ORIGINAL ARTICLE

Epidemiological and Clinical Features of People with Malta Fever in central Iran, 2013–2018: results from national surveillance system

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ABSTRACT

Background: Malta fever is one of the most common diseases among humans and animals in some areas of Iran. This study investigated the epidemiological features of People with Malta Fever in Yazd province in central Iran.
Methods: In this cross-sectional study, 1117 cases of Malta Fever that registered by brucellosis national surveillance system at Yazd University of Medical Sciences from January 2013 and December 2018 were extracted. All analyses were done using GIS version 10.3 and SPSS. The significance level was set at <0.05.
Results: The average cumulative incidence of Malta Fever was 16.35 (14.18-18.51) per 100,000 over the 6-year study in the province. The highest occurrence in khatam and Abarkuh counties and the lowest in the capital of Yazd Province, i.e., Yazd City (116.69 (114.10-119.27) vs. 8.60(6.95-10.24) in 100000). About 56.4% of patient were males with the mean age of 37.38 ±19.46 years. 65.4% of the patients lived in urban areas and 81.3% had a history of consuming of unpasteurized dairy products. The highest proportion was observed among housewives(32.8%) and livestock breeders(14.3%).The most common clinical manifestations recorded were fever (75.4%) and chills (59%) Myalgia (49%), Back pain(47.4%) and Sweating(43.2%), respectively.
Conclusion: The findings of the present study reveal that at-risk groups for Malta Fever in Yazd province include young and middle-aged men, housewives, livestock breeders, people have a history of contact with animals and consuming of unpasteurized dairy products especially raw milk and cheese in south districts and urban areas of Yazd province.
Keywords: Brucellosis, Epidemiology, Clinical manifestation, Iran

INTRODUCTION

Brucellosis or Malta fever is a very infectious disease between animals and humans. Malta fever is caused via Brucella bacteria, in particular Brucella melitensis, Brucella abortus, and Brucella suis species[1].

The transmission most regularly occurs as a result of close contact by animals or their produces (concluded the consumption of unpasteurized milk and dairy produces, herding, and lambing) and via work-related contact [2, 3]. Direct human to humans transmission rarely happens, though it has been described that transmission may happen by feeding, breast and sexual contact[4] So, Professions with animal contact, such as farm labors, veterinarians, ranchers, abattoir workers and lab staffs are classified as high risk groups[5].

Malta fever is one of the common multi-systemic disease (known as the disease of a thousand faces) with over 500,000 cases in the world every year. [6-8]. The prevalence of diseases are more than 10 cases per 100,000 population in some countries[9, 10].

Brucellosis is still the most important public health problem worldwide, But mostly and especially in the Mediterranean region, comprising Iran, Turkey, the Arabian Peninsula, the Indian subcontinent, Mexico, parts of Central and South America[11, 12].

Despite abundant efforts made by the ministry of health, Iran remains an endemic area for the Malta fever. According to the report of Center for Disease Control and Prevention (Iran) [13] the four types of provinces for incidence of human brucellosis are as follows: Type 1: very high (31-41 per 100000 populations), Type 2: high incidence regions, (21-30 per 100000 populations), Type 3: moderate incidence regions, (11-20 per 100000 populations) and Type 4: low incidence regions(0-10 per 100000 populations). Based on this classification, the province of Yazd is located in the moderate incidence regions.

Public health surveillance is a tool to assessment the health status and population behavior served by ministries of health. The key purpose of surveillance is to provide information for action and enable decision makers to lead and manage more efficiently by providing well-timed, valuable evidence[14].

In response to the spread of Malta fever, and due to the zoonotic and economic importance of this disease, an early warning system epidemic was immediately required in the epidemic area [15]. So brucellosis surveillance systems was established that registered data brucellosis cases, every case of brucellosis must be reported within 7 day through National Notifiable Disease Surveillance System by medical works in Iran. Thus, the identification of the major risk factors for Malta fever it play a crucial role in understanding of the nature of the disease for prevention programs. This study investigated the epidemiological

characteristic of People with Malta Fever in Yazd province in central Iran.

