



Brucellosis is a public health problem in southern Italy: Burden and epidemiological trend of human and animal disease

Alessio Facciola^a, Maria A.R. Palamara^b, Giuseppa D'Andrea^c, Fernanda Marano^c, Domenico Magliarditi^d, Giovanni Puglisi^c, Isa Picerno^b, Angela Di Pietro^b, Giuseppa Visalli^{b,*}

^a Department of Clinical and Experimental Medicine, University of Messina, Italy

^b Department of Biomedical and Dental Sciences and Morphofunctional Imaging, University of Messina, Italy

^c Epidemiology Operative Unit, Department of Prevention, Sanitary Provincial Agency, Messina, Italy

^d Veterinary Epidemiology Operative Unit, Veterinary Prevention Department, Sanitary Provincial Agency, Messina, Italy

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ABSTRACT

Background: Brucellosis is the most common global bacterial zoonotic disease. Italian annual 2015 report on animal brucellosis control that was submitted to the Integrated National Plan of the Italian Health Ministry showed that the Italian region with the highest prevalence and incidence of brucellosis was Sicily (3.3%). This study aims to demonstrate the burden of disease and the epidemiological trend of human and animal brucellosis in Messina, Sicily, from 1997 to 2016.

Methods: The analysis was conducted in the twenty-years 1997–2016. We examined the computerised and paper registers of the Messina Provincial Health Agency n.5 to evaluate human and animal brucellosis reports.

Results: 1462 cases of human brucellosis were reported with an important outbreak in 2016 in which were reported 137 cases while the prevalence of infected cattle and sheep/goats decreased from 3.8% and 8%, respectively, in 1997 to 1.7% for both in 2016. A statistically significant correlation was observed between the decrease of both animal and human cases during the considered period.

Conclusions: Our study demonstrate that brucellosis is still present in Sicily with a number of cases identified in both animals and humans and it hypothesises a large number of probable underreported cases. Our findings confirm the need to improve knowledge of the risks associated with consuming raw milk and its derivatives, mainly from sheep and goats, and demonstrates that public health would benefit from cooperation between human and veterinary health services.

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Introduction

Zoonoses are diseases transmissible from animals to humans through direct contact or through food, water and environment and represent an important public health problem [1–3]. Brucellosis is the most common global bacterial zoonotic disease [4–6]. Ruminant brucellosis is generally transmitted to humans through the ingestion of unpasteurised milk derived from infected animals (usually cattle, goats and sheep), contaminated undercooked food or through an occupational exposure. However, the high temperatures during cooking and pasteurisation rapidly kill *Brucella* spp. [7–9]. In countries where it is common practice to pasteurise milk,

brucellosis has become more of occupational disease, especially in those working with infected animals or their tissues (i.e. farmers, livestock breeders, veterinarians and laboratory workers) [10–12]. However, brucellosis remains an important zoonotic disease in areas where *Brucella* spp. is endemic in sheep and goats, such as the Mediterranean basin, Southwest Asia and parts of Latin America [13].

In 2015, 27 countries in the European Union reported a total of 437 confirmed cases of human brucellosis, with a notification rate of 0.09/100,000 individuals. As in previous years, the countries that reported the highest rates of brucellosis were Greece (109 confirmed cases with a notification rate of 1/100,000 individuals), Italy (105 confirmed cases with a notification rate of 0.17/100,000 individuals) and Portugal (46 confirmed cases with a notification rate of 0.44/100,000 individuals), which collectively accounted for 59.5% strongly of all confirmed cases that year. Spain was fourth,

* Corresponding author.

E-mail address: gvisalli@unime.it (G. Visalli).

with 33 confirmed cases and a notification rate of 0.07/100,000 individuals [14]. These countries are not officially brucellosis-free in either cattle, sheep or goats. Between 1998 and 2010, 8483 cases of human brucellosis were reported to the Italian Informative System of Infectious Diseases and 6260 (74%) of these individuals were hospitalised. A total of 89% of reported cases occurred in the south of Italy, particularly in Campania, Puglia, Calabria and Sicilia. However, the number of reported cases decreased during these 13 years. This observation was noted in all Italian territories, even in the southern regions where the annual number of reports has dropped significantly over time [15]. Despite this positive trend, brucellosis remains an important health problem in Sicily. Of the total 316 cases notified in Italy in 2005, 92.4% were reported in this region, even with the well-known problem of underreporting [16,17].

