Reemergence of Human Brucellosis in Israel

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ABSTRACT: **Background:** The epidemiology of human brucellosis (HB) continues to evolve.

Objectives: To describe the current epidemiology of HB in Israel in general and in the population at risk.

Methods: We calculated the incidence of HB in Israel for the period 2009–2015, overall and for the Arab population. Data are based on mandatory reporting of HB in Israel, defined clinically with either laboratory confirmation or epidemiological linkage to a laboratory-confirmed case. We mapped the geographic distribution of HB throughout the study period according to localities. We specified localities with high incidence (≥ 10 per 100,000 population) and mapped the distribution of dense localities with time.

Results: The incidence of HB in the general population in Israel increased sharply from 1.9 per 100,000 in 2009 to a peak of 7.3 per 100,000 in 2014. Each year, 95–100% of cases occurred among Arabs, thus the incidence in the Arab population increased from 10 per 100,000 in 2009 to 33.5 per 100,000 in 2014. Throughout this period 133 different localities reported at least one case of HB, and of these 20 were high-incidence localities during one year at least. During the period 2009–2013 the number of affected localities ranged from 35 to 44 per year and the disease was local, while in 2014 there were 82 localities distributed across the country.

Conclusions: We demonstrate the importance of analyzing incidence in the population at risk for a disease. HB is an urgent public health issue in the Arab population in Israel, mandating an immediate and long-term eradication and control program.

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KEY WORDS: human brucellosis, epidemiology, Israel, Arab population

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Human brucellosis (HB), one of the most common zoonotic diseases worldwide [1-4], is an endemic disease in the Middle East including Israel [5]. *Brucella melitensis*, acquired mainly from infected goats and sheep, has been the only identified causative agent of brucellosis in Israel since 1985 [6] when *B. abortus* was eradicated following the introduction of the S19 vaccine for animals by the Veterinary Service [7]. This disease occurs mainly in the Arab population, which comprises about 20% of the Israeli population and lives mostly in segregated communities in southern, northern and eastern central regions. We aimed to evaluate the incidence of HB in Israel and its geographic distribution in recent years.

METHODS

Data for the present study were obtained from the Epidemiology Division of the Ministry of Health. HB has been a mandatory reported disease in Israel since 1951 [5]. Case definition is based on clinical presentation, with either laboratory confirmation and/or epidemiological linkage to a laboratory-confirmed case. Laboratory confirmation includes a positive culture or a serum agglutination test, IgG > 1:160. Testing is performed locally and results are confirmed by the national reference laboratory in the Kimron Veterinary Institute at Beit Dagan [5]. The reporting system relies on dual reporting performed by microbiology laboratories and the treating physician.

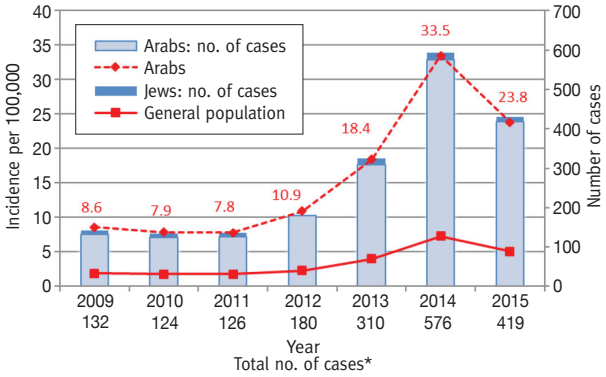
To describe the geographic distribution of the disease, we extracted the residence locality of all reported cases between the years 2009 and 2015. In order to identify areas with high activity of the disease, we further defined high-incidence localities as those having at least 10 reported cases of HB and an annual incidence of ≥ 10 per 100,000 populations in the same year. HB incidence was calculated as the number of cases per 100,000 population per year. Population-size data were obtained from the website of the Israel Central Bureau of Statistics (CBS, www.cbs.gov.il). HB incidence among Arabs was calculated as the number of cases of HB reported among Arabs during a year divided by the number of Arab inhabitants in Israel in the same year. To calculate the HB incidence in the Arab population of Jerusalem we used the number of Arab inhabitants of the city as given by the CBS data. In 2015, data on the classification of HB for Arabs and Jews were unavailable and the incidence was calculated using the total number of cases in 2015 minus the average percentage of Jews between 2009 and 2014.

