salmonella control.

**Stratified analysis**

We performed a stratified analysis of risk factors for infection with: (a) *S. typhimurium*, (b) *S. enteritidis*, and (c) all other serovars combined. For groups (b) and (c) the numbers of cases were too low to enable meaningful analyses, and none of the exposures recorded achieved statistical significance. A separate analysis of *S. typhimurium* infections showed that consumption of the following foods was associated with an increased risk: poultry purchased abroad (OR = 6.1, CI = 1.2–30.2, \( P = 0.03 \)), food from a catering establishment (OR = 5.4, CI = 1.1–27.3, \( P = 0.04 \)), poultry (regardless of origin) (OR = 2.3, CI = 1.0–5.4, \( P = 0.09 \)), pork purchased abroad (OR = 3.8, CI = 0.9–15.5, \( P = 0.11 \)), and recent foreign travel among household members (OR = 7.8, CI = 2.0–31.2, \( P = 0.005 \)). A decreased risk was detected for consumption of the following food items: beef (OR = 0.3, CI = 0.1–0.6, \( P = 0.002 \)), homemade meat or fish items (OR = 0.5, CI = 0.2–1.0, \( P = 0.09 \)), and minced or forced meat products (OR = 0.2, CI = 0.1–1.0, \( P = 0.09 \)).

**Multivariate analysis**

Consumption of poultry purchased abroad was the only factor which remained independently associated with an increased risk of salmonella infection in conditional logistic regression analysis. The estimated attributable fraction related to this exposure was 10.4%. Pork, sausages or cold cuts purchased abroad were not independent risk factors. The apparent association between these exposures and salmonellosis was attributable to the fact that many persons who ate foreign poultry, also ate other imported items. Eating of beef was independently associated with a decreased risk.

To test whether consumptions of domestically produced poultry, red meat or eggs were associated with an increased risk of infection, aggregate food variables representing these exposures were generated,
and each was entered separately into a regression model together with its corresponding variable for imported food. The slightly increased risk associated with poultry consumption overall was eliminated after controlling for consumption of poultry from abroad. Likewise, no risk was detectable for red meat consumption. None of the enrollees ate imported eggs. Thus, the analysis failed to demonstrate any statistically significant association between salmonellosis and consumption of domestically produced red meat, poultry or eggs.

In a separate logistic regression analysis, the following factors were independently related to S. typhimurium infection (Table 2): consumption of poultry purchased abroad, eating food from a catering establishment, and foreign travel among household members. A negative association was detected for beef consumption.

DISCUSSION

The epidemiological progression of salmonellosis in Norway is parallel to trends noted elsewhere in Europe [3, 5]. The proportion of reported cases related to foreign travel varies considerably across Europe [3]. However, in contrast to most other European countries, a majority of the Norwegian patients have acquired their infection abroad, and the indigenous level is comparatively low. This favourable situation is not unique, but is shared with the neighbouring countries of Finland and Sweden [16, 17]. Although the possibility cannot be excluded that a selection bias may have been introduced by potential oversampling of travellers relative to domestic cases, it is unlikely that this factor is sufficient to explain completely the observed dominance of imported cases. It is also important to emphasize that the wide variation in the incidence of human salmonellosis reported from different countries, largely reflects the efficiency of the surveillance or notification systems [3]. Thus, direct comparison of national incidence estimates is not warranted.

Our finding of an apparently low incidence of domestic cases is supported by veterinary investigations documenting a low level of salmonella in the Norwegian food chain. Based on a national survey conducted in 1991, which encompassed 23000 randomly selected samples, the prevalence of salmonella in meat and meat products of Norwegian origin was estimated to be 0.1% or less [18]. Likewise, a nationwide screening of 7931 eggs in 1994 failed to isolate salmonella [19]. In 1995 a programme for the surveillance and control of salmonella in live animals, animal carcasses, slaughterhouses and meat processing plants was launched [20, 21]. During its first 2 years, the programme which entails the analysis of approximately 30000 samples annually, found that less than 1% of the domestic animals and food products under surveillance harboured salmonella [22].