Italy issued laws to eliminate bovine, sheep and goat brucellosis, which have led to a substantial decline of brucellosis and to the eradication of the disease in the northern Italian regions. In 2002, Sicily issued the decree 519/2002 entitled “Implementation of the extraordinary plans for the control of bovine, ovine and caprine brucellosis”. Moreover, in November 2006, the Ministry of Health issued the ‘Extraordinary veterinary police measures on tuberculosis, bovine and buffalo brucellosis, ovo-caprine brucellosis, bovine leukosis in Calabria, Campania, Puglia and Sicily’, which was modified and updated in 2012 and 2015 [18–20]. However, eradication programmes in the south of Italy, especially in Sicily, were hindered by the incomplete control of movement, the identification of animals, the lack of putting down of infected animals and the traditional breeding practices described above.

In 2014, in Sicily and Puglia were positive for brucellosis 1519 cattle on a total of 1723 animals culled during the year. A total of 13,529 sheep and goat were positive in Calabria and Sicily in 2015 and 16,170 were culled [21].

According to the Regional Veterinary Epidemiological Bulletin (which is published by the Regional Experimental Zooprophyllactic Institute) in December 2016, of the total official regionally-controlled infected cattle/sheep and goat farms, 76.3% and 69.1%, respectively, were in Messina [22].

This descriptive study aims to demonstrate the epidemiological trend of human and animal brucellosis in Messina, Sicily, from 1997 to 2016, showing the persistence of this infection and the necessity of increasing the official control to improve the health condition of breeding animals and human safety.

Material and methods

Data collection

The analysis was conducted in the twenty-years 1997–2016. In these years, the population resident in the entire Messina province, from 1997/12/31 to 2016/12/31 decreased of 3.1% ranging from 656,646 to 636,653 in the two years respectively. 37.3% of inhabitants live in Messina town. The entire provincial territory is the Provincial Health Agency n.5 (ASP 5) of the Sicilian Region. The all Agency is subdivided in 8 districts, one of these includes the Messina town. The computerised and paper registers of the Public Health, Epidemiology and Preventive Medicine Unit of the Messina ASP 5 Prevention Department collect all the human brucellosis reports from all districts. These registers were used to identify human cases, which were subsequently subdivided by gender, age and the month of occurrence.

Similarly, the computerised and paper registers of the Veterinary Epidemiology Unit of the Messina ASP 5 Prevention Department collect all cases of animal brucellosis of the entire provincial territory and were used to identify all animal cases.

Statistical analysis

Statistical processing was performed using version 10 of StatSoft® software. Descriptive statistics were used to find the percentages. Linear regression and Pearson’s correlation tests were performed to assess the relationship between animal and human cases. Significance was assessed at the $P < 0.05$ level.

Results

Human cases

A total of 1462 cases of human brucellosis were reported between 1997 and 2016. Interestingly, the first 7 years (1997–2003) were characterised by more intense peaks than the rest of the considered period, which can be attributed to the increasing levels of official controls after the emanation of decree 519/2002. Despite the decreasing numbers of notified cases during the considered period, the infection persists in our territories with a number of cases that, in 2016, resulted in an important outbreak totalling 137 notified cases. The outbreak then ended as evidenced by only 8 expected cases reported between January and August 2017 (data not shown). The numbers of cases reported per year and the incidences are shown in Fig. 1A.

During 1997–2015, males accounted for 60% of all cases and females accounted for 40%. The 25–64 age group was the most affected, accounted for 58% of all cases, and was followed by the ≥ 65 (15%), 15–24 (14%) and 0–14 (13%) age groups. The hospitalisation rate was 82% and only 6% was accounted for by workers who were at risk of contracting brucellosis (i.e. veterinarians, breeders, farmers and butchers). Concerning the 2016 outbreak, there was no significant difference between affected males and females. The age groups percentages during this time were very similar to those of the entire period. The hospitalisation rate was 46% and only 2% were at-risk workers. The monthly reporting trend during the 2016 outbreak is shown in Fig. 1B.