MATERIAL AND METHODS

Yazd province is sited in the central of Islamic Republic of Iran, and founded on the General Population and Housing Census, it had a population of 1,138,533 (971355 urban, 167178 rural area) in 2016. The city of Yazd is the center for Yazd province. It also consists of ten county. The production of 233,000 tons of raw milk during 2016 that ranked fifteen in the country in expressions of production milk. A total of 436980, 426000 and 154400 sheep, goats and cows were reported in 2016 in this province by Yazd veterinary organization, respectively.

Data source: In this cross-sectional study, data of Malta Fever cases that recorded by brucellosis national surveillance system at Yazd University of Medical Sciences from January 2013 and December 2018 were enrolled. In this study, all Malta Fever cases were confirmed by laboratory diagnosis. The cumulative incidence for Malta Fever was calculated on a annually (cases/ total population) and described per 100,000 inhabitants.

Information on these patients was recorded in specific forms. Required data, such as age, gender, education level, job, place of residence (city or rural), History of animal contact, Type of contact with animals, History of consuming unpasteurized dairy products, Type of dairy product, nationality, herd and animal vaccination, relapse after systemic and local treatment was extracted from the related forms.

Statistical Analysis: In this way, data of 1117 patients was extracted and analyzed using GIS version 10.3 and Statistical Package for the Social Sciences Version 17.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics (frequency and relative frequency) and chi-square test at the significance level of 0.05 were employed to analyze the collected data.

Ethical considerations: In using raw data from the national brucellosis surveillance system, all principles have been considered to protect the confidentiality of personal information of individuals.

RESULTS

Between January 2013 and December 2018, 1117 confirmed Malta Fever cases were reported from Yazd province, in the central of Iran.

The cumulative incidence of Malta Fever increased from 11.95 (10.04-13.85) cases/100,000 population in 2013 to 14.40 (12.34-16.45)cases/100,000 population at the ending of 2018. However, the average incidence of Malta Fever was 16.35 (14.18-18.51) per 100,000 over the 6-year study in the province: 12.53 (10.58-14.47) per100,000 in the city population and 38.58 (35.42-41.43) 100,000 in the rural population (Fig. 1).

Furthermore the highest occurrence in khatam and Abarkuh counties and the lowest in the capital of Yazd Province, i.e., Yazd City (116.69(114.10-119.27) vs. 8.60(6.95-10.24) in 100000) (Fig. 2).

Table 1: Distribution of demographic characteristics and potential risk factors in the patients with Malta Fever in Yazd province

Variables	Frequency	%age	P value
Gender			
Male	630	56.4	p<0.001
Female	487	43.6	
Age (year)			
0-20	262	23.5	
21-40	397	35.5	
41-60	301	26.9	p<0.001
61-80	149	13.3	
>81	8	0.7	
Location			
Urban	730	65.4	p<0.001
Rural	387	34.6	
Occupation			
Housewife	366	32.8	
livestock breeders	160	14.3	
farmer	90	8.1	
Worker	131	11.7	p<0.001
student	131	11.7	
Staff	56	5	
Free job	129	11.5	
NO(children)	54	4.8	
History Contact with animals			
Yes	661	59.2	p<0.001
No	456	40.8	
Using unpasteurized dairy products			
Yes	908	81.3	p<0.001
No	209	18.7	
Type of dairy product			
Raw milk	500	44.7	
Fresh cheese	295	26.4	
Ice cream	59	5.3	
Cream	20	1.8	p<0.001
Butter	10	0.9	
Colostrum	19	1.7	
No Interviewed	214	19.2	
Season			
Spring	330	29.5	
Summer	371	33.2	
Autumn	260	23.3	p<0.001
Winter	156	14	

Table 2: Distribution of clinical manifestations, complications and laboratory findings of the patients with Malta Fever in Yazd

Variables	%age
Clinical manifestations	
Fever	75.4
Chills	59
Myalgia	49
Sweating	43.2
Headache	29
Back pain	47.4
Testicular pain	18.1
Complications	
Arthritis	3.4
Spondylitis	0.26
Epididymo orchitis	0.35
No complication	95.99
Wright. Test	
1/40	2.4
1/80	14.8
1/160	26.1
1/320	22.4
1/640	14.2
1/1280	20.1

Distribution of Malta Fever in the spring, summer, autumn and winter was 29.5%,33.2%, 23.3% and 14%, respectively (p<0.001).

