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Investigation of the Epidemiological Situation of Malta Fever in the Cities under Mashhad University of Medical Sciences during the years 2016 to 2022

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Abstract:

Background: Management of Malta fever disease requires policy-making and accurate epidemiological statistics and information.

Aim: The present study was conducted to determine the epidemiological status of Malta fever.

Materials and Methods: This study is of the secondary data analysis type, which was conducted using the recorded data of patients with brucellosis in the health center of Mashhad City from 2016 to 2022. Data related to 12,714 cases of brucellosis were analyzed using R software and Chi-2, Pearson, and independent t-statistical tests.

Results: The average age of the patients was 33.18 ± 18.81 years. About 87% of disease cases were related to rural areas and 13% to urban areas. The average annual incidence of the disease was 287 cases per 100,000 population at risk of the disease. The highest incidence rate was in 2020, and the lowest incidence rate was in 2016. The most cases of disease were related to the first three months of the year, and the least cases were related to the last three months of the year. Most cases of the disease were related to housewives, cattle breeders, and farmers.

Conclusion: The incidence of the disease increased from the beginning of the study to 2020 and decreased from 2020 to the end of the study. Health policymakers should integrate medicine, ecology, and education for the prevention and control of brucellosis. This holistic strategy recognizes the interconnectedness of human, animal, and environmental health, emphasizing the need for collaborative efforts across sectors to address the multifaceted nature of the disease.

Keywords: Malta fever, Epidemiology, Brucellosis, Disease, Infectious, Health, Treatment, Human, Animal.

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1. INTRODUCTION

Brucellosis, also known as Malta fever disease, is a common illness that affects both humans and animals, leading to significant financial burdens on societies [1, 2]. It is considered one of the most important and well-known diseases worldwide, particularly in Iran [3, 4]. Brucellosis presents with nonspecific signs and symptoms, resembling other febrile illnesses [5, 6]. Common symptoms include fever, chills, sweating, body and muscle aches, joint and spine pain, as well as gastrointestinal, respiratory, urinary, and cardiovascular issues. Nervous system involvement and depression are also reported. Although not typically fatal, brucellosis is a cause for concern due to its economic impact on societies [7-9].

According to the World Health Organization, approximately 500,000 cases of brucellosis are reported annually worldwide, with rates ranging from 4 to 10% in developed countries [10]. The distribution of the disease varies globally, with regions like North America, Canada, and Australia reporting very low incidence rates [less than 2 cases per 100,000 people], while the Mediterranean region and the Middle East have higher rates [1 to 78 cases per 100,000 people] [11]. In Iran, despite having an extensive healthcare system, brucellosis remains endemic and ranks fourth in terms of incidence. The incidence of brucellosis varies across different regions of Iran, with an average reported annual incidence of 43 cases per 100,000 people based on research conducted between 1370 and 1387 [12].

Razavi Khorasan province is one of the areas with a high prevalence of brucellosis in Iran due to having suitable weather conditions for animal husbandry and the use of traditional animal husbandry methods [13]. According to the results of the studies conducted in Razavi Khorasan during the years 1388-1392, the average incidence of brucellosis was reported as 26 per hundred thousand people. More than 70% of the total cases of brucellosis were related to rural areas and urban outskirts [14].

Malaria deaths are rare, but it imposes a huge economic burden on countries. With a decrease in productivity and the loss of livestock, it has caused a significant drop in the economy of countries. So, in many parts of the world, it is considered an important economic and public health issue. This disease is mainly transmitted to humans through the consumption of contaminated dairy products, meat, and other contaminated meat products, direct contact with infected animals, and skin scratches [15-17]. Because a large part of the Iranian population lives and earns their livelihood through agriculture, animal husbandry, and related professions, brucellosis has a high prevalence [18-20]. Health measures, including vaccination of animals, improvement of the animal-keeping environment, veterinary care, and education of people who are at risk of Malta fever, are useful solutions to prevent Malta fever. Also, preventing contact with infected animals, not consuming non-pasteurized dairy products, and early diagnosis and treatment of patients are other ways to fight human Malta fever [21-23].

