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Original Article

Incidence Patterns and Occupational Risk Factors of Human Brucellosis in Greece, 2004–2015

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Abstract

Background: Brucellosis is the most common bacterial zoonosis worldwide. Greece has the highest reported incidence among EU countries. However, occupational risk factors have not been well described.

Objective: To determine the incidence patterns and exposure risk factors of brucellosis in Greece.

Methods: We used national-level surveillance and occupational denominator data to estimate the incidence patterns and exposure risk factors of brucellosis in Greece, with particular emphasis on occupation.

Results: Between November 2003 and December 2015 a total of 2159 human brucellosis cases was reported. The mean incidence rate was 1.62 per 100 000 population per year. A large majority of cases (77.1%) reported consumption of unpasteurized milk or contact with livestock animals. Most cases occured in farmers and livestock breeders (1079 [87.7%] of 1231 cases reporting their occupation), corresponding to an annual incidence of 7.1 per 100 000. However, there were other occupations with a similar or higher risk: butchers and abattoir workers (12.7 per 100 000), laboratory personnel (3.1 per 100 000), while the highest risk was for veterinarians (53.2 per 100 000).

Conclusion: Brucellosis incidence in specific occupational groups was much higher than in the general population. These results underline the importance of collecting information on occupation, both during the diagnostic process and in the surveillance system. Besides efforts to control brucellosis in animals, organized prevention efforts are needed within an occupational health framework, especially for the most vulnerable workers.

Keywords: *Brucella*; Brucellosis; Occupational exposure; Communicable diseases; Occupational diseases; Epidemiology

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Introduction

Brucellosis is the most common bacterial zoonotic disease worldwide, with global distribution, causing more than 500 000 new human cases each year.[1] It is transmitted to humans from infected animals, usually goats, cattle, pigs, sheep, and dogs, either through direct inoculation or consumption of contaminated food and milk. *Brucella* is a small Gram-negative aerobic bacterium, which is readily killed by boiling or pasteurization; thus food-borne exposure is normally limited

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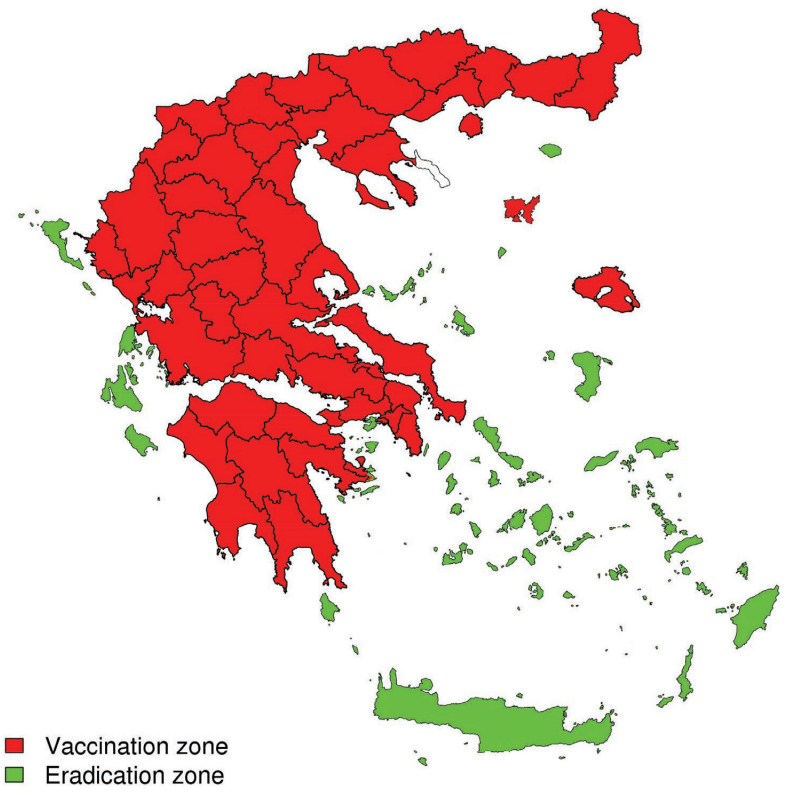

