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Research article

Human brucellosis and associated risk factors in the Middle East region: A comprehensive systematic review, meta-analysis, and meta-regression

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A R T I C L E I N F O

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A B S T R A C T

Introduction: Human brucellosis, caused by the bacteria *Brucella*, is a significant infectious disease globally, also known as Mediterranean fever or Malta fever.
Methods: This meta-analysis and systematic review focuses on the prevalence rate, risk factors, and diagnostic methods of human brucellosis in Middle Eastern countries, where the disease remains a significant public health issue. The analysis included 92 studies conducted between 1993 and 2024, following specified inclusion and exclusion criteria among symptomatic patients across these countries. The prevalence rate was calculated by dividing positive samples by total samples. The I2 index and Chi-squared test assessed study heterogeneity. Significant heterogeneity occurred when I2 exceeded 50 %.
Results: The highest prevalence rate was observed in Oman, Lebanon, and Kuwait countries, emphasizing a notable burden of *Brucella* infection in these regions. Risk factors associated with human brucellosis were identified, with unpasteurized dairy consumption and close animal contact being predominant. Various professions such as farmers, dairy factory workers, and agriculture workers showed higher prevalence rate. Gender analysis indicated a prevalence rate of 18.02 % (95 % CI: 11.55–25.51 %) in males and 13.61 % (95 % CI: 10.8–16.68 %) in females, with no significant difference in hospitalization rates. The prevalence rate of *Brucella* spp. was varied across detection methods, with immunocapture agglutination assay (Brucellacapt) showing the highest estimated prevalence rate of (44.04 %, 95 % CI: 27.71–61.04), followed by PCR (39.84 %, 95 % CI: 20.14–61.39) and culture (29.22 %, 95 % CI: 17.89–42.03). Among *Brucella* species, *Brucella melitensis (B. melitensis)* and *Brucella abortus (B. abortus)* were the highest prevalence rate. Although statistically insignificant, the meta-analysis also revealed an upward trend in prevalence rate from 1993 to 2024, (P value = 0.277).
Discussion: This comprehensive review emphasizes the need for tailored strategies to control brucellosis in the Middle East, highlighting the importance of timely diagnosis, public awareness,

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and effective treatment protocols. These findings provide valuable insights for policymakers and healthcare professionals working to mitigate the impact of this disease in the region.

1. Introduction

Human brucellosis is caused by Gram-negative coccobacillus bacteria of the *Brucella* genus. These bacteria are primarily transmitted to humans through direct contact with infected animals or by consuming contaminated animal products, such as unpasteurized dairy products [1,2]. The present classification of his genus comprises 13 species, with the possibility of further species being counted in the future [3]. A comparative genetic analysis of *Ochrobactrum* and *Brucella* strains revealed significant differences in gene content, genome size, and the absence of *Brucella*-specific genes and virulence factors in *Ochrobactrum*. Additionally, notable differences in antimicrobial resistance genes and plasmid presence were observed, with genome alignment showing a maximum similarity of 85.7 % between the genera. These findings support the classification of *Brucella* and *Ochrobactrum* as separate genera [4]. *Brucella* spp. have the ability to infect various animal hosts, including humans [5]. *B. melitensis* and *B. abortus* are two popular species of *Brucella* that pose significant public health problems globally. *B. melitensis* primarily infects small ruminants, such as goats and sheep, while *B. abortus* mainly affects cattle. Humans are considered accompanying hosts who may get infected through direct contact with animals or products derived from animals [5,6]. The acute infection of human brucellosis displays as a severe flu-like syndrome characterized by non-specific clinical symptoms such as sweating, undulating fever, headaches, myalgia, chills, fatigue, joint pain, and arthralgia [7,8]. In case a disease is not diagnosed early, it may progress into a chronic condition, persisting for an extended period. Prolonged exposure to infection allows bacteria to spread to various tissues and organs, posing serious complications such as hepatobiliary, osteoarticular, cardiovascular, and central nervous system involvement [9]. In some cases, it can cause long-term complications such as arthritis, swelling of the testicles, and chronic fatigue [10,11]. In rare cases, it can cause inflammation of the heart, liver, or spleen [12,13]. Treatment typically involves antibiotics, such as doxycycline or rifampin, for several weeks [14,15]. It is important to practice good hygiene and avoid contact with infected animals or their products. This precaution is necessary because vaccines for brucellosis are currently available only for animals and are not completely effective [16]. The causative agents of human brucellosis include *B. melitensis*, *B. abortus*, *B. suis*, and *B. canis*. These species are associated with different animal reservoirs (such as goats, cattle, pigs, and dogs, respectively) and can cause varying degrees of illness in humans through direct contact with infected animals or consumption of contaminated animal products. However, *B. melitensis* is recognized as the predominant cause of human brucellosis in endemic regions worldwide. It is also considered a significant foodborne pathogen in economically developing countries, based on numerous investigations conducted globally [17–19]. The primary route through which animals transmit diseases to humans is via the consumption of unpasteurized milk and dairy products obtained from infected livestock [8]. The evidence-based conservative estimate of the global prevalence rate of human brucellosis is 2.1 million, significantly higher than previously believed. Furthermore, these models indicate that Africa and Asia bear the majority of the global risk and cases, but the Americas and Europe also remain vulnerable [20]. It also continues to be an important public health concern across the Middle East, with tens of thousands of new cases reported annually, despite incremental advances in disease management [21,22]. The prevalence rate of brucellosis in the region underscores its intricate interplay with socioeconomic and political factors, notably influenced by variables such as population literacy rates, demographic distribution, and the efficacy of healthcare infrastructure [6]. Currently, Middle Eastern countries are experiencing a remarkable rise in human cases of brucellosis, providing an opportunity to collect significant data on the clinical symptoms of the disease, diagnostic