The peak number of reports occurred in the first part of the year, from February to July. This trend was consequent to the origin of the outbreak. Seven different sources of the outbreak were identified, of which 40 cases were related to the distribution of a local cheese (‘tuma’) during the living nativity scene at Christmas 2015 in a village in the southern suburbs of the city. The rest of the reported cases were all concentrated in the southern part of the city and were related to the consumption of fresh cheeses bought in shops supplied by small local retailers.

Analysing the reported and the hospitalized human cases, we observed a rather overlap during the years except in the 2016 outbreak in which the hospitalization rate was 46% compared to an 81% average hospitalization rate of all previous years (Fig. 2).

Animal cases

During the considered period, the number of controlled farms for cattle and sheep/goats has increased considerably from 44% and 37%, respectively, in 1997 to 100% for both in 2016. The number of controlled cattle and sheep/goats also increased during this period from 36.2% and 30.1%, respectively, in 1997 to 100% for both in 2016 (Fig. 3A–B). The increase was consequent to the implementation of decree 519/2002, which led to an overlap between controllable and controlled farms (Fig. 3C–D).

In addition, the prevalence of infected cattle and sheep/goats decreased from 3.85% and 8%, respectively, in 1997 to 1.7% for both in 2016 (Fig. 3E–F). A similar decrease was also observed for the number of infected animals that were culled or died (data not shown).

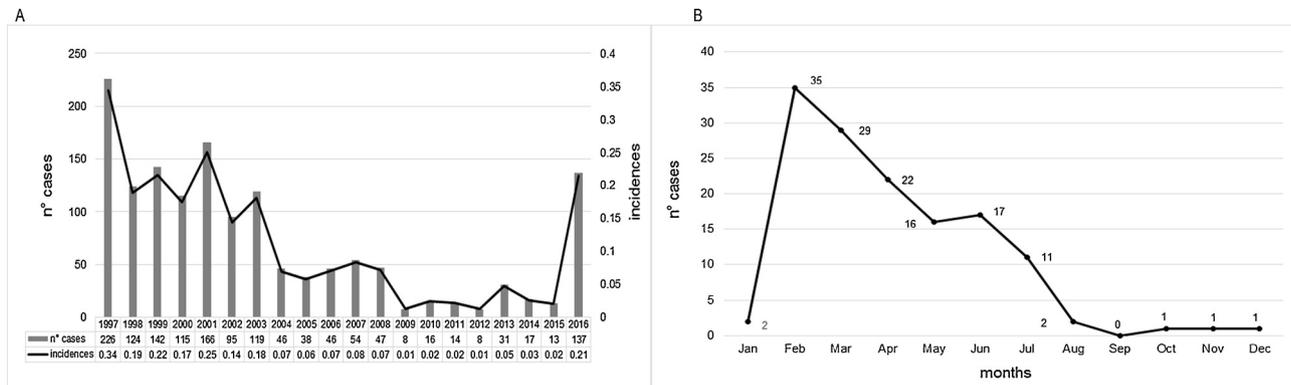


Fig. 1. Epidemiological trend of reported human cases during the twenty years 1997–2016 (A) and monthly trend of reported cases during the 2016 outbreak (B).

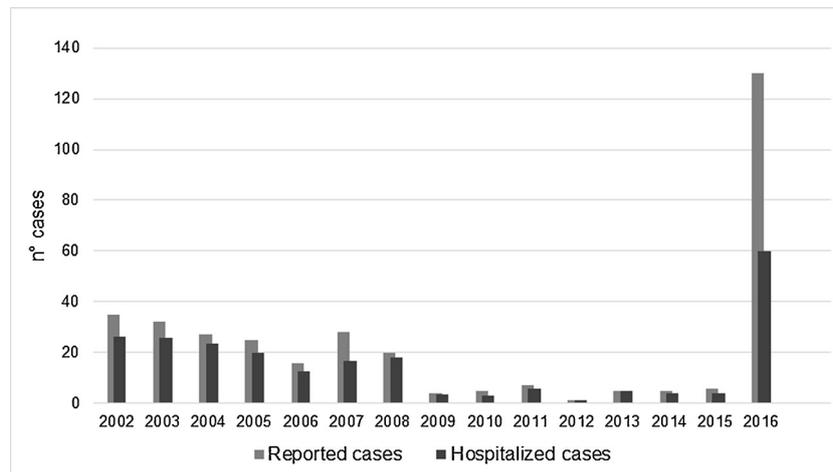


Fig. 2. Comparison between number of reported and hospitalized human cases.