The steady increase in international food trade represents a significant health problem of considerable complexity modulated by political overtones [7]. Among the factors contributing to an explanation of Norway’s favourable situation regarding salmonella are effective legislative measures which restrict the import of meat, live animals and feed, and strict control and preventive measures [9, 18]. In contrast to many other European countries, more than 95% of the meat products sold at retail outlets are domestically produced [23]. Other factors which may have reduced the introduction and dissemination of salmonella, are Norway’s geographically isolated location in the northern part of Europe where a cold climate prevails, and the structure of the animal husbandry which is characterized by small, scattered production units with a relatively low degree of industrialization [9, 18].

The apparently low level of salmonella in the Norwegian food chain is further substantiated by the present case-control study which failed to demonstrate any statistically significant association between human salmonellosis and the consumption of domestically produced red meat, poultry or eggs. This result is in contrast with previous case-control studies conducted in Switzerland, the United States and the United Kingdom which incriminated eggs, poultry or both as vehicles of infection [24–28]. In our study, the only factor which remained independently associated with an increased risk of salmonellosis, was consumption of poultry purchased abroad during holiday visits to neighbouring countries. This finding parallels the results of a previous study of sporadic campylobacter infections in Norway which found an association with poultry from foreign sources [29]. Although publicity linking foreign poultry with salmonellosis could have biased recall of food histories, it is unlikely that this is sufficient to explain the observed effect, since the exposure concerned is an especial event which is readily recalled.

The fact that consumption of foreign poultry remained independently associated with infection in
the multivariate analysis reinforces its importance, but the attributable fraction implies that it would only account for a small part (10%) of the salmonella problem. The majority of the cases may probably be explained by a variety of factors, the individual effects of which are too small to precipitate statistically significant risks, or by factors not included in the questionnaire. The univariate analysis indicates that consumption of pork, sausages or cold cuts purchased abroad, contact with wild birds and working offshore in the oil industry, are all exposures which may contribute to an explanation of the indigenous cases. Consumption of catered food and foreign travel among household members were independently related to *S. typhimurium* infection, but did not achieve statistical significance when all salmonella infections were lumped. The last mentioned factor may reflect secondary spread of infection within the family or consumption of contaminated food bought while being abroad. It is also possible that the apparent risk factor status of both of these exposures is due to an association with dietary patterns more directly related to the modes of infection, thereby creating a confounding effect.

Consumption of untreated water has figured prominently in previous epidemiological studies in Norway as a risk factor for infections with campylobacter and *Yersinia enterocolitica* [29–31]. In this study, no significant link between salmonellosis and untreated water was detected. However, as cases and controls were matched by geographic area, we may have underestimated the importance of water as a risk factor, because people living in the same area are likely to have the same or a similar drinking water supply. In a concurrent case-control study in Norway, drinking of untreated water, contact with wild birds and consumption of snow, sand and soil were found to be associated with an increased risk of sporadic infection with a particular variant of *S. typhimurium* 0:4–12 [32], which was responsible for the nationwide outbreak in 1987 [15]. Unlike most other salmonellae, this variant has established an indigenous reservoir in the avian wildlife fauna, with contamination of the environment, including surface water sources, as a likely consequence [32]. The lack of association with untreated water for all salmonella infections combined, is in accordance with the suggestion that most serovars have so far failed to establish stable reservoirs in Norway.

In accordance with previous case-control studies of salmonellosis, several factors were associated with a reduced risk of infection [24, 28]. Only beef consumption remained as an independent factor in the multivariate analysis. It is possible that this exposure represents dietary behaviour generally conferring a lower risk of infection, thereby creating a spurious protective effect.

Although the epidemiology of human salmonellosis in Norway show close similarities to trends noted elsewhere in the industrialized world, several distinguishing features are evident. The high proportion of cases related to foreign travel, the relative low level of indigenous infections, the low prevalence of the organism in the domestic food chain and the lack of association with consumption of domestically produced meat and eggs, are all features which differ from the situation in most European countries. The progressive trend towards globalization of the food trade represents a contemporary challenge to Norway’s favourable salmonella status, and predicates the need for renewed alertness and appropriate intersectorial actions.

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