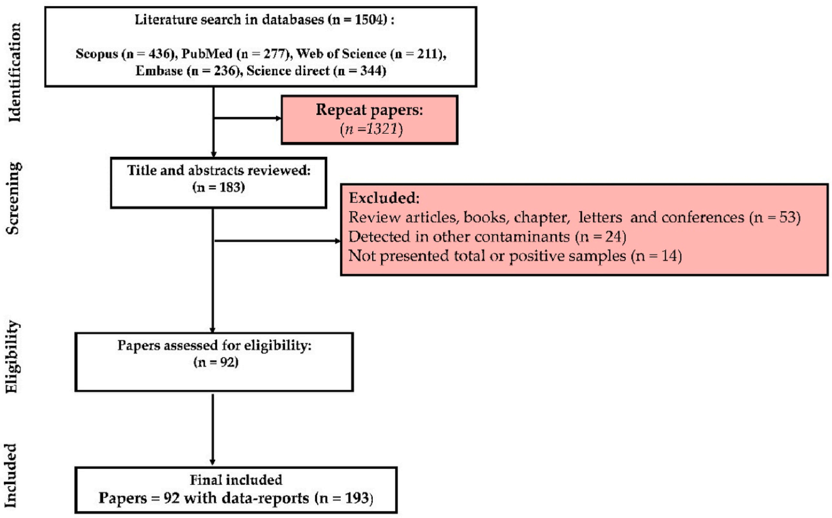

Fig. 1. PRISMA flow diagram summarizing the articles' selection process.

techniques, and therapeutic interventions. Traditional practices, like engaging in widespread pastoralism, and consuming unpasteurized dairy products increase the likelihood of animal-to-human disease transmission [23–25]. Additionally, political and social instability, coupled with insufficient financial and labor resources, hinder the development and execution of a consistent disease control program [23,26]. Considering the socioeconomic factors that impact the spread of brucellosis, it is crucial to prioritize the development of customized strategies. These strategies should focus on enabling timely and easily accessible diagnosis, as well as implementing effective and cost-efficient treatment protocols. The severity and harmful impact of this infection emphasize the critical importance of timely and precise diagnosis, as well as effective treatment, to mitigate the risk of subsequent disability [27,28]. This review article aims to provide a comprehensive overview of the prevalence rate of brucellosis in Middle Eastern countries, where the prevalence rate of the disease is notably higher compared to other regions worldwide. Additionally, it examines the risk factors associated with these infections through regression modeling analysis. In the present review, we also describe the key diagnostic methods for detecting human brucellosis in the Middle East, and we propose a regional approach toward public awareness of brucellosis as the first step in controlling the disease.