A statistically significant correlation was observed between animal and human cases during the considered period (r 0.461 for cattle and r 0.426 for sheep/goats) (Fig. 4A–B). Particularly, the slope was significant both for cattle and sheep/goats ($P < 0.01$ for both). Analysing the steepness of the slope we observed that a 5% reduction of seropositivity in cattle and sheep/goats leads to a decrease of 208 (95% CI: 184.21–288.37) and 62 (95% CI: 56.72–81.51) human cases respectively.

Discussion

Brucellosis is still one of the most common zoonoses in the world. *Brucella melitensis* is known to be the most pathogenic species of the *Brucellaceae* family, producing the most intense symptoms, the greatest tissue damage and the highest incidence of localisation in body organs, systems or tissues [23]. However, a separate study reported that there was no evidence that *B. melitensis* was more virulent than *Brucella abortus* or that infections due to *B. abortus* were less severe than infections with *B. melitensis*, despite the higher prevalence of *B. melitensis* in humans [24]. Bovine brucellosis is mainly sustained by *B. abortus*, as cattle are the natural host and reservoir of this microorganism; secondary hosts include bison, buffalo, camel and moose, while casual hosts include pigs, horses and dogs. *B. melitensis* is the primary etiologic agent of sheep and goat brucellosis.

Brucellosis has been a compulsory notification disease in Italy since 1934 and reached its highest incidence in humans in the late 1940s after World War II (20 cases per 100,000 inhabitants). Starting from the second half of the 1950s, following the adoption of

national and regional control plans, a decrease in the incidence of the disease in humans and animals was observed [25]. Due to these efforts, the majority of Italian provinces are now classified as “officially undamaged territories”; however, brucellosis continues to be an important disease in many areas of the Mediterranean region [26].

Indeed, brucellosis is still present in Sicily with a number of cases identified in both animals and humans. This situation is strongly linked to the persistence of a large number of infected animals in this territory, especially in the sheep and goat population. In fact, sheep and goat breeding is the main zootechnical activity of the region and is one of the most important resources for the regional economy. The production of local cheese by smallholders and small-scale farmers is frequent in this region. In addition, the promiscuity of the different animals (sheep, goats and cattle) is very common and increases the possibility of contamination, transmission and the spread of infections [27].

The annual 2015 report on brucellosis control that was submitted to the Integrated National Plan of the Italian Health Ministry showed that 99.6% of companies covered by the programme for the elimination of bovine brucellosis were checked and that the region with the highest prevalence and incidence was Sicily (3.3%). The same report also showed that 97.4% of the companies covered by the eradication programme of sheep and goat brucellosis were checked and that the regions with the highest prevalence and incidence were Sicily (3.7%) and Calabria (1.1%).

Sheep, goats, and their products appear to be the major sources of infection, as demonstrated by the elevated number of brucellosis cases in these animals compared to cattle; the prevalence of