Figure 1: Zones of animal brucellosis control program in Greece

to persons consuming unpasteurized milk and dairy products. On the other hand brucellosis is considered primarily an occupational hazard affecting those working with infected animals or their tissues—farmers, livestock breeders, veterinarians, abattoir workers, *etc.*[2] These occupations are exposed through inhalation, contact with conjunctival mucosa, or entry of the bacteria through cuts and abrasions in the skin. Brucellosis is also a hazard affecting laboratory workers handling specimens containing *Brucella* species, as the pathogen is readily aerosolized and has a low infective dose.[3]

Incidence of brucellosis in humans is declining in many countries due to systematic efforts to control the disease in animals, particularly in the developed nations. According to the latest epidemiological data (2012), in Europe the annual incidence rate is low, at less than 0.1 per 100 000 population. However, four countries in the EU account for the majority (73%) of reported cases, namely Greece, Italy, Spain and Portugal.[4] Greece, in particular, has a brucellosis control program in animals since 1975. The country is divided into two control zones (Fig 1); in the "vaccination zone" (comprising of continental Greece plus the islands of Evoia, Lesvos, Limnos and Thasos) reproductive animals are legally required to be inoculated against *Brucella*, while in the "eradication zone" (all remaining islands) inoculation is prohibited, regular serologic monitoring is performed, and no animals from the "vaccination zone" may be introduced.

Despite these efforts, Greece still has the highest incidence rate of human brucellosis among EU countries.[4] At the same time, there is a lack of recent published data on the epidemiology of human brucellosis in Greece, particularly regarding exposure risk factors and occupation. This is important, because symptoms and signs of brucellosis in humans are highly non-specific and often present as fever of unknown origin. Therefore, its diagnosis requires a high index of clinical suspicion.[5] A clear understanding of who is at risk of

TAKE-HOME MESSAGE

- Brucellosis is a known but underappreciated occupational hazard.
- In Greece, which has the highest reported brucellosis incidence among EU countries, most cases occur in farmers and livestock breeders. However, other occupations have similar or higher risk of infection with *Brucella*, most notably veterinarians.
- Occupational history is a vital part of the diagnostic process and should be consistently collected during surveillance of human brucellosis cases.

Brucella infections can facilitate early diagnosis and treatment of the disease, preventing unnecessary complications and morbidity.

We therefore, used the available surveillance data (at the national level) to examine the incidence patterns of human brucellosis in Greece. Our objective was to elucidate the main exposure risk factors for the disease, especially occupational risk factors, and draw useful conclusions for clinical and public health practice.

Materials and Methods

Brucellosis in humans is a notifiable disease in Greece, with physicians and laboratories countrywide reporting every case that met the EU case definition[6] to the Hellenic Centre for Disease Control and Prevention (HCDCP) using a standard paper notification form, available at the HCDCP Web site (*http://goo.gl/n9q6p4*). The form includes basic demographic and clinical information, as well as information about risk factors, including occupation. The item in the form about occupation specifically enquires about working in particular high-risk jobs (*ie*, farmer, livestock breeder, butcher or abattoir worker, and veterinarian) or any other job that the notifying physician assesses as "high-risk." Working in a laboratory that handles specimens containing *Brucella* species is not included as a prespecified option in the form.

We used all notifications data from November 2003, when the current national surveillance system was established, until the end of 2015. We undertook a descriptive analysis, focusing on exposure risk factors and reported occupations. Apart from the four main high-risk jobs prespecified in the notification form, other jobs were reported as free text; therefore we ran through the list and grouped together similar job descriptions to the maximum

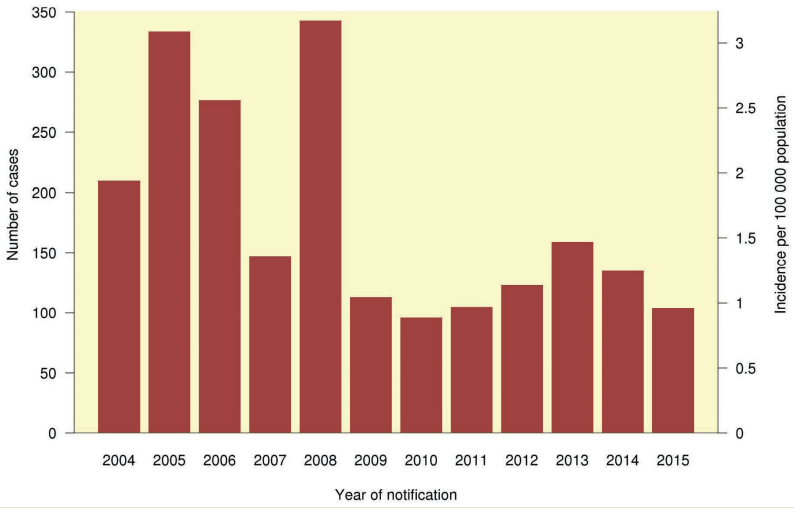

Figure 2: Notified cases of human brucellosis in Greece, 2004–2015

meaningful extent, with discrepancies resolved by consensus. Data from the 2011 population census and other official surveys performed by the Hellenic Statistical Authority (such as the 2013 farm structure survey) were used as denominators for the