RESULTS

The incidence of HB in the general population in Israel increased sharply from 1.9 per 100,000 in 2009 to a peak of 7.3 per 100,000

in 2014 [Figure 1]. The increase started in 2012 with 182 cases of HB reported, representing a 32% increase over the preceding year. The highest number of cases was recorded in 2014 with 595 cases of HB. Each year, 95–100% of cases occurred among Arabs, thus the incidence in the Arab population increased from 10 per 100,000 in 2009 to 33.5 per 100,000 in 2014 (internal report of epidemiology division published in 2015) [Figure 1].

Figure 1. Human brucellosis overall and among Arabs in Israel 2009–15



*Total number of cases with available ethnicity data (ranging from 93 to 99% of total reported cases per a single year)

Table 1. Number of localities and cases of HB per region in Israel between 2009 and 2015

Health office	No. of localities (no. of cases)						
	2009	2010	2011	2012	2013	2014	2015
South	17 (64)	17(69)	28 (72)	27 (160)	42 (273)	50 (344)	38 (240)
Jerusalem	1(9)	3 (20)	1(16)	2 (2)	2 (9)	3 (37)	2 (50)
Hadera	2 (4)	2 (11)	2 (5)	3 (3)	0	7 (65)	5 (29)
Acre	11 (39)	12 (18)	13 (18)	4 (7)	13 (22)	20 (139)	14 (54)
Others	7 (11)	1 (1)	–	2(2)	2 (4)	2(2)	4(9)
Total*	38 (127)	35 (119)	44 (111)	38 (174)	59 (308)	82 (587)	63 (382)

*Number of localities with available data for reported cases (ranging between 80% and 98% per year)

Residence data were available for 83–97% of HB cases reported per year between 2009 and 2015; 133 different localities reported at least one case of HB. The number of affected localities ranged between 35 and 44 per year for the years 2009 to 2012. During the following 3 years and in parallel with the increase in HB incidence, the number of localities reporting HB increased to 59, 82 and 63, respectively [Table 1]. The disease spread from the south to the north. In 2012, 92% of HB cases (160/174) were from 27 localities in the south from among 38 localities reporting HB cases, while in 2014 and 2015 more than 40% of HB cases were reported in other parts of the country [Table 1].

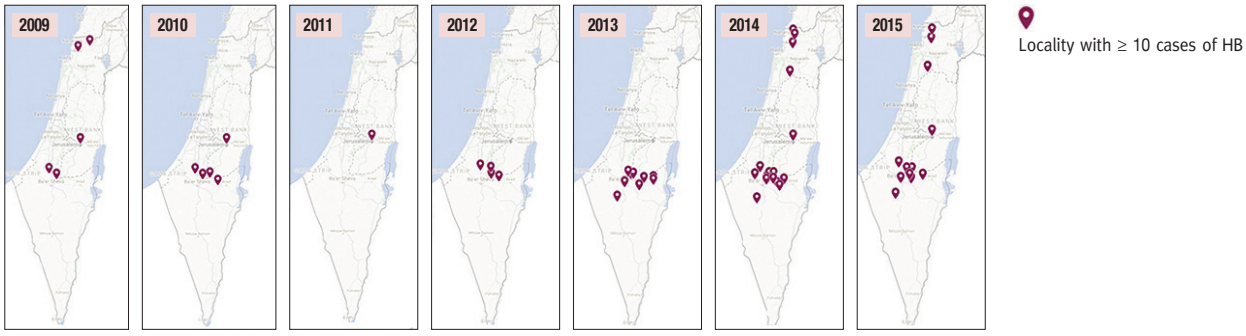
Twenty localities fulfilled the criteria for high HB incidence. While these localities were all in the south for the period 2010–2013, they spread countrywide in 2014–2015 [Figure 2].