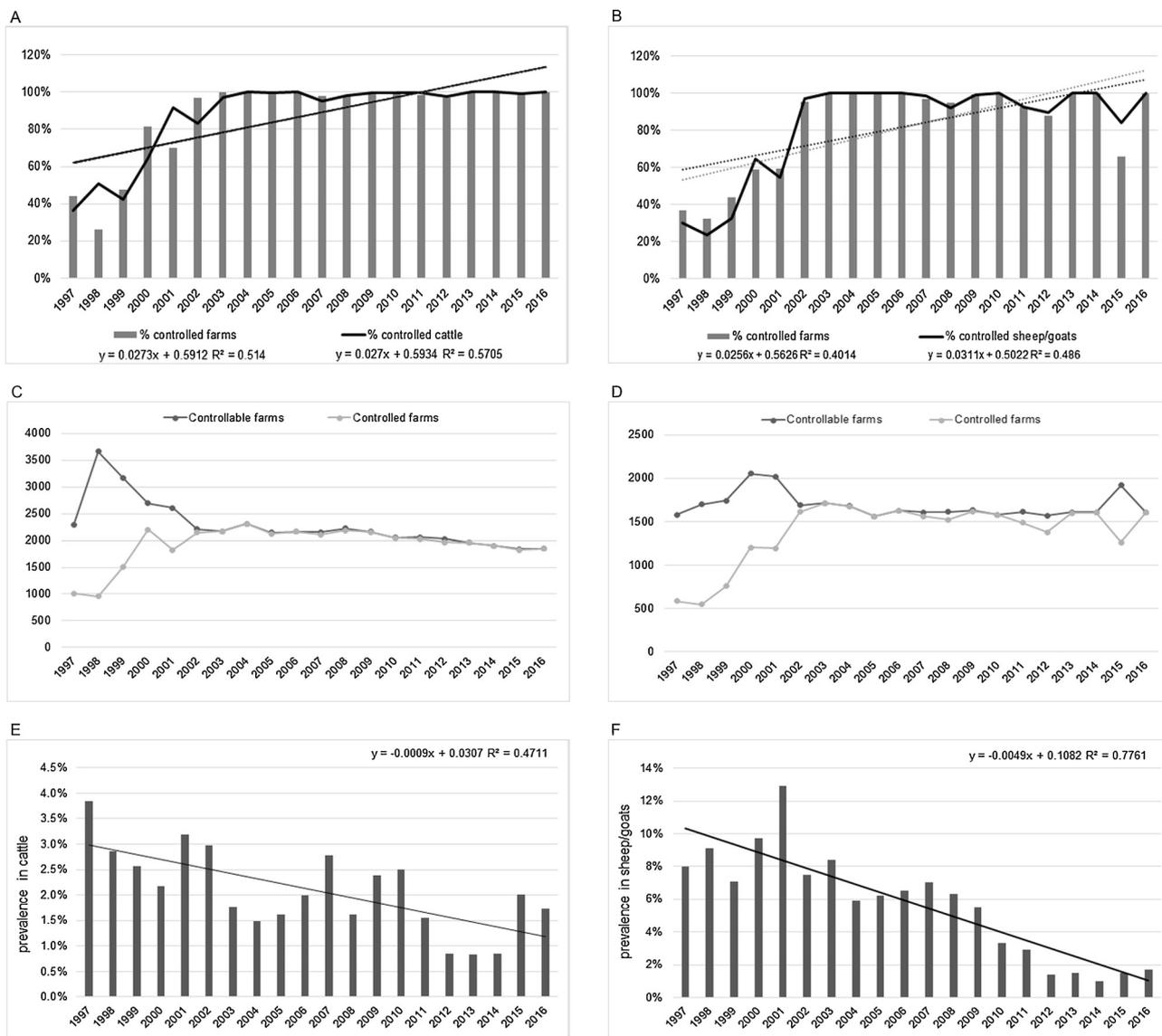


Fig. 3. Comparison between controlled farms and animals for cattle (A) and sheep/goats (B). Graphics C and D show the overlap between controlled and controllable farms for cattle and sheep/goats respectively. Prevalence of cattle (E) and sheep/goats (F) brucellosis in the considered period.

