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Correlation between animal and human brucellosis in Italy during the period 1997–2002

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ABSTRACT

The aim of this study was to test the hypothesis that brucellosis in Italy is a food-borne, rather than an occupational disease. This hypothesis was tested using data for both human and animal populations from the period 1997–2002. The correlation between the distribution of the disease in the human, sheep and goat populations was analysed, as were the risk factors for the disease, with respect to gender, age, occupation and residence of the individuals involved. Notifications of human brucellosis, which are mandatory in Italy, reach a peak between April and June. However, considering the standard incubation period of 2–4 weeks, and the fact that lamb slaughter is traditionally at a peak during the Easter period, it might be expected that occupational exposure would result in a peak of human cases between March and May. The observed peak between April and June could be related to the production and consumption of fresh cheese, starting just after lamb slaughter. The age of patients showed a fairly uniform distribution, and analysis of incidence rates of human brucellosis between 1997 and 2002 showed that the incidence rates were consistent with an occupational exposure risk of about 25%.

Keywords Brucellosis, cheese, food consumption, incidence rates, lambs, occupational risk

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INTRODUCTION

Worldwide, brucellosis remains a major source of disease in man and farmed animals [1]. Consumption of contaminated foods and occupational contact remain the major sources of infection. Examples of human-to-human transmission following tissue transplantation or sexual contact are reported occasionally [2], but most human cases involving wild-type strains of *Brucella* spp. can be traced to food animals. In the past, cattle have been the major source of human infection in most countries, and programmes to eradicate the disease have been aimed largely at bovine brucellosis. Success has been achieved in northern and eastern European countries, Australia, New Zealand, Japan, Canada and the USA. Cattle remain the source of brucellosis in most African countries, where large numbers of cattle are maintained and drinking raw milk is a custom. In countries with near universal pasteurisation of milk, brucellosis has become an occupational disease. Brucellosis remains a serious zoonosis in areas of the world where *Brucella melitensis* is endemic in sheep and goats. These areas include the Mediterranean littoral, southwest Asia and parts of Latin America [3].

Prevention of human brucellosis depends on control of the disease in animals. Although success has been achieved in eradicating the bovine disease, *B. melitensis* infection in sheep and goats has proved more intractable, and success has been limited [1]. Previous studies in Italy regarding the impact of animal brucellosis on human disease have suggested an overlap between the distribution of disease in humans and that in the cattle and ovi-caprine populations [4], although it seems unlikely that the disease was transmitted to humans in the same proportion from cattle, sheep and goats. Caporale *et al.* [5] reported that *B. melitensis* was the pathogen isolated most frequently in human cases of brucellosis in Italy between 1970 and 1990,

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accounting for 99% of total cases. Therefore, the problem in Italy seems to focus on the ovi-caprine population, rather than the cattle population, and the correlation between the distribution of the disease in cattle and in human populations seems to be spurious, since there is a higher prevalence of bovine brucellosis in the same areas of southern Italy where ovi-caprine brucellosis is widespread.

Data on *Brucella* strains isolated from humans in Italy have not been updated since 1990, even though animal, mainly ovi-caprine, trends remained relatively high in the succeeding years [4]. The possible routes of infection have not been assessed formally in Italy, but there are consistent seasonal incidence peaks, which suggest that foodborne infection could be the main route of dissemination for the disease. The aim of the present study was to test the hypothesis that brucellosis in Italy is a food-borne, rather than an occupational disease. This hypothesis was tested using data for both human and animal populations during the period 1997–2002 for the whole of Italy, with particular reference to some regions where more detailed information was available. The correlation between the distribution of the disease in the human, sheep and goat populations was analysed, as were the risk-factors for the disease in human populations in Italy, with respect to gender, age, occupation and residence of the individuals involved.

MATERIALS AND METHODS

Data sources

National population data, subdivided by gender, age, occupation and residence, for the period 1997–2002 were provided by the Italian National Institute for Statistics [6]. National data regarding human cases of brucellosis, subdivided by gender, age, and month of occurrence, notified during the period 1997–2002 in Italian provinces and regions, were provided by the Italian Ministry of Health [7]. Regional data regarding the occupations of individuals involved in cases of brucellosis notified during the period 1997–2002 were provided by the University of Bari (Faculty of Medicine) for the Apulia region, by the Regional Epidemiological Centre for the Campania region, and by the Regional Health Unit for the Abruzzi region. National data on the number of flocks infected with brucellosis in Italian regions, as well as data regarding the ovi-caprine population density, were provided by the Italian Ministry of Health as part of national eradication campaigns for sheep and goat brucellosis. National data regarding the monthly number of lamb slaughters during 1997–2002 were provided by the Italian Institute of Services for Agricultural Food Market [8].

Statistical analysis

Regression model

The correlation between the incidence of human brucellosis in Italian regions and the number of brucellosis-infected flocks was investigated by least squares linear regression.