Information on the prevalence of brucellosis in animals and, if possible, in the human population should be obtained before any control program implementation. One way to research is to determine if age, job, place of residence, season, consumption of dairy products, and history of contact with animals have a significant relationship with the incidence of Malta fever. However, brucellosis is considered an occupational hazard for people in direct contact with infected animals, as well as a non-occupational hazard for those who consume unpasteurized dairy products. Due to the economic burden caused by the disease, the lack of public knowledge about its spread and management, especially in rural areas, and other related factors, it is necessary to prioritize this disease in different regions [24, 25]. The prevalence of the disease varies in different regions based on weather conditions, livestock species, animal health levels, access to pasteurized products, and diagnostic tests used. In general, the diagnosis of brucellosis should consider epidemiological, clinical, and laboratory information simultaneously. Understanding the number of cases and disease incidence in humans and animals, as well as the epidemiological characteristics in infected areas, can lead to successful prevention and control of the disease through information exchange between health and veterinary departments [26, 27].

In general, Iran is among the countries with a high incidence of Malta fever in the Eastern Mediterranean region. Considering that the northern provinces of the country have a high prevalence, Razavi Khorasan province and especially Mashhad city are considered areas of interest in the control and prevention of this disease [13]. Therefore, this study was conducted for an epidemiological investigation of Malta fever in Mashhad City.

2. MATERIALS AND METHODS

This study is a secondary data analysis. In this study, the recorded data of patients with brucellosis who visited health centers, offices, outpatient clinics, and hospitals in the cities covered by Mashhad University of Medical Sciences were analyzed during the years 2016 to 2022. The tool for collecting information was a checklist including 7 items: age, place of residence, occupation, season, history of contact with infected animals, history of consumption of non-pasteurized dairy products, and history of vaccination.

The inclusion criteria of the patients included those who, in addition to having symptoms, had a positive serological test (Wright greater than 1.80 and 2ME test greater than 1.40) and had been treated by a doctor with the diagnosis of Malta fever. From the years 2016 to 2022, 12,714 cases of Malta fever were registered in the city, which was fully investigated. After collecting the information, the pre-processing stage was performed, and actions, such as removing extra fields, unifying the data unit and format, merging and generating new fields, *etc*., were performed using Microsoft Excel software. Finally, the data were analyzed using R software. The chi-square

test was used to measure the relationships between qualitative variables, and Pearson's correlation test was used to measure the correlation between quantitative variables. Independent t-test was also used to compare the average of independent groups. ArcGIS and GeoDa software were used for geographic analysis.

In this research, first, the data of Malta fever patients were entered into ArcGIS software separately for each region. To show the spatial distribution of patients based on the mentioned period, density points were used. In this study, all patient information was kept confidential, and the researchers followed the ethical principles of Helsinki in all research cases.

3. RESULTS

The present study was conducted in the subset of cities of Mashhad University of Medical Sciences during the years 2016 to 2022. In this study, a total of 12,714 cases of Malta fever were examined. Of these, 7193 (56.5%) were men and 5551 (43.5%) were women. The average age of the patients was 33.18±18.81 years during the years under investigation. The average age of onset of Malta fever in men was 35.39±18.03 years, and in women, it was 30.96±19.01 years, and this difference was statistically significant (p-value < 0.00). The lowest age of onset of the disease among all examined patients was 1 year, and the highest age of onset was 101 years. The most cases of the disease, with some 7909 (62%) cases, were in the age group of 50-16 years, and the least cases of the disease were in the age group of under 15 years; so that in both sexes, the frequency of the disease was higher in this age group. According to the results of this study, 11,068 (87%) cases of Malta fever were reported in rural areas, and 1,634 (13%) were reported in urban areas (Table **1**). The average annual incidence of the disease was 287 cases per 100,000 people at risk of the disease, so the highest incidence rate was in 2020, and the lowest incidence rate was in 2016.

The incidence of brucellosis in the subset of cities of Mashhad University of Medical Sciences increased from the beginning of the study to 2020. It decreased from 2020 to the end of the study (Fig. **1**). The incidence of the disease in terms of different months of the year shows that the highest incidence of Malta fever was reported at the beginning of February, May, June, and July. The lowest incidence was reported from November to March.