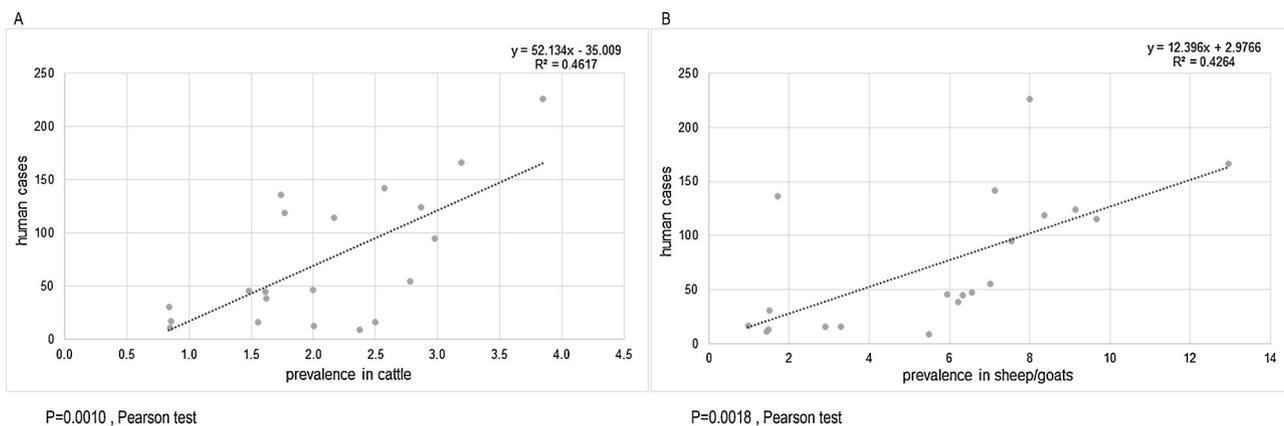


Fig. 4. Correlation between human and animal cases in cattle (A) and sheep/goats (B).

Brucella infection in sheep and goats in Messina is the highest in Italy. Moreover, sheep and goats play a key role in the spread of brucellosis in cattle and in humans; in fact, cattle are not the usual reservoir of *Brucella* spp. [23]. The incidence rates of animal bucel-

losis are variable in different countries. In Argentina the average incidence rate is 1.7 [28], in Nigeria ranges from 9.9 to 15% in cattle [29], in Libya the prevalence of the disease is 0.2% in cattle, 8.3% in sheep, and 14.8% in goats [30].

Epidemiological data on the incidence of human brucellosis are most likely underestimated, as the disease has nonspecific signs and symptoms [9,31].

During the period considered in this study, the affected subjects were commonly young adult males and there was no correlation between infection and working risk, as the percentage of at-risk workers was very low during all periods, probably because the outbreaks did not originate from controlled farms but from unofficial farming families. This finding is not in agreement with other studies [12]. Because the difference between the sexes is not linked to occupational risks, probably males are less careful about drinking unpasteurised or raw milk or eating uncontrolled cheese than females.

This study also showed that official controls efficiently reduced the incidence of the disease in animals and humans, with a significant decrement of infected compared to controlled animals following the enactment of decree 519/2002. This finding was in line with those seen in other studies [32]. The statistically significant correlation between animal and human infection means that veterinary surveillance could eliminate human brucellosis, as was seen in the northern regions [33].

However, the infection persistence indicates that small breeders, often in the form of farming families who produce and distribute homemade cheese, could evade the official controls and be a major cause of the current situation. Particularly, the habit of adding raw milk to finished cheese to improve its taste is one of the principle causes of the infection. In fact, when it was possible to identify the cause of the infection, the major implicated foods were always local cheeses (“primosale”, “tuma” and “ricotta”).

Moreover, the difference in the hospitalisation rate between 1997–2015 and the 2016 outbreak reveals a probable and significant underreporting rate. Indeed, in light of the high hospitalisation rate registered in the first period, it is very likely that only the hospitalised cases were reported and not those treated at home. Probably, the media attention focused on the most recent outbreak has prompted physicians to also report the cases treated at home. Probably, a large number of non-hospitalized cases were not reported by family physicians, thus escaping official surveillance.

Conclusions

Brucellosis remain an important public health problem worldwide. Our findings, although related to a local area, are surely overlapping to the epidemiological situation of endemic Mediterranean countries. The main public health goal is to decrease the prevalence of brucellosis among humans by eliminating the infection sources. Prevention should include implementing of the governmental surveillance programme to collect all suspected cases of brucellosis and fight the underreporting which is still much probable in the studied area; creating a smooth and fast flow of data reporting from peripheral laboratories to the specific national centre and endowing peripheral centres with the qualified laboratory personnel and equipment. Moreover, it is also necessary to enforce animal controls, vaccinate all susceptible animals and increase the level of education and awareness among people, especially regarding the consumption of not controlled milk and derivatives. Finally, the constant prevalence of the infection in animals, particularly sheep and goats, suggests the need to improve the official control measures and eradication efforts, especially in breeds that are currently not controlled and in which a high prevalence of animal brucellosis is often present. This confirms the need to improve knowledge of the risks associated with consuming raw milk and its derivatives, mainly from sheep and goats, and demonstrates that public health would benefit from cooperation between human and veterinary health services.