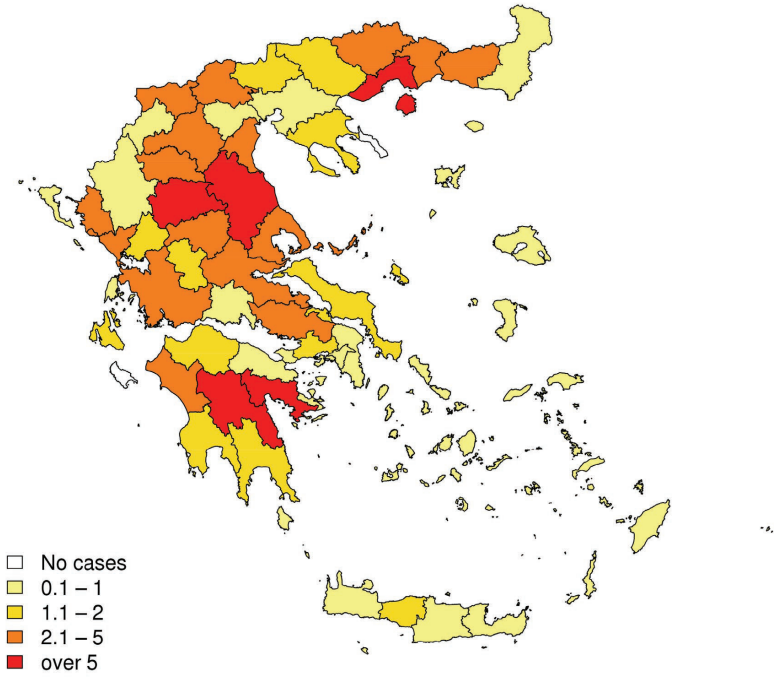

Figure 3: Mean annual human brucellosis incidence in Greece, 2004–2015, per 100 000 population