In general, the spatial distribution of brucellosis was higher in the northeastern and southeastern regions than in the western regions in the studied cities. The incidence of brucellosis was low in the cities of Kashmar, Bardaskan, Khalil Abad, Mashhad, Khaf, Bakharz, and Quchan, moderate in the cities of Taibad, Rashtkhwar, Chenaran, and Darghs, and high in the cities of Kalat, Sarakhs, and Fariman (Fig. **2**). The cities of Mashhad and Khaf were characterized by low incidence in all years, and the city of Kalat had a low incidence in the last year of the study and high incidence in other years (Fig. **3**). The incidence of Brucellosis disease in Kalat city in the studied years ranked first, with Sarakhs and Roshtkhar cities ranking second and third respectively. The lowest incidence was related to Mashhad City (Fig. **4**).

Regarding the occurrence of Malta fever in different occupations, the highest occurrences were related to housewives (37.2%), ranchers and farmers (28%), students (10.6%), and workers (9.3%); 14.9% of cases were in other occupations. According to the results of this study, a history of consumption of unpasteurized dairy products was seen in 78% of disease cases, indicating a lack of sufficient awareness and attention to health standards regarding disease transmission in this region. About 18.6% of the investigated patients had a history of vaccination, 48.6% had no history of vaccination, and the rest had an unknown vaccination history. In terms of treatment, 89.4% of patients were successfully treated, while 10.6% reported treatment failure. There were no reported deaths related to Malaria disease among the studied patients.

Table 1. Frequency distribution of brucellosis patients based on demographic information from 2016 to 2022 in Northeast of Iran.

Residence		Age(n)			Gender(n)		Total	Year
Rural	Urban	>50	16-50	0-15	Female	Male		
740	123	180	560	128	355	513	868	2016
1119	121	308	753	182	544	699	1243	2017
1327	218	342	975	229	697	849	1546	2018
2045	361	574	1494	338	1033	1373	2406	2019
2528	406	679	1870	387	1245	1691	2936	2020
2005	225	488	1406	337	963	1268	2231	2021
1304	180	441	851	192	684	800	1484	2022
11068 (87%)	1634 (13%)	3012 (24%)	7909 (62%)	1793 (14%)	5551 (43,5%)	7193 (56.5%)	12714 (100%)	Total (%)