The majority of the patients (95.1%) had been diagnosed for the first time (new cases), 630 (56.4%) males and 487 (43.6%) females with the mean age of 37.38±19.46 years ranged from 5 to 94 years were enrolled. 730(65.4%) of the patients lived in urban areas. 661 (59.2%) of patients had a history of contact with animals, and 908 (81.3%) had a history of consuming of unpasteurized dairy products. The highest frequency was observed among housewives (32.8%) and livestock breeders (14.3%), respectively (p<0.001).

Among consumed unpasteurized dairy products, milk (44.7%, n=500 patients), cheese (26.4%, n = 295 patients) and Ice cream (5.3%, n=59 patients) had the highest consumption rate among patients, respectively (p<0.001). Also, 356 (31.9%) patients had a History of morbidity in family members. Moreover, 108 patients (9.66%) were hospitalized due to their disease, and 38 (3.4%) patients were diagnosed with Arthritis, as complications of the disease. A total of 26.1% and 22.4% of patients had Wright test with titer of 1.160 and 1.320 test, respectively. The most common clinical manifestations recorded were fever (75.4%) and chills (59%) (Table1,2).

Fig. 1 Trend of cumulative incidence of Malta Fever in Yazd province, Iran in urban, rural and total populations (2013-2018).

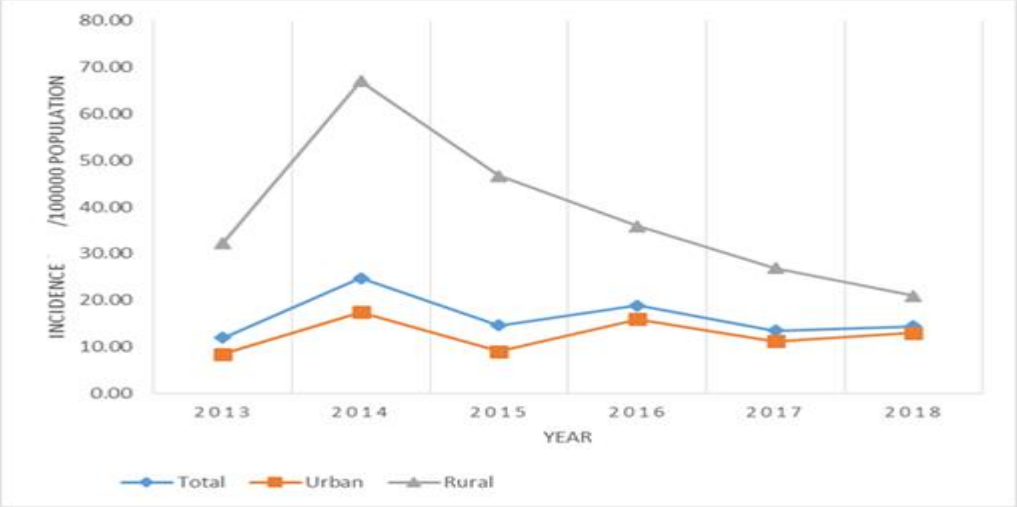
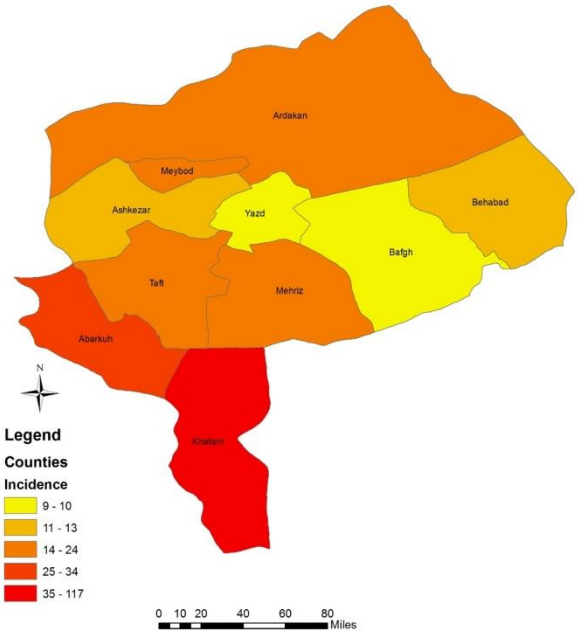