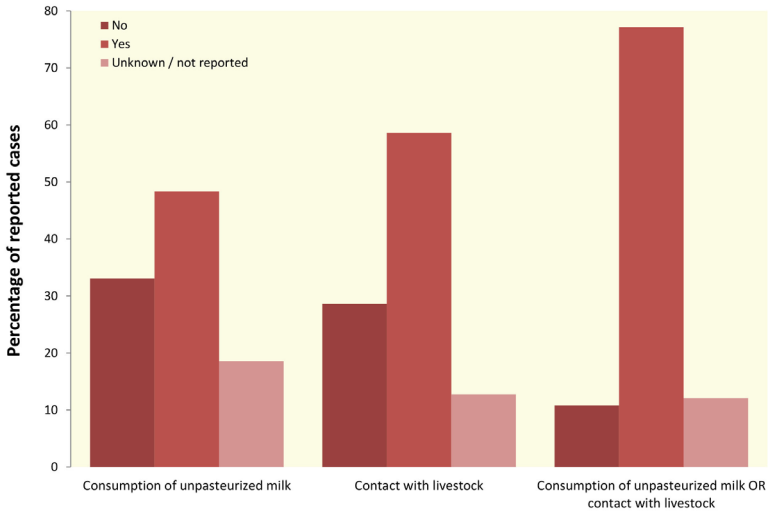

Figure 4: Main reported risk factors for human brucellosis

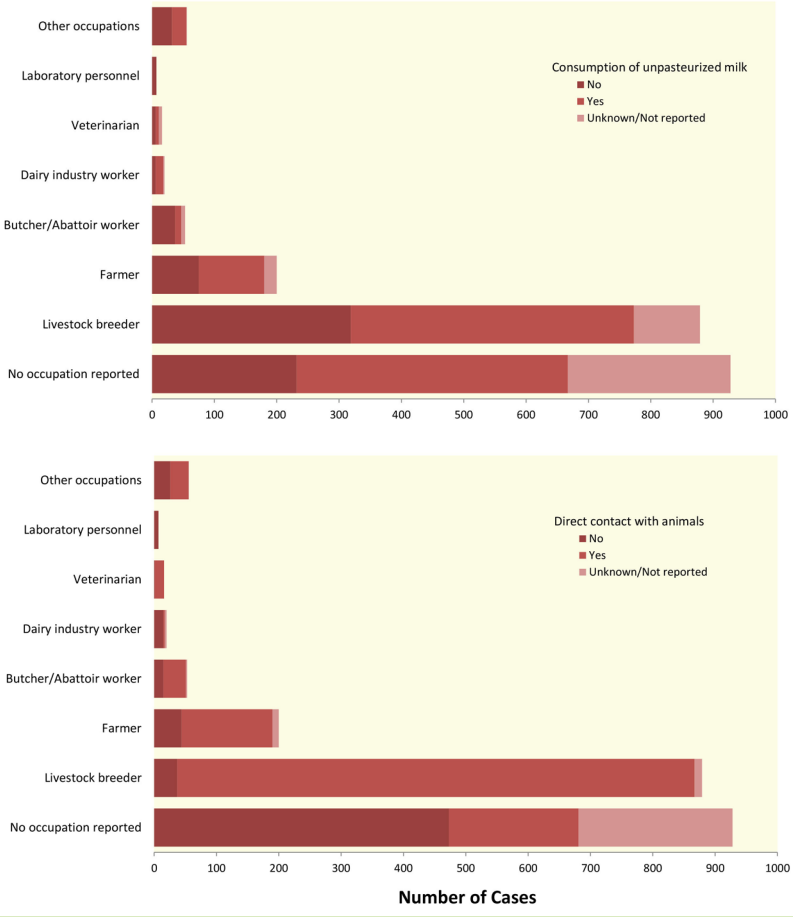

Figure 5: Notified cases of human brucellosis in Greece, 2004–2015, by occupation

calculation of incidence rates among different occupational groups. All analyses were performed using the R software environment, version 3.2.3.[7]

Results

From November 2003 to December 2015, 2159 human brucellosis cases were reported, translating to a mean incidence rate of 1.62 per 100 000 population per year (Fig 2). The sharp rise in incidence during 2008 was caused by an large outbreak in the northern Aegean island of Thasos, with 98 reported human cases,[8] after which the annual incidence fell to about 1 per 100 000 population. The median age of patients was 44 (range 0 to 95) years; 68% of cases were male (*ie*, a male:female ratio of 2.2), reflecting exposure patterns in the community. Diagnosis was confirmed by serology in 79% of cases; a positive culture was found in 31%. The overall majority of cases occured within the "vaccination zone" compared to the "eradication zone" (2091 *vs* 50 cases, corresponding to an annual incidence of 1.77 *vs* 0.34 cases per 100 000 population, respectively). The geographical pattern of incidence was widespread, and more intense in rural areas with substantial livestock breeding activity (Fig 3). The species of *Brucella* was characterized in 206 cases (9.5%), of which 88% were *B. melitensis* and 12% were *B. abortus*.

The two most commonly reported risk factors for contracting human brucellosis were consumption of unpasteurized milk (48%, 1044 cases) and contact with livestock animals (59%, 1266 cases), with most cases (77.1%) reporting at least one of the two (Fig 4). Occupation was reported by 928 cases (43%), most of them working as livestock breeders (71.4%, 879 cases) or farmers (16.2%, 200 cases). In addition, 4.3% (53 cases) worked as butchers or abattoir workers, 1.6% (20 cases) worked in the dairy industry, 1.3% (16 cases) were

veterinarians, and 0.6% (7 cases) were laboratory personnel, presumably working with *Brucella* isolates. Most of these workers reported consumption of unpasteurized milk and contact with livestock animals, as did cases who did not report their occupation; the major exception was laboratory personnel, none of whom reported either risk factor (Fig 5).