Mathematical model for occupational exposure

It was assumed that the number of expected cases of human brucellosis in a given age group, with respect to a given percentage of occupational exposure risk (Fig. 1), can be derived from the sum of: (1) the number of cases expected in that age group related to a given professional exposure risk, i.e., the number of observed cases multiplied by the percentage of occupational exposure risk and by the ratio between the population employed in the age group under consideration and the total population employed in all age groups; and (2) the number of cases expected in an age group that are related to non-professional exposure, i.e., the number of observed cases multiplied by 1 – the assumed percentage of occupational exposure risk and by the ratio between the total population in the age group considered and the total population in all age groups. The age groups considered were 0–14 years, 15–24 years, 25–64 years and ≥65 years. The percentages of occupational exposure risk were 0%, 25%, 59%, 75% and 100%. Validation of the mathematical model was based on surveillance data from the Abruzzi, Campania and Apulia regions, considering a north–south incidence gradient of human and animal brucellosis infection.

RESULTS

Incidence of brucellosis in humans and its relationship with animal brucellosis

The incidence of human brucellosis in Italy during 1990–2002 decreased from 2.7 cases/100 000 inhabitants in 1990 to 1.4 cases/100 000 inhabitants in 2002, with a peak of

$$\left(\begin{pmatrix}\text{Total}\\ \text{observed}\\ \text{cases}\end{pmatrix} * \begin{pmatrix}\text{Percentage}\\ \text{occupational}\\ \text{exposure}\end{pmatrix} * \begin{pmatrix}\dfrac{\text{Population employed in.age.class}}{\text{Total. population. employed}}\end{pmatrix}\right) + \left(\begin{pmatrix}\text{Total}\\ \text{observed}\\ \text{cases}\end{pmatrix} * \left(1 - \begin{pmatrix}\text{Percentage}\\ \text{occupational}\\ \text{exposure}\end{pmatrix}\right) * \begin{pmatrix}\dfrac{\text{Total population in.age.class}}{\text{Total population}}\end{pmatrix}\right)$$

Fig. 1. Number of expected cases of human brucellosis in a given age group related to a given percentage of occupational exposure risk.

3.3 cases/100 000 inhabitants in 1996. The disease is more widespread in southern regions of Italy, especially in Sicily, in the human, sheep and goat populations (Fig. 2). The incidence in Sicily of human brucellosis increased from 5.5 cases/100 000 inhabitants in 1990 to 8.0 cases/100 000 inhabitants in 2002, with a peak of 18.8 cases/100 000 inhabitants in 1997. Southern regions of Italy are territories in which the ovi-caprine population density is higher than that in the rest of the country.

A particularly interesting region was Sardinia, which, despite the highest ovi-caprine population density in Italy, had a very low incidence of human cases of brucellosis in the period 1996–2002, reaching 0.12 cases/100 000 inhabitants (Fig. 2). Regression analysis demonstrated a significant relationship between the incidence of cases of human brucellosis and the number of infected flocks for 1997–2002, as well as between the incidence of human brucellosis and the number of infected herds for the same period (Table 1).

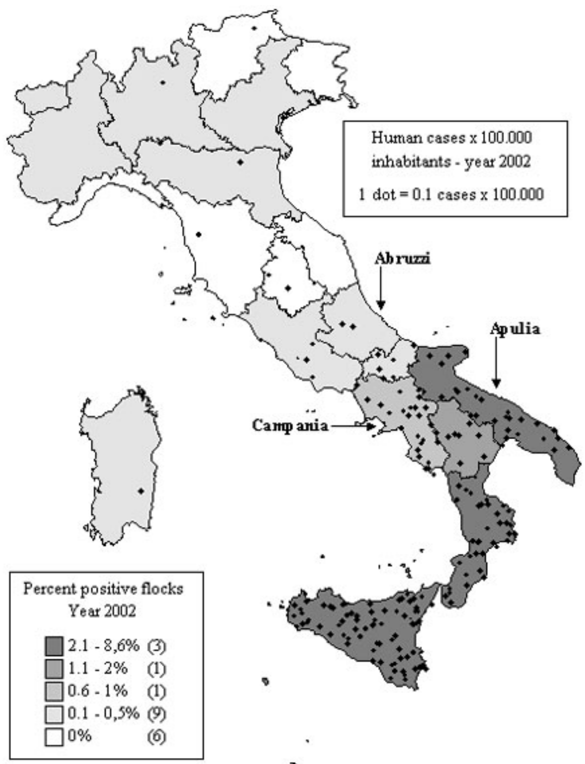

Fig. 2. Relationship between the percentage of sheep and goat flocks positive for brucellosis and the incidence of human brucellosis in Italy (year 2002).