DISCUSSION

The largest previous outbreak of HB in Israel peaked in 1988 when the incidence increased to 11 per 100,000. This outbreak was controlled following a national intervention program for the control of livestock brucellosis that was initiated in 1994 [8]. In the last overview summarizing the global epidemiology of HB, Israel was presented as one of the countries achieving control of brucellosis [4]. In fact, in the relevant, Arab, population of Israel, control of HB has never been achieved. Moreover, the eradication program was discontinued only 4 years after its initiation [8]. As expected, HB incidence re-increased to a level of 10 per 100,000 in the Arab population between the years 2003 and 2012, followed by the ongoing outbreak since then.

The present study shows that the disease was restricted to the southern part of Israel between 2010 and 2013 and spread to other parts of the country in 2014–2015. The number of localities in Israel reporting brucellosis increased from 38 in 2009 to 82 in 2014, including 17 high-incidence localities in four different regions of the country. This probably reflects the spread of uncontrolled livestock brucellosis and emphasizes the missed opportunity to contain the disease in 2012 when

Figure 2. Spread of HB between 2009 and 2015: high-incidence localities



most cases were confined to a specific region in the country [Figure 2]. Furthermore, the persistence of HB endemicity for years in some Arab localities may indicate the non-satisfactory functioning of the veterinary services in such places, combined with cultural practices of dairy product preparation, trading of unvaccinated goats, unawareness and knowledge gaps [9], and other social issues [10] beyond the scope of this report.

The high activity of the disease seemed to continue in 2016 and 2017, as shown by weekly data updated in the Ministry of Health website (http://www.health.gov.il/UnitsOffice/HD/PH/epidemiology/Pages/epidemiology_report.aspx). Human brucellosis results in complications, as reported recently in almost one-fifth of a series of patients with *Brucella* bacteremia from southern Israel, including infective endocarditis in 13% of cases as well as abortions in 4 of 11 pregnant women diagnosed with brucellosis during pregnancy [11]. Other severe, although rare, complications have been reported, including endovascular infection [12] and severe fatal neurobrucellosis [13]. Such a burden of disease also carries financial and health resources costs, acknowledged in part in a recent local study [14].

The main limitation of the present study is its reliance on passive surveillance. Despite mandatory reporting guidelines of the Health Ministry, under-reporting is likely. Variable compliance of HB reporting was observed in different countries and sometimes in different regions of the same country [15]. The under-reporting rate was found to be as high as 25% in Greece [16]. Yet, since no changes were introduced to the reporting methods in Israel during the study period, longitudinal incidence data can be deemed indicative of actual epidemiological trends. The absence of data regarding disease in animals makes the picture incomplete.

Our study emphasizes the importance of investigating a disease in the affected population rather than in the general population. If continued endemicity in certain Arab localities had not been ignored, perhaps the eradication efforts would not have been cancelled and the current outbreak prevented. The long-term persistence of brucellosis in Arab localities in Israel is most probably the source of the recent outbreak reported from different parts of the country [17], affecting all age groups of the population [11,17,18] in different types of localities. The current incidence of HB among Arabs in Israel mandates an immediate long-term interventional national plan for eradication of the disease.

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"Pedantry and mastery are opposite attitudes toward rules. To apply a rule to the letter, rigidly, unquestioningly, in cases where it fits and in cases where it does not fit, is pedantry... To apply a rule with natural ease, with judgment, noticing the cases where it fits, and without ever letting the words of the rule obscure the purpose of the action or the opportunities of the situation, is mastery"

George Polya (1887–1985), Hungarian mathematician