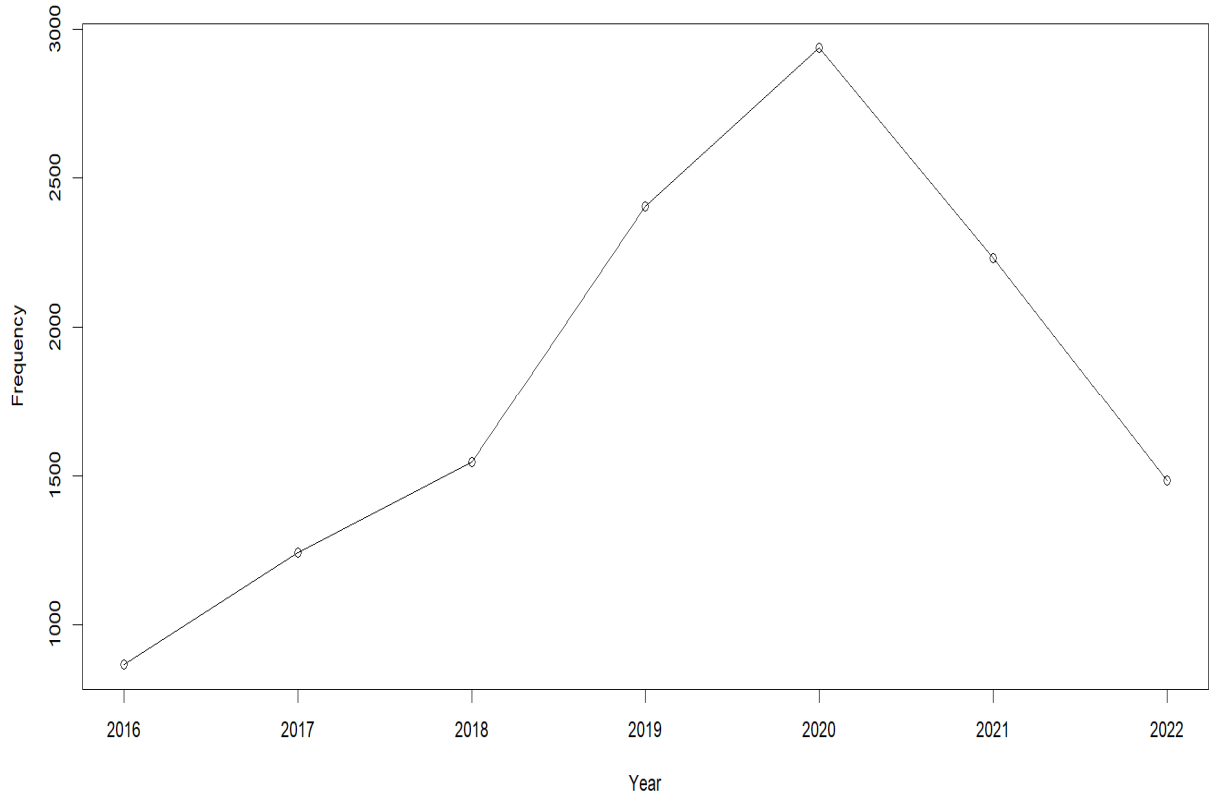

Fig. (1). Trends of brucellosis in Northeast of Iran during 2016–2022.

Fig. (2). Location of Razavi khorasan province in Iran. Forteen study regions are shown with red coulure.