Table 1. Regression analysis of the incidence of human brucellosis and the number of sheep and goats/bovine infected flocks/herds during 1997–2002

	Human incidence vs. ovi-caprine		Human incidence vs. bovine	
Year	R^2	p	R^2	p
1997	0.9458	< 0.00001	0.9447	< 0.00001
1998	0.8106	< 0.00001	0.7552	< 0.00001
1999	0.7472	< 0.00001	0.7615	< 0.00001
2000	0.8695	< 0.00001	0.8905	< 0.00001
2001	0.8632	< 0.00001	0.8249	< 0.00001
2002	0.907	< 0.00001	0.9339	< 0.00001

Residence of patients with brucellosis

Residence data for patients affected by brucellosis were available only for the Abruzzi, Campania and Apulia regions. The incidence of brucellosis was compared by dividing the municipalities in these three regions into two groups based on the number of inhabitants, i.e., >50 000 inhabitants ('urban areas'), and <50 000 inhabitants ('rural areas'). Chi-square analysis revealed no significant differences with respect to the residences of patients infected with brucellosis.

Relationship between occupational exposure and exposure via food

Fig. 3 shows the monthly distribution of human cases in relation to monthly percentage of lamb

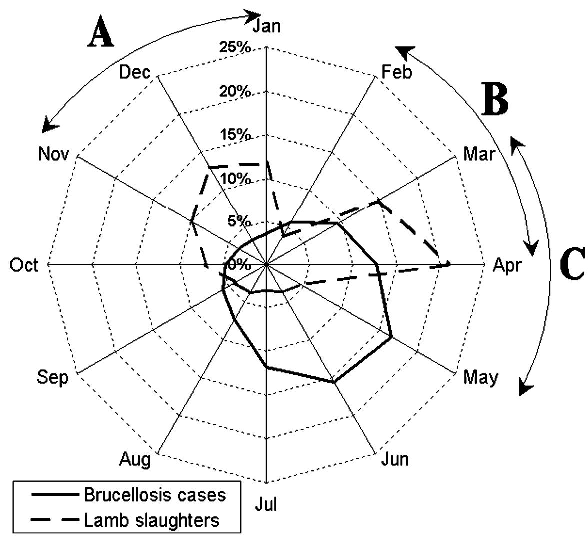

Fig. 3. Relationship between the monthly distribution of human cases of brucellosis in Italy and the percentage of lamb slaughters (1997–2002). A, secondary period of peak incidence (expected for occupational exposure). B, expected period of peak incidence for occupational exposure. C, expected period of peak incidence for foodborne exposure.

slaughters during the period 1997–2002, with a seasonal peak from April to June. The age distribution of human cases of brucellosis for the same period did not show clustering of patients in a particular age class or group of age classes, but rather a fairly uniform distribution (Table 2). The expected age distribution and number of human cases of brucellosis in relation to different levels of professional exposure are shown in Fig. 4.

Occupation and gender of patients with brucellosis

The overall incidence of human brucellosis in Italy during the period 1997–2002 was 15.6 cases/100 000 males and 9.5 cases/100 000 females (62% vs. 38%). Detailed data regarding the gender and occupation of patients were available only for the Abruzzi, Campania and Apulia regions. Animal breeders, shepherds, farmers, butchers, veterinarians and laboratory workers were considered to be at risk for occupational brucellosis. In Abruzzi, 32% of cases belonged to 'at risk' categories, compared to 7% of cases in Campania, and 13% of cases in Apulia. Thus, the data available for these three regions confirmed that the 25% scenario for occupational exposure (Fig. 4) was closest to the surveillance data. Within the 'at risk' categories, 81% of patients were males and 19% were females. Unfortunately, the occupation of people involved in brucellosis cases is often under-reported. During the period 1997–2002, the occupation of the patient was not recorded for 35 of 60 cases in Abruzzo, 399 of 1243 cases in Campania, and 118 of 1048 cases in Apulia.

Table 2. Incidence of human brucellosis in Italy during 1997–2002, grouped according to the age of patients

Age group (years)	Cases/100 000 inhabitants
0–14	1.57
15–24	2.10
25–64	2.39
≥ 65	1.61

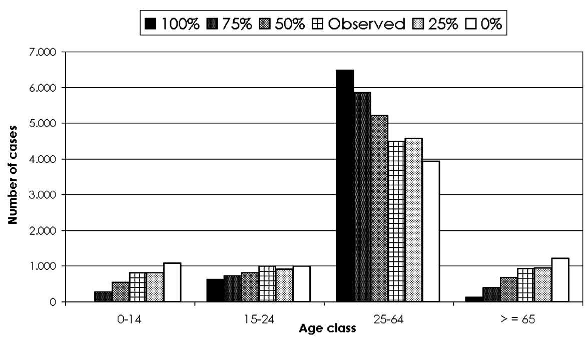

Fig. 4. Expected distribution of the number of human cases of brucellosis in Italy by age class in relation to different levels of professional exposure.