Limit of the study

This research focused the attention on a problem that has present in many parts of world but that has become uncommon in high-income countries such as Northern Europe and United States. For this reason, the findings could not interest the public health actions in the latter. Moreover, we hypothesise an important under-notification rate of the disease but we are not able to demonstrate or quantify it.

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Competing interests

None declared.

Ethical approval

Not required.

References

- [1] De Knecht LV, Pires SM, Hald T. Attributing foodborne salmonellosis in humans to animal reservoirs in the European Union using a multi-country stochastic model. *Epidemiol Infect* 2015;143(6):1175–86.
- [2] Facciola A, Riso R, Avventuroso E, Visalli G, Delia SA, Laganà P. *Campylobacter*: from microbiology to prevention. *J Prev Med Hyg* 2017;58(2):E79–92.
- [3] World Health Organization (WHO). Zoonoses; 2018 <http://www.who.int/zoonoses/en/>.
- [4] Nenova R, Tomova I, Saparevska R, Kantardjiev T. A new outbreak of brucellosis in Bulgaria detected in July 2011—preliminary report. *Euro Surveill* 2015;20(39).
- [5] Aloufi AD, Memish ZA, Assiri AM, McNabb SJ. Trends of reported human cases of brucellosis, Kingdom of Saudi Arabia, 2004–2012. *J Epidemiol Glob Health* 2016;6(1):11–8.
- [6] Lai S, Zhou H, Xiong W, Gilbert M, Huang Z, Yu J, et al. Changing epidemiology of human brucellosis, China, 1955–2014. *Emerg Infect Dis* 2017;23(2):184–94.
- [7] Pappas G, Akritidis N, Bosilkovski M, Tsianos EV. Brucellosis. *N Engl J Med* 2005;352:2325–36.
- [8] Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. *Lancet Infect Dis* 2006;6:91–9.
- [9] Franco MP, Mulder M, Gilman RH, Smits HL. Human brucellosis. *Lancet Infect Dis* 2007;7:775–86.
- [10] Seleem MN, Boyle SM, Sriranganathan N. Brucellosis: a re-emerging zoonosis. *Vet Microbiol* 2010;140:392–8.
- [11] Traxler RM, Lehman MW, Bosserman EA, Guerra MA, Smith TL. A literature review of laboratory-acquired brucellosis. *J Clin Microbiol* 2013;51:3055–62.
- [12] Lytras T, Danis K, Dounias G. Incidence patterns and occupational risk factors of human brucellosis in Greece, 2004–2015. *Int J Occup Environ Med* 2016;7:221–6.
- [13] Nicoletti P. Relationship between animal and human disease. In: Young EJ, Corbel MJ, editors. *Brucellosis: clinical and laboratory aspects*. Boca Raton, FL: CRC Press; 1989. p. 41–51.
- [14] European Food Safety Authority (EFSA). 2015: EU summary report on zoonoses, zoonotic agents and food-borne outbreaks. *EFSA J* 2016;14(12):4634 <https://www.efsa.europa.eu/it/efsajournal/pub/4634>.
- [15] Graziani C, Mancini FR, Adone R, Marianelli C, Pasquali P, Rizzo C, et al. La brucellosi in Italia dal 1998 al 2011. Roma: Istituto Superiore di Sanità; 2013 (Rapporti ISTISAN 13/45).
- [16] Mancini FR, Bella A, Graziani C, Marianelli C, Mughini-Gras L, Pasquali P, et al. Trends of human brucellosis in Italy, 1998–2010. *Epidemiol Infect* 2014 Jun;142(6):1188–95.
- [17] De Massis F, Di Girolamo A, Petrini A, Pizzigallo E, Giovannini A. Correlation between animal and human brucellosis in Italy during the period 1997–2002. *Clin Microbiol Infect* 2005;11(August (8)):632–6.
- [18] Gazzetta Ufficiale della Repubblica Italiana, Serie Generale n.285 del 07-12-2006 — Suppl. Ordinario n. 230. Misure straordinarie di polizia veterinaria in materia di tubercolosi, brucellosi bovina e bufalina, brucellosi ovi-caprina, leucosi in Calabria, Campania, Puglia e Sicilia.
- [19] Gazzetta Ufficiale della Repubblica Italiana, Serie Generale n.212 del 11-09-2012. Misure straordinarie di polizia veterinaria in materia di tubercolosi, brucellosi bovina e bufalina, brucellosi ovi-caprina, leucosi, nelle regioni Calabria, Campania, Puglia e Sicilia (12A09729).
- [20] Gazzetta Ufficiale della Repubblica Italiana, Serie Generale n.144 del 24-06-2015. Misure straordinarie di polizia veterinaria in materia di tubercolosi, brucellosi bovina e bufalina, brucellosi ovi-caprina, leucosi bovina enzootica (15A04879).