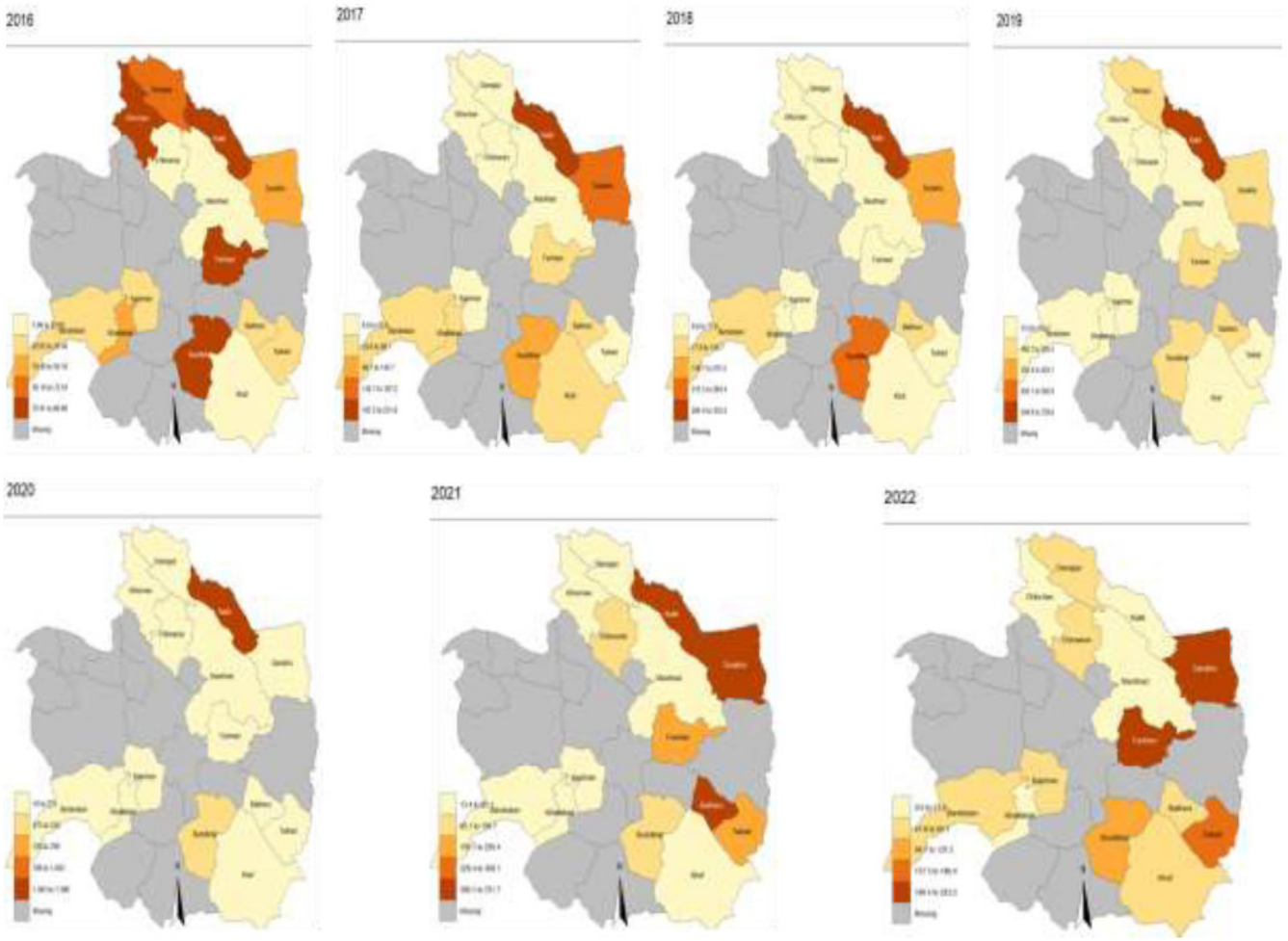

Fig. (3). Spatial distribution of incidence rates of brucellosis in Northeast of Iran (2016–2022). This map was created using R software by Tma and the tydyvers package.

4. DISCUSSION

The present study was conducted to determine the epidemiological status of Malta fever in the cities under Mashhad University of Medical Sciences during the years 2016 to 2022. Although Malta fever has been eradicated in some countries, unfortunately, it still exists as an endemic health problem in our country.

The findings of the present study showed that the prevalence of Malta fever in men was higher than in women, with a prevalence of 56.5% in men and 43.5% in women. In terms of the occurrence of Malta fever in different occupations, the highest occurrences were related to housewives, livestock farmers, farmers, students, and workers, respectively. In interpreting this research finding, it can be pointed out that Malta fever is generally a work-related disease, the prevalence of which is higher in men than in women. Therefore, the high percentage of the disease in men can be attributed to the greater activity of men in these areas. Occupations, such as agriculture, shepherding, animal husbandry, butchery, and work in slaughterhouses are related to traditional methods. On the other hand, the spread of Malta fever in housewives can also be due to hand milking and accompanying them in livestock and agricultural affairs. In line with this finding of the present study, the results of several studies also indicate that the prevalence of Malta fever is higher in men than in women [28-31]. However, the results of the studies conducted in Kurdistan and Lorestan show that the prevalence of Malta fever is higher in housewives than in men [26, 32]. In interpreting the discrepancy between the results of these studies and the findings of the present research, it is possible to point to the different geographical, cultural, and social conditions in different regions.