Fig. 2. Cumulative Incidence (per 100000 population) of Malta Fever in Yazd Province (2013–2018



DISCUSSION

Malta Fever is endemic in, Middle East, Latin America, Africa, Central Asia, and the Mediterranean Basin. The Eastern Mediterranean district entails of 22 countries, including the Iran. The annual incidence of Malta Fever in Middle Eastern and Mediterranean littoral varies between 1 and 78 patient per 100,000 population[16, 17]. However, it seems that only a small proportion of cases are reported due to absence of diagnostic facilities in the poor and remote countries of this district. Most province of Iran are endemic for the Malta Fever, especially the regions where human lives in close contact with livestock[18].

In the present study, the average incidence of Malta Fever was 16.35/ 100,000 over the 6-year study in the province: 12.53/100,000 in the urban population and 38.58 /100,000 in the village population. However, the cumulative incidence of Malta Fever increased from 11.95 cases/100,000 population in 2013 to 14.40 cases/100,000 population at the ending of 2018.

According to one study, the average incidence of Malta Fever in the Iranian population was 21 / 100,000 population, although this changed between 1.5 and 107.5 per 100,000 population in different province of Iran[19]. In a study, Dastjerdi et al. [20] reported the average annual cumulative incidence of 12.1 cases per 100000 people. In a study, Etminani et al. reported the incidence of 26 cases per 1000000 people in Khorasan Razavi Province [21]. Also, Soofian et al. in Arak Province reported the average cumulative incidence of 60 per population [22]. The results of these studies similar to estimation Center for Disease Control and Prevention, Ministry of Health and Medical Education (Iran)[13] indicates that province of Yazd is located in the moderate incidence regions in Islamic Republic of Iran.

In this study, the highest occurrence in khatam and Abarkuh counties and the lowest in the capital of Yazd Province, i.e., Yazd City (116.69 vs. 8.60 in 100000) (Fig. 2). Khatam and Abarkuh are the main livestock breeding pole in Yazd province. The main occupation of the people living in these regions are animal husbandry. These can be attributed to the higher incidence of Malta Fever in these regions.

The results of this study showed that, both genders were vulnerable to the Malta Fever But, the proportion of the disease was more common in the male sex with a mean age of 37.38 ±19.46 years which is similar to some studies[23, 24]. Malta Fever can happen in both genders and any age group[25]. The majority of age group was between 21-40 yr (35.5%) which was similar to other studies[24, 26].

In this study, 65.4% of patients were from urban regions; Haj Abdolbaghi et al.[27] and Haddadi et al. [28]reported 84.3% and 59.5% of patients from urban areas, respectively. In Yazd, the percentage of population who live in urban regions is more than rural regions; in contrast, Eini et al study were done in Hamadan (Most people live in rural areas) 72.2% of patients were from rural regions[24].

In the current study, 81.3% of patients had a history of consuming of unpasteurized dairy products and raw milk, cheese and Ice cream were the dairy product consumed most commonly by patients, respectively which was similar to Rahmanian et al. and Haj Abdolbaghi et al. studies, a consumption of unpasteurized dairy products was reported in 87.7% or 88.3% of patients[23, 27].

Cases of Malta Fever happened throughout the year, but 29.5% and 33.2% happened in the spring and summer which was similar to other studies [19, 23, 24].