According to the 2013 farm structure survey, 1 243 288 persons were working in the agricultural sector (including livestock breeding).[9] Therefore, the 1079 brucellosis cases in farmers and livestock breeders corresponded to a mean annual incidence rate of 7.1 per 100 000 population. According to the 2011 census, Greece had 2473 veterinarians and 3665 microbiologists; the number of laboratory personnel is not known, but we assume (conservatively) that it could be five times the number of microbiologists. Therefore, the incidence of brucellosis in laboratory personnel could be at least 3.1 per 100 000 per year, and in veterinarians 53.2 per 100 000 per year. Similarly, although the number of butchers, abattoir workers and workers in the dairy industry is not known, according to the 2011 census 47 199 persons were classified as "food processing workers and related occupations," thus the 73 cases in this group corresponded to a conservative annual incidence estimate of 12.7 per 100 000 (Fig 6).

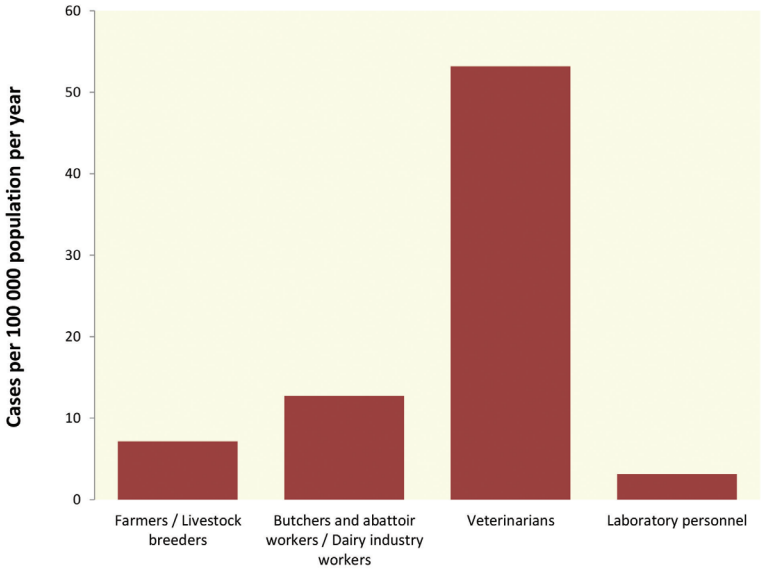

Figure 6: Incidence rate of human brucellosis in Greece, 2004–2015, by occupation

Discussion

This analysis confirms that brucellosis in humans is primarily an occupational hazard. Although the majority of cases occured in farmers and livestock breeders, other occupations appear more vulnerable in terms of risk. This must be taken into account when considering brucellosis in a patient with fever of unknown origin, and indicates a need for targeted occupational health interventions in these groups. In particular, the relatively few veterinarians with brucellosis translate into a substantially higher incidence rate compared to other occupations. In addition, the seven cases of brucellosis in laboratory personnel represent a known but underappreciated occupational hazard. In fact, such events should prompt a review of biosafety precautions in the laboratory, in order to prevent further infections in the same setting.[10]

The finding that half of all notified cases reported consumption of unpasteurized milk, even among high-risk occupations, indicates that many cases can be prevented just by raising awareness of the importance of consuming only pasteurized or treated (*eg*, boiled or properly prepared) milk and dairy products. However, more than 20% of reported cases did not report consumption of unpasteurized milk or contact with animals. Although this might be due to poor patient recall, it could also be due to less thorough investigation of the cases. Enhancing case investigation is an important component of a successfull brucellosis control program.

The message for clinicians is that occupation forms an indispensable part of the patient's history and should always be queried, particularly when the illness is nonspecific or in patients with fever of unknown origin. In similar fashion, brucellosis surveillance in Greece should systematically collect detailed occupational information from all cases, not just those deemed to be working in a high-risk job. This will allow identification of other potentially vulnerable jobs, and more comprehensive quantification of risk.

Under-reporting is a potential problem in any surveillance system, particularly for less common diseases.[11] The completeness of our data, both in terms of case ascertainment and in terms of reporting, is not known; this is a limitation of our study. Due to the phrasing of the relevant reporting form item, occupations have not been comprehensively reported, particularly those not perceived to be as high-risk. In addition, although we used the best available denominators to calculate incidence rates by occupation, these should still be regarded as approximate estimates, sufficient only to make general comparisons.

Surveillance of human cases is an essential indicator of progress towards brucellosis control; strengthening it should be a priority. At the same time, it is important to raise awareness of brucellosis as an occupational health hazard. Organized preventive interventions should be targeted to those workers with the highest risk, and surveillance data can guide these efforts, as our results illustrate.

Conflicts of Interest: None declared.

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