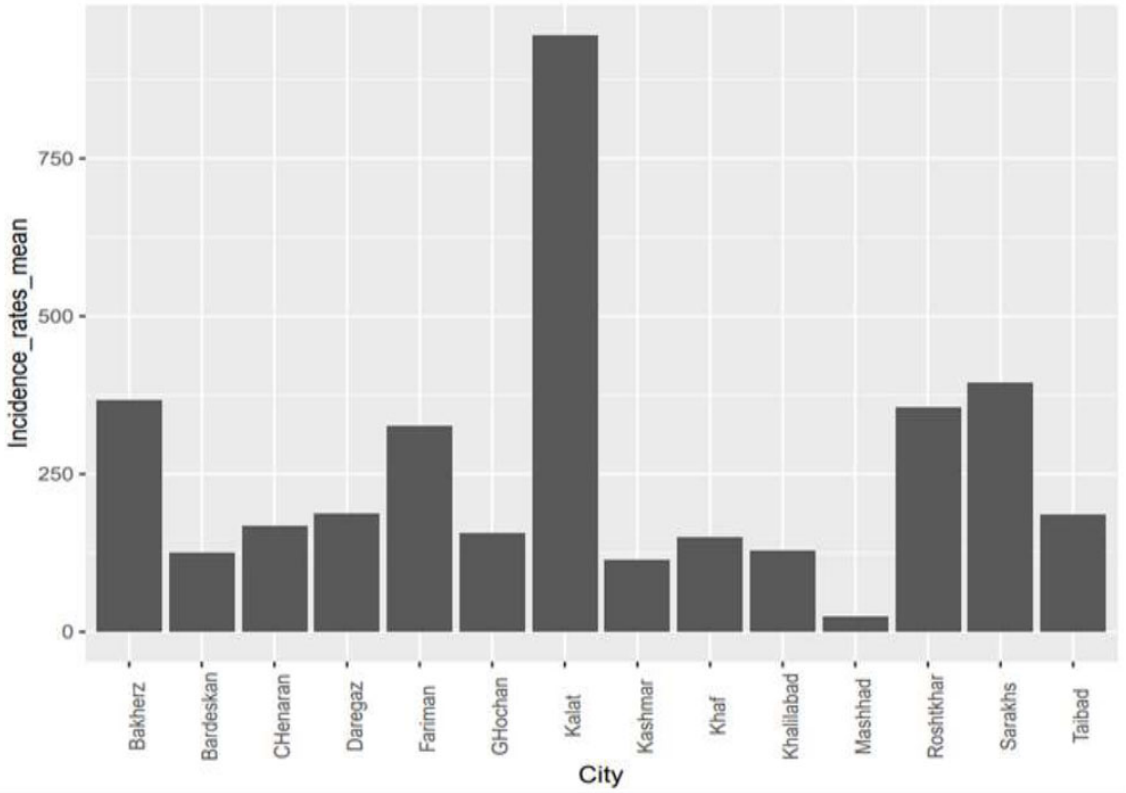

Fig. (4). Distribution of brucellosis in cities affiliated to Mashhad University of Medical Sciences of Razavi Khorasan province during 2016–2022.

The findings of the present study showed that the average age of the patients during the investigated years was 33.18 years. The average age of onset of Malta fever was 35.39 years in men and 30.96 years in women. The most cases of the disease were in the age group of 16-50 years and the least cases of the disease were in the age group of under 15 years. In the interpretation of this research finding, it can be mentioned that Malta fever is more common in the middle-aged group who are active in livestock and agriculture. Therefore, because this age group is active economically and socially, it needs special attention in the matter of education for this group of people. In line with this research finding, the results of the study of Gozidehkar *et al*. study showed that the average age of Malta fever patients was 36 [31]. In the study of Shirzadi *et al*., the highest frequency of the disease occurred at the age of 30-59 years [28] and in the studies of Bagheri and Bagherizadeh and their colleagues at the age of 33 [30, 33]. Also, in a study in the north and northwest of Iran, the average age of patients at the time of diagnosis was 34 years [34]. The results of a study in Mashhad showed that most of the patients suffering from Malta fever were young people and were in the age group of 16-24 [25].

The findings of the current research showed that 87% of the cases of Malta fever were reported in rural areas, and 13% of the cases were reported in urban areas. In the interpretation of this research finding, it can be pointed out that consumption of non-pasteurized dairy products, more contact of villagers with livestock and animal excrement, and the presence of more livestock in rural areas can be among the reasons for the higher prevalence of Malta fever in rural areas. Along with this finding of the present study, the results of the study by Gozidehkar *et al*. in Qaenat City [31] and the results of other studies in Khorasan and Kurdistan also showed that the prevalence of Malta fever in rural areas is significantly higher than in urban areas [25, 32].

The findings of the current research showed that the average annual incidence of the disease was 287 cases per 100,000 population. The highest incidence rate was in 2020, and the lowest incidence rate was in 2016. The incidence of brucellosis in the subset of cities of Mashhad University of Medical Sciences kept increasing from the beginning of the study to 2020, and it has been decreasing from 2020 to the end of the study. In the interpretation of this research finding, it can be pointed out that the rising trend of the disease in the cities under Mashhad University of Medical Sciences can be due to more access of people to laboratory services, improvement of the diagnosis process, and accurate recording of information and statistics. Also, the increase in the prevalence of the disease in the livestock population and the importation of unhealthy livestock from the southern parts of the country,

which are illegal and lack vaccination, are other reasons related to this finding of the present study.