2. Methods

2.1. Search strategy

The Cochrane procedure was employed to conduct a meta-analysis of published data on human brucellosis in several Middle Eastern countries [29]. The data were retrieved and selected using the PRISMA techniques (Fig. 1) [30]. All publications on human brucellosis in Middle Eastern countries from January 1, 1993 to February 10, 2024 were obtained by searching Databases such as Web of Science, PubMed, Scopus, Science Direct CABI, Cochrane, Embase, and Scielo. The Medical Subject Headings (MeSH) term of human brucellosis and associated terms “Malta Fever'', "prevalence", " Middle Eastern countries ", “*Brucella* infection'', OR "human" OR "*Brucella* spp.*" OR* "*B. abortus*" OR "*Brucella*" OR "*B. melitensis*" OR *"B. canis*" OR *"B. suis*" OR "brucellosis" OR "seroprevalence " OR "human risk factor" OR "*Brucella* isolation". The material selected from each database was imported into Endnote X7.8, where it was verified and cleaned to exclude any duplicate entries. Subsequently, the reference list of all pertinent papers was carefully scrutinized to pinpoint additional qualifying studies. The status of human brucellosis in Middle Eastern countries, risk factors associated with the disease and diagnostic methods were all topics of interest.

2.2. Inclusion and exclusion criteria

This study considered specific inclusion criteria as follows: 1) the material must be written entirely in English; 2) It must address issues related to human brucellosis in Middle Eastern countries; 3) It should comprise descriptive and original publications derived from qualitative or quantitative data, such as case series, cross-sectional studies, cohort studies, case-control studies, and case reports; 4)The research should focus on human brucellosis and risk factors in Middle Eastern countries, demonstrating both positive outcomes and adequate sample sizes. Documents lacking peer review, such as books, clinical trial dissertations, and workshops, as well as sources beyond scholarly journals and review articles, were excluded [31,32].

2.3. Data extraction

Data pertaining to human brucellosis in Middle Eastern nations were meticulously collected from all relevant articles. The extracted information encompassed elements such as the primary author, geographical location, study duration, total sample size, number of positive samples, sample type, diagnostic methodologies employed, isolated *Brucella* species and their respective biovars, identified risk factors, gender distribution, and documented symptoms (if any). The articles were classified according to the detection techniques utilized. These techniques include indirect methods like the Rose Bengal Plate Test (RBPT), Serum Agglutination Test (SAT), 2-Mercaptoethanol Test (2-ME), Buffered Acidified Plate Antigen Test (BAPAT), Complement Fixation Test (CFT), indirect Enzyme-Linked Immunosorbent Assay (i-ELISA), Brucellacapt tests (Immunocapture agglutination assay), and competitive Enzyme-Linked Immunosorbent Assay (c-ELISA). Additionally, bacterial culture and the detection of nucleic acids through molecular methodologies such as Polymerase Chain Reaction (PCR), Real-Time Polymerase Chain Reaction (RT-PCR), or Quantitative Polymerase Chain Reaction (QPCR) represent direct methods employed in the diagnosis of brucellosis.

2.4. Meta-epidemiological analysis of human brucellosis

The prevalence rate was determined by calculating the ratio of positive samples to the total sample size. Study heterogeneity was analyzed using the I^2 index and Chi-squared test. Heterogeneity was considered significant if the I^2 value exceeded 50 % [33–35].The combined odds ratio (OR) from the studies was calculated using a random effect model (REM) to evaluate the overall prevalence rate of human brucellosis across the studied countries [36,37]. Furthermore, the prevalence rate of human brucellosis in Middle Eastern countries throughout time was examined using meta-regression analysis [38,39]. Statistical analyses were performed utilizing STATA program version 12.0 (STATA Corp, College Station, TX, USA), with significance determined at a threshold of $P < 0.05$.