The most common clinical manifestations of the patients were fever, chills, Myalgia, Back pain and Sweating, respectively. In a study by Djalalinia et al sweating, fever and Splenomegaly were the most common clinical manifestations of Pediatric [29]. However, Malic et al. reported fever, sweating, bone pain; back pain and headache were the most common signs and symptoms in Malta Fever[30]. In addition, in our study 4.01% of patients had complications (Arthritis, Spondylitis and Epididymo orchitis). The complication of Malta Fever was reported 7.4% to 10.9% in other studies in Iran [24, 28, 31].

CONCLUSION

The findings of the present study reveal that at-risk groups for Malta Fever in Yazd province include young and middle-aged men, housewives, livestock breeders, people have a history of contact with animals and consuming of unpasteurized dairy products particularly raw milk and cheese in south districts and urban areas of Yazd province. Malta fever is one of the common multisystem diseases (known as the disease of a thousand faces) which can involve different parts of the human body with different clinical manifestations in patients, and early identification and treatment of Malta fever may help to prevent from complications and relapse.

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Conflict of interest: The authors report no conflict of interest.

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REFERENCES

1. Alizadeh M, Safarzadeh A, Bahmani M, et al. Brucellosis: Pathophysiology and new promising treatments with medicinal plants and natural antioxidants. *Asian Pacific Journal of Tropical Medicine.* 2018;11(11):597.
2. Zheng R, Xie S, Lu X, Sun L. A Systematic Review and Meta-Analysis of Epidemiology and Clinical Manifestations of Human Brucellosis in China. 2018;2018:5712920.
3. Cash-Goldwasser S, Maze MJ, Rubach MP, et al. Risk factors for human brucellosis in northern Tanzania. *The American journal of tropical medicine and hygiene.* 2018;98(2):598-606.
4. Ceylan A, Kostu M, Tuncer O, Peker E, Kirimi E. Neonatal brucellosis and breast milk. *Indian journal of pediatrics.* Mar 2012;79(3):389-391.
5. Ali S, Nawaz Z, Akhtar A, Aslam R, Zahoor MA, Ashraf M. Epidemiological Investigation of Human Brucellosis in Pakistan. *Jundishapur Journal of Microbiology.* 2018;11(7).