DISCUSSION

The results of this study confirmed that, in Italy, human brucellosis is more widespread where the prevalence of infection in sheep and goats is highest (Fig. 1), and a significant correlation between human and animal infections during 1997–2002 was demonstrated by regression analysis. Three species of pathogenic *Brucella* cause infection in humans in Italy (*Brucella abortus*, *B. melitensis* and *Brucella suis*). Caporale *et al.* [5,9] observed that *B. melitensis* was the species isolated most frequently, with *c.* 99% of cases in Italy being caused by this species. Therefore, human brucellosis seems to be related more to ovi-caprine than to cattle infection, and the correlation between the distribution of the disease in cattle and human populations may be spurious because of the higher prevalence of bovine brucellosis in the same areas of southern Italy where ovi-caprine brucellosis is widespread.

The surveillance data regarding the occupation of brucellosis patients suggests that occupational exposure may not be the primary route of infection, despite the fact that the difference in the incidence of disease between males and females could be explained by the observation that most cases within 'at risk' categories are males. However, the seasonal peak noted in the distribution of human cases of brucellosis (Fig. 3), as well as the age group distribution (Table 2), suggests that the main route of human infection could be related to exposure through food.

The seasonal trend in human cases of brucellosis showed a peak from April to June The peak of lamb slaughters is March–April (Easter), and there is a secondary peak in November–January (Christmas; Fig. 3). Since lambs are generally aged 30–60 days at the time of slaughter, and considering that the standard incubation period for human brucellosis is 2–4 weeks [10], the peak incidence of human cases resulting from occupational exposure should be between March and April, with a secondary peak between November and January. However, the seasonal peak noted from April to June (Fig. 3) is consistent with the consumption of fresh sheep cheese. After lamb slaughtering, milking of ewes and the production of cheese from non-pasteurised milk follows. These seasonal milk products are usually sold fresh and pose a serious risk of infection for consumers. This hypothesis is supported by the fairly uniform distribution observed in human cases of brucellosis (Table 2), and the fact that the incidence rates of human brucellosis between 1997 and 2002 were similar to those expected for an assumed occupational exposure rate of *c*. 25% (Fig. 4).

Overall, the findings confirmed the geographical clustering of cases of human brucellosis in Italy, as well as the strong association with infection in animals, mainly sheep and goats. This suggests a need to focus appropriate control measures and eradication efforts on areas in which a high prevalence of animal brucellosis is present. The findings of this study also indicate that brucellosis in Italy is now predominantly a foodborne zoonosis, rather than an occupational disease. This confirms the need to enforce public awareness of the risk associated with consumption of non-pasteurised milk and dairy products, mainly from sheep and goats, and demonstrates that public health would benefit from a strengthening of cooperation between human and veterinary health services.

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REFERENCES

1. Corbel MJ. Brucellosis: an overview. *Emerg Infect Dis* 1997; **3**: 213–21.
2. Mantur BG, Mangalgi SS, Mulimani B. *Brucella melitensis*—a sexually transmissible agent. *Lancet* 1996; **347**: 1763.
3. Nicoletti P. Relationship between animal and human disease. In: Young EJ, Corbel MJ, eds. *Brucellosis: clinical and laboratory aspects*. Boca Raton, FL: CRC Press, 1989; 41–51.
4. Salmaso S, Bella A, D'Ancona F, De Mei B, Mandolini D. Epidemiologia della brucellosi in Italia. *Notiziario Dell'istituto Superiore Sanità* 2000; **13**: 4–8.
5. Caporale V, Nannini D, Giovannini A, Morelli D, Ramasco M. Prophylaxis and control of brucellosis due to *Brucella melitensis* in Italy: acquired and expected results. In: *Prevention of brucellosis in the Mediterranean countries. Proceedings of the International Seminar CIHEAM CEC, MINAG (Malta), FIS (Malta).* Valletta: CIHEAM, 1992; 127–145.
6. Repubblica Italiana. Istituto Nazionale di Statistica. *Popolazione*. Rome: ISTAT, 2003. http://www.istat.it
7. Repubblica Italiana. Ministero della Salute. *Malatie infettive*. Rome: Ministero della Salute, 2003. http://www.ministerosalute.it
8. Repubblica Italiana. Istituto di Servizi per il Mercato Agricolo Alimentare. *Animal e carni*. Rome: ISMEA, 2003. http://www.ismea.it
9. Caporale V, Nannini D, Petracca G, Paganico G. Epidemiology and control of *Brucella melitensis* in Italy. In: Verger M, Plommet M, eds. *Brucella melitensis.* Dordrecht: Martinus-Nijhoff, 1985; 51–83.
10. Young EJ. Human brucellosis. *Rev Infect Dis* 1983; **5**: 821–842.