3. Results

3.1. Literature selection process

The approach and criteria for including and excluding publications are detailed in Fig. 1. In this context, 1504 papers have been identified in international databases, including Scopus (n = 436), PubMed (n = 277), Web of Science (n = 211) and Embase (n = 236) from January 1, 1993 to February 10, 2024. Duplicates were deleted with EndNote 8x program (Philadelphia, PA, USA). The 183 articles were chosen as potentially suitable based on their titles, whereas 1321 articles were rejected for having irrelevant content. Out of the 183 publications, 91 were excluded after reviewing their abstracts. Only 92 articles met the inclusion criteria, which included papers with clear prevalence rate and risk factor analysis, comprising a total of 193 data reports and/or studies. This is because some articles studied multiple methods or genders for brucellosis analysis, with each method and gender at one location considered as a data report and/or study. Table S1 displays the key characteristics of the studies that were included.

3.2. Geographical and temporal distribution of studies

As indicated in Table 1, out of the 92 selected studies, the majority were conducted in Iran (n = 47). The countries ranked by the number of studies were as follows: Iran (47) > Turkey ~ Saudi Arabia (35) > Egypt (30) > Jordan (9) ~ Iraq (8) > Palestine/Israel (7) > Lebanon (5) ~ Yemen (5) ~ Kuwait (5) > Syria (3) > Qatar ~ Oman (2). Fig. 2 shows that most relevant research was conducted between 2011 and 2023 (n = 131), followed by the periods 2003–2010 (n = 40) and 1993–2002 (n = 22). The highest prevalence rate of *Brucella* spp. in human was observed in 2011–2023 years with 23.14 % (Table 2). Additionally, the results of meta-regression show that prevalence rate increased insignificantly over time (P value = 0.277) (Fig. 2).

3.3. Prevalence rates of Brucella in Middle Eastern countries

Among the Middle Eastern countries included in the analysis, different prevalence rates were observed. Oman, Lebanon, Palestine, Jordan, and Kuwait reported relatively higher prevalence rates, ranging from 27.87 % to 57.09 %. These findings indicate a significant presence of *Brucella* spp. in these regions. Iran and Saudi Arabia had prevalence rates of 18.21 % and 17.83 % respectively. Despite having a relatively large number of studies in Iran (47 studies), the prevalence rate remained within the range observed for other Middle Eastern countries. Türkiye and Egypt, from the Eastern Mediterranean region, reported prevalence rates of 15.03 % and 21.90 %, respectively. These prevalence rates are comparable to those found in other Middle Eastern countries, indicating a moderate prevalence rate of *Brucella* infection. Qatar, with a notably higher prevalence rate of 71.43 %, and Kuwait, with a prevalence rate of 57.09 %, exhibited the highest prevalence rates among the countries studied. These findings highlight a particularly significant burden of *Brucella* infection in these Gulf states. The meta-analysis included data from 193 studies on the prevalence rate of *Brucella* spp. (%) in humans across various countries. The overall prevalence rate across all countries was found to be 20.45 % (95 % CI: 17.85 %–23.19 %) (Table 1). The overall heterogeneity across all studies was high (I2 = 99.44 %, p < 0.001), indicating significant variability in the reported prevalence rate. This suggests that factors such as geographic location, diagnostic methods, and population characteristics may contribute to the observed differences in *Brucella* spp. prevalence rate among the included countries (Fig. 3).

3.4. Risk factors influencing human brucellosis prevalence rates

As showed in Fig. 4 several factors could contribute to the observed differences in *Brucella* spp. prevalence rate among these countries. Consumption of unpasteurized dairy products (n = 118) and close contact with animals (n = 85) emerge as the most

Table 1
Meta-analysis prevalence of *Brucella* spp. (%) in human based on country subgroup.