In line with this current research finding, the results of the study of Gozidehkar *et al*. [31] showed that the trend of Malta fever in Qaenat City was on the rise from 1994 to 1400. Also, in this regard, the results of Shirzadi *et al*.'s study showed that the trend of Malta fever in Khorasan from 2009 to 2011 was upward. In 2012, this trend decreased, and again, from 2013 to 2015, it was upward [28]. However, in some studies, such as Jafarnejad's study during the years 2009 to 2016 and Norouzinezhad's study in Lorestan during the years 2015 to 2016, presenting programs, such as control of livestock infection with vaccination and face-to-face training of livestock farmers, the process of contracting Malta fever has been reduced [29, 32].

The findings of the present study show that the trend of disease incidence varies according to different months of the year. The highest incidence of Malta fever was from April to July, and the lowest incidence was from November to March. In interpreting this research finding, it can be pointed out that in the first four seasons of the year, there is more livestock birth. Additionally, due to the increased contact of livestock farmers with aborted animal fetuses and more people using non-pasteurized dairy products, it can lead to more disease incidence. In line with this current research finding, the results of the study by Gozidehkar *et al*. [31] showed that Malta fever disease is more common in summer and spring, which is the breeding season of livestock. In their study, 62.9% of disease cases were seen in the first half of the year, and 37.1% occurred in the second half of the year. This finding of the present study is also consistent with other similar studies [26, 32].

The findings of the current research indicate that in 78% of disease cases, there is a history of consuming non-pasteurized dairy products, which shows a lack of sufficient knowledge and attention to health standards regarding disease transmission in this region. In line with this finding of the present study, the results of Gozidehkar *et al*. [31] showed that contact with livestock and non-pasteurized dairy products, especially non-pasteurized milk and cheese, was most frequent among those suffering from Malta fever. Additionally, in studies conducted in Fasa, Lorestan, and Isfahan, the consumption of cheese and unpasteurized milk was the most frequent (27%, 30%, 37%). Despite the confirmation of the relationship between the consumption of unpasteurized dairy products and disease in previous studies, unpasteurized dairy products, especially local cheese made from unboiled milk, are still consumed fresh. The common culture of drinking milk immediately after milking domestic animals, especially in rural areas, is unfortunately considered one of the risk factors for disease outbreaks, and it is necessary to raise the awareness level of people in this field. The findings of the present study showed that in terms of the treatment of the investigated patients, 89.4% of the patients were successfully treated, and 10.6% of the patients reported treatment failure. There were no reported deaths related to Malta fever among the patients studied. In line with this finding of the current research, the results of the study of numerous studies indicate that the treatment has been successful in the majority of patients suffering from Malta fever, and the failure of the treatment has been reported in a limited number of patients, which indicates the effectiveness of the treatment in affected patients [29, 31, 35, 36]. In some studies, male and occupational contact (animal husbandry), disease duration, presence of hepatosplenomegaly, and thrombocytopenia have been mentioned as risk factors for recurrence or failure of Malta fever treatment [36].

CONCLUSION

The study reveals a distinct epidemiological pattern for Malta fever, with the average age of patients being 33.18 years, indicating a broad age distribution. The highest incidence occurring in the age group of 16-50 years suggests a significant risk within this demographic data, while lower cases in those below 15 years highlight potential age-related immunity or exposure factors. The predominance of cases in rural areas (87%) compared to urban areas (13%) underscores the importance of environmental and occupational factors in disease transmission. The temporal analysis of Malta fever incidence demonstrates fluctuations over time, with the highest annual incidence recorded in 2020 and the lowest in 2016. The seasonal variation, with a peak in the first three months of the year and a decline in the last three months, suggests a possible link to climatic or behavioral factors influencing disease transmission. These findings can guide public health interventions and resource allocation to target high-risk periods effectively. The study identifies specific occupational groups, such as housewives, cattle breeders, and farmers, as being at higher risk for Malta fever. This highlights occupational exposure as a significant risk factor for disease acquisition, emphasizing the need for targeted preventive measures and education for these vulnerable populations. Understanding the occupational dynamics of disease transmission can inform tailored interventions to reduce the burden of Malta fever in at-risk communities. The high treatment success rate of 89.4% among patients underscores the effectiveness of current therapeutic approaches for Malta fever. The absence of reported deaths related to the disease within the studied population is a positive outcome, indicating the potential for a favorable prognosis with timely diagnosis and appropriate management. These findings emphasize the importance of early detection and access to quality healthcare services in improving patient outcomes and reducing mortality associated with Malta fever.