6. Godfroid J, Al Dahouk S, Pappas G, et al. A “One Health” surveillance and control of brucellosis in developing countries: moving away from improvisation. *Comparative immunology, microbiology and infectious diseases.* 2013;36(3):241-248.
7. Berger S. *Brucellosis: Global Status: 2018 edition*: GIDEON Informatics Inc; 2018.
8. Dadar M, Shahali Y, Whatmore AM. Human brucellosis caused by raw dairy products: A review on the occurrence, major risk factors and prevention. *International journal of food microbiology.* Dec 12 2018;292:39-47.
9. Fallah Rostami F, Borzoueisileh S, Ebrahimpour S. An overview of brucellosis epidemic in Iran. *Crescent Journal of Medical and Biological Sciences.* 2016;3(1):35-36.
10. Migisha R, Nyehangane D, Boum Y, et al. Prevalence and risk factors of brucellosis among febrile patients attending a community hospital in south western Uganda. *Scientific reports.* 2018;8(1):15465.
11. Facciolà A, Palamara MAR, D'Andrea G, et al. Brucellosis is a public health problem in southern Italy: Burden and epidemiological trend of human and animal disease. *Journal of Infection and Public Health.* 2018/11/01/ 2018;11(6):861-866.
12. Khazaei S, Karami M, Mohammadbeigi A, et al. Spatio-Temporal analysis of brucellosis in Hamadan Province, West of Iran: 2009–2015. *Advances in Human Biology.* 2018;8(3):145.
13. Zeinali M, Shirzadi M, Haj rasuliha H. *National Guideline for Brucellosis Control*. Second ed. Tehran: Raz Nahan Publishing; 2012.
14. Peck ME, Chanachai K, Jenpanich C, Amonsin A, Alexander BH, Bender JB. Seroprevalence of brucellosis in goats and sheep in Thailand: Results from the Thai National Brucellosis Surveillance System from 2013 to 2015. *Transboundary and emerging diseases.* Jun 2018;65(3):799-805.
15. Yang L, Bi ZW, Kou ZQ, et al. Time-Series Analysis on Human Brucellosis During 2004–2013 in Shandong Province, China. *Zoonoses and public health.* 2015;62(3):228-235.
16. Al Shehhi N, Aziz F, Al Hosani F, Aden B, Blair I. Human brucellosis in the Emirate of Abu Dhabi, United Arab Emirates, 2010-2015. Oct 12 2016;16(1):558.
17. Musallam, II, Abo-Shehada MN, Hegazy YM, Holt HR, Guitian FJ. Systematic review of brucellosis in the Middle East: disease frequency in ruminants and humans and risk factors for human infection. *Epidemiology and infection.* Mar 2016;144(4):671-685.
18. Mirnejad R, Jazi FM, Mostafaei S, Sedighi M. Epidemiology of brucellosis in Iran: A comprehensive systematic review and meta-analysis study. *Microbial pathogenesis.* 2017;109:239-247.
19. Moradi G, Kanani S, Majidpour M, Ghaderi A. Epidemiological status survey of 3880 case of brucellosis in Kurdistan. *Iranian Journal Of Infectious Diseases And Tropical Medicine.* 2006;11(33):27-33.
20. Dastjerdi MZ, Nobari RF, Ramazanpour J. Epidemiological features of human brucellosis in central Iran, 2006–2011. *Public Health.* 2012;126(12):1058-1062.
21. Hashtarkhani S AM, Jarrahi L, Etminani K. Epidemiological characteristics and trend of incidence of human brucellosis in Razavi Khorasan province. *Mashhad University of Medical Sciences.* 2015;58(9):531-538.
22. Farahani S, Shah Mohamadi S, Navidi I, Sofian M. An investigation of the epidemiology of brucellosis in Arak City, Iran,(2001-2010). *Arak Medical University Journal.* 2012;14(7):49-54.
23. Rahmanian V, Rahmanian K, Mansoorian E, Jahromi AS, Madani A. Epidemiological characteristics and temporal trend of human and bovine brucellosis cases, Southern Iran, 2009-2016. *Pakistan Journal of Medical and Health Sciences.* 2018;12(1):488-495.
24. Eini P, Keramat F, Hasanzadehhoseinabadi M. Epidemiologic, clinical and laboratory findings of patients with brucellosis in Hamadan, west of Iran. *Journal of research in health sciences.* 2012;12(2):105-108.
25. Roushan MRH, Ebrahimpour S. Human brucellosis: An overview. *Caspian journal of internal medicine.* 2015;6(1):46.
26. Rajabi J, Hamidi-Farahani R, Mansouri F, Soleiman-Meigooni S. Incidence and risk factors of brucellosis in Kermanshah province, Iran during 2010-2014. *Infectious disorders drug targets.* Dec 11 2018.
27. Zadeh Y. Epidemiological, clinical, diagnostic and therapeutic survey in 505 cases with Brucellosis. *Tehran University Medical Journal.* 2001;59(4):34-46.
28. Hadadi A, Rasoulinezhad M, Afhami S, Mohraz M. Epidemiological, clinical, para clinical aspects of brucellosis in Imam Khomeini and Sina Hospital of Tehran (1998-2005). *Journal Of Kermanshah University Of Medical Sciences.* 2006;10(3):242-251.
29. Djalalinia S, Arjmand R, Gholami M, et al. Frequency and Clinical Manifestations of Pediatric Brucellosis in Iran: A Systematic Review. *International Journal of Pediatrics.* 2019;7(2):9037-9047.
30. Akhvlediani T, Bautista CT, Garuchava N, et al. Epidemiological and Clinical Features of Brucellosis in the Country of Georgia. *PloS one.* 2017;12(1):e0170376.
31. Ebrahimpour S, Bayani M, Moulana Z, Hasanjani Roushan MR. Skeletal complications of brucellosis: A study of 464 cases in Babol, Iran. *Caspian J Intern Med.* Winter 2017;8(1):44-48.