Subgroups	NS*	ES**	lower	Upper	Weight	Heterogeneity statistic	Degrees of freedom	P value	I^2
Oman	2	27.87	25.04	30.79	1.06	.	1	.	.%
Iran	47	18.21	12.74	24.40	24.39	8926.96	46	0	99.48%
Saudi Arabia	35	17.83	13.25	22.89	17.95	9676.96	34	0	99.65%
Lebanon	5	29.93	7.03	60.25	2.65	977.15	4	0	99.59%
Palestine	7	31.77	9.95	58.96	3.64	1048.35	6	0	99.43%
Jordan	9	34.70	25.50	44.51	4.65	294.53	8	0	97.28%
Yemen	5	10.14	0.62	28.70	2.66	739.9	4	0	99.46%
Türkiye	35	15.03	10.85	19.74	18.41	1823.26	34	0	98.14%
Egypt	30	21.90	12.62	32.80	15.09	3136.77	29	0	99.08%
Iraq	8	12.85	10.63	15.24	4.20	16.72	7	0.02	58.14%
Syria	3	11.74	9.26	14.47	1.60	.	2	.	.%
Qatar	2	71.43	66.97	75.69	1.03	.	1	.	.%
Kuwait	5	57.09	30.65	81.53	2.64	563.6	4	0	99.29%
Overall	**193**	**20.45**	**17.85**	**23.19**	**100.00**	**34106.04**	**192**	**0**	**99.44%**

*Number of studies

**Effect size or pooled prevalence

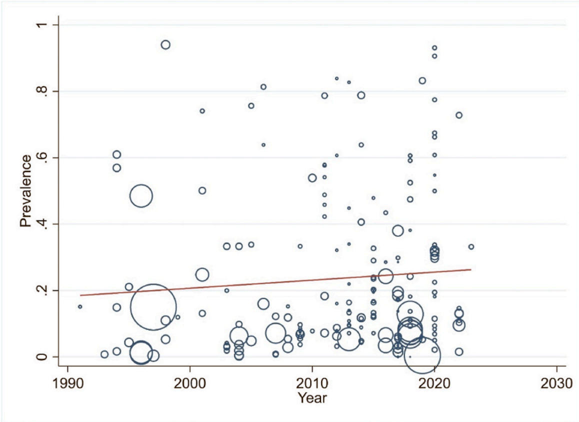

Fig. 2. Meta-regression prevalence of *Brucella* spp. in human by years of study.

Table 2
Meta-analysis prevalence of *Brucella* spp *(%)* in human by years, method of detection and sex.

Subgroups	Study	NS*	ES**	lower	Upper	Weight	Heterogeneity statistic	Degrees of freedom	P value	I^2
Year of study	1993–2002	22	22.13	13.10	32.72	11.68	12510.73	21	0	99.83 %
	2003–2010	40	12.09	8.09	16.74	21.07	4037.01	39	0	99.03 %
	2011–2023	131	23.14	19.98	26.45	67.25	16694.79	130	0	99.22 %
Method of detection	SAT	82	18.39	14.84	22.22	42.51	15794.55	81	0	99.49 %
	2-ME	7	4.81	2.10	8.53	3.74	304.78	6	0	98.03 %
	Culture	19	29.22	17.89	42.03	9.97	2239.36	18	0	99.20 %
	Coombs	3	4.51	0.00	16.00	1.60	.	2	.	.%
	ELISA	47	20.31	15.85	25.15	24.54	4862.84	46	0	99.05 %
	RBT	18	16.69	7.48	28.54	9.36	4630.03	17	0	99.63 %
	PCR	8	39.84	20.14	61.39	4.10	343.97	7	0	97.96 %
	Brucellacapt	9	44.04	27.71	61.04	4.18	218.94	8	0	96.35 %
Sex	Male	21	18.02	11.55	25.51	10.8	666.02	20	0	97.00 %
	Female	25	13.61	10.8	16.68	12.73	958.41	24	0	97.50 %
	ND	147	22.14	18.81	25.66	76.48	32002.99	146	0	99.54 %

*Number of studies.
**Effect size or pooled prevalence.
***Not mentioned.

frequently reported factors across the studies (Fig. 4). The other risk factors include rural populations (n = 31), occupation (n = 30), age of human (n = 27), male gender (n = 26), seropositive sheep (n = 25), season (n = 17), family history (n = 14), urbanicity (n = 10), consumption of raw-meat (n = 8), low knowledge about brucellosis (n = 3), vaccination (n = 3) (Fig. 4).