Health policymakers should embrace a One Health approach that integrates medicine, ecology, socio-economics, policy, science, management, and education for the prevention and control of brucellosis. This holistic strategy recognizes the interconnectedness of human, animal, and environmental health, emphasizing the need

for collaborative efforts across sectors to address the multifaceted nature of the disease. Policymakers should prioritize the enhancement of surveillance systems to monitor the prevalence and distribution of brucellosis in both animals and humans. Furthermore, timely and accurate data collection is essential for early detection, effective response, and targeted interventions to prevent the spread of the disease.

Health policymakers should promote and support vaccination programs for cattle, goats, and sheep in enzootic areas with high prevalence rates of brucellosis. Vaccination plays a crucial role in reducing the infection rate in animals, thereby decreasing the risk of transmission to humans and preventing outbreaks. Policymakers should focus on raising public awareness about the risks associated with brucellosis, especially among individuals working in the livestock sector. Education campaigns on the importance of food safety measures, occupational hygiene, and proper handling of animal products can help prevent human infections and reduce the disease burden.

Health policymakers should advocate for the implementation of occupational safety measures in settings where individuals are at high risk of exposure to Brucella species, such as laboratories, veterinary settings, and agricultural environments. Providing appropriate personal protective equipment, training on safe handling practices, and establishing medical surveillance programs can help mitigate occupational risks and prevent infections. By incorporating these recommendations into health policies and programs, policymakers can effectively combat brucellosis, reduce its impact on public health, and create a safer environment for both humans and animals.

Based on the epidemiological and clinical features of Malta fever in Iran, the following recommendations can be followed for future studies:

1. Investigate age-related immunity or exposure factors that contribute to the lower incidence of Malta fever in individuals under 15 years of age compared to the 16-50 years age group.

2. Explore environmental and occupational factors that lead to the significantly higher incidence of Malta fever in rural areas (87%) compared to urban areas (13%).

3. Analyze the potential link between climatic or behavioral factors and the observed seasonal variation in Malta fever incidence, with a peak in the first three months of the year and a decline in the last three months.

4. Develop and evaluate targeted preventive measures and educational programs for specific occupational groups at higher risk, such as housewives, cattle breeders, and farmers, to reduce the burden of Malta fever in these vulnerable populations.

5. Continue monitoring the treatment success rate and mortality associated with Malta fever to ensure the effectiveness of current therapeutic approaches and identify areas for improvement in patient management.

6. Expand the geographical coverage of studies to include other regions of Iran to provide a more comprehensive understanding of the epidemiological patterns and potential regional variations in Malta fever incidence.

By following these recommendations, future studies can contribute to a deeper understanding of Malta fever epidemiology, guide the development of targeted interventions, and ultimately improve the prevention and management of this disease in Iran.

AUTHORS' CONTRIBUTIONS

It is hereby acknowledged that all authors have accepted responsibility for the manuscript's content and consented to its submission. They have meticulously reviewed all results and unanimously approved the final version of the manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article reports the results of a research project approved by Torbat Jam Faculty of Medical Sciences, Iran with the code of ethics IR.TRJUMS.REC.1401.007.

HUMAN AND ANIMAL RIGHTS

All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1975 Helsinki Declaration and its later amendments or comparable ethical standards.

CONSENT FOR PUBLICATION

Considering that this study is of a secondary type, the data for this research was obtained from the archived findings of patients at Mashhad University of Medical Sciences. Therefore, there was no need to obtain informed consent or written consent from the patients.

STANDARDS OF REPORTING

STROBE guidelines were followed.

AVAILABILITY OF DATA AND MATERIALS

The data and supportive information are available within the article.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

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