- [21] Ministero della Salute. Relazione annuale al PNI; 2015 <http://www.salute.gov.it/relazioneAnnuale2015/stampaDettaglioRA2015.jsp?id=991>.
- [22] Veterinary Epidemiological Bulletin. Experimental Zoo-prophylactic Institute. December 2016. <https://docs.google.com/viewer?a=v&pid=sites&srcid=aXpzc2ljaWxpYS5pdHxpenN8Z3g6MWnkNzExM2Y5N2MZZGM0Ng>.
- [23] Marianelli C, Graziani C, Santangelo C, Xibilia MT, Imbriani A, Amato R, et al. Molecular epidemiological and antibiotic susceptibility characterization of *Brucella* isolates from humans in Sicily, Italy. *J Clin Microbiol* 2007;45(9):2923–8.
- [24] Dokuzoguz B, Ergonul O, Baykam N, Esener H, Kiliç S, Celikbaş A, et al. Characteristics of *B. melitensis* versus *B. abortus* bacteraemias. *J Infect* 2005;50:41–5.
- [25] Salmaso S, Bella A, D'Ancona F, De Mei B, Mandolini D, Rota C, et al. Epidemiologia della brucellosi in Italia. *Notiziario dell'Istituto Superiore Sanità* 2000;13:4–8.
- [26] Currò V, Marineo S, Vicari D, Galuppo L, Galluzzo P, Nifosì D, et al. The isolation of *Brucella* spp. from sheep and goat farms in Sicily. *Small Rumin* 2012;106S:S2–5.
- [27] Caracappa S. Livestock production and animal health in Sicily, Italy. *Parassitologia* 1999;41:17–23.
- [28] Russo AM, Mancebo OA, Monzón CM, Gait JJ, Casco RD, Torioni de Echaide SM. Epidemiology of caprine and ovine brucellosis in Formosa province, Argentina. *Rev Argent Microbiol* 2016;48(April–June (2)):147–53.
- [29] Njeru J, Wareth G, Melzer F, Henning K, Pletz MW, Heller R, et al. Systematic review of brucellosis in Kenya: disease frequency in humans and animals and risk factors for human infection. *BMC Public Health* 2016;16(August (1)):853.
- [30] Al-Griw HH, Kraim ES, Farhat ME, Perrett LL, Whatmore AM. Evidence of ongoing brucellosis in livestock animals in North West Libya. *J Epidemiol Glob Health* 2017;7(December (4)):285–8.
- [31] Mandell, Douglas and Bennett's principles and practice of infectious diseases. sixth edition Elsevier Inc.; 2005. p. 2669–74.
- [32] Zinsstag J, Schelling E, Roth F, Bonfoh B, de Savigny D, Tanner M. Human benefits of animal interventions for zoonosis control. *Emerg Infect Dis* 2007;13:527–31.
- [33] Farina F, Fuser R, Rossi M, Scotton PG. Brucellosis outbreak in Treviso province caused by infected cheese from an endemic area. *Infez Med* 2008;16(3):154–7.