3.5. The prevalence rate of Brucella spp. Through different methods

The prevalence rate of *Brucella* spp. in humans varied across different methods of detection. Brucellacapt (44.04 %, 95 % CI: 27.71–61.04), followed by PCR (39.84 %, 95 % CI: 20.14–61.39) and culture-based detection (29.22 %, 95 % CI: 17.89–42.03) had the highest estimated prevalence rate. Conversely, Coombs test had the lowest estimated prevalence rate (4.51 %, 95 % CI: 0.00–16.00) (Table 2). ELISA also showed a substantial prevalence rate, while Brucellacapt had the highest prevalence rate but the lowest weight among all methods. Heterogeneity was generally high across all methods, indicating variability in the study results. The meta-analysis provided insights into the prevalence rate of different *Brucella* detection methods in humans. From the 82 studies on SAT, the prevalence rate was found to be 18.39 % (CI 14.84–22.22), carrying a substantial weight of 42.51 %. 2-ME (2-Mercaptoethanol Test) from 7 studies showed a prevalence rate of 4.81 % (CI 15.85- 8.53) with a lower weight of 3.74 %. Culture, based on 19 studies, had a prevalence rate of 29.22 % (CI 17.89–42.03) and a weight of 9.97 %. Coombs Test, analyzed in 3 studies, exhibited a prevalence rate of 4.51 % (CI 0.00–16.00) with insufficient data for weight and heterogeneity. I-ELISA and c-ELISA from 47 studies showed a prevalence rate of 20.31 % (CI 15.96–25.15) with a substantial weight of 24.00 %. RBPT from 18 studies indicated a prevalence rate of 16.69 % (CI 7.48–28.54) with a weight of 9.36 %. PCR from 8 studies displayed the highest prevalence rate at 39.84 % (CI 20.14–61.39) but with a low weight of 4.10 %.

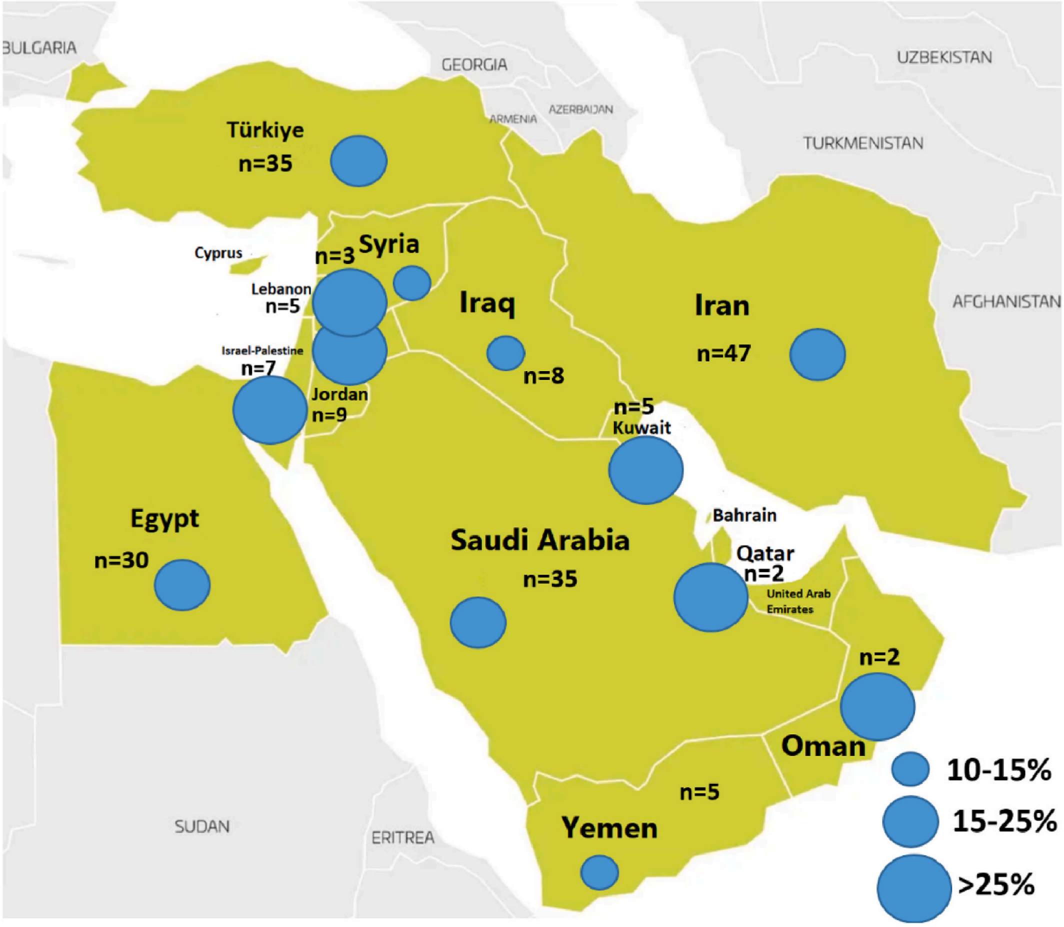

Fig. 3. Map of the Middle East showing countries included with the number of studies per country deemed relevant and of sufficient quality. The blue circle represents the prevalence rates of human brucellosis based on various sizes and corresponding prevalence rates.

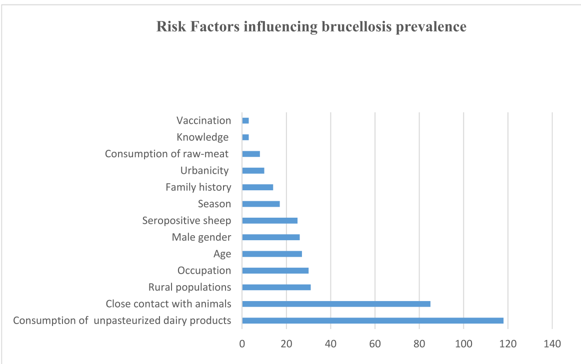

Fig. 4. Ranked risk factors influencing brucellosis prevalence. The x-axis displays the number of studies presenting risk factors for human brucellosis, while the y-axis represents the various risk factors reported across these studies.

3.6. The prevalence rate of Brucella in different gender, age and occupations

The study examined various occupations in relation to the prevalence rate of human brucellosis, comparing the general population to those in high-risk occupations. Among the general population including housewife children, and pregnant women, 117 cases were identified, with a prevalence rate of 21.71 %, ranging from 18.54 to 25.06. When looking at specific occupations within the high-risk category, some interesting trends emerge. Four occupations with highest prevalence rate of human brucellosis were non-permanent job of farmer (60.66 %), dairy factory worker (36.48 %), non-animal related works (33.33 %) and agriculture workers (26.87 %) (Table 3). The rank order of other occupations countries based on the prevalence rate was butchers (21.91 %), livestock farmers (17.33 %), veterinarians (14.95 %), slaughterers (11.96 %), abattoir workers (10.65 %), laboratory workers (6.06 %), rural communities (3.32 %), and blood donors (0.43 %). The single non-permanent job case had a prevalence rate of 60.66 %. Among those classified as "NM" (not mentioned), there were 14 cases identified, resulting in a prevalence rate of 34 %, ranging from 20.42 to 49.07. Non-animal related occupations had one case, resulting in a prevalence rate of 33.33 %, with a range of 25.86–41.48. Regarding the human age, the prevalence of human brucellosis in ≥30 age class and 30 < age was observed at 35.46 % and 22.43, respectively (Table 3).

With respect to gender-wise prevalence rate findings (Table 2), in the "Male" subgroup, there were 21 studies with a total of 10.8 wt, indicating a prevalence rate of 18.02 % (95 % CI: 11.55–25.51 %). The heterogeneity statistic (I^2) is 97.00 %, suggesting high variation across the studies. In the "Female" subgroup, there were 25 studies with a total weight of 12.73, indicating a prevalence rate of 13.61 % (95 % CI: 10.8–16.68 %). The heterogeneity statistic (I^2) is 97.50 %, also indicating high variation across the studies (Table 2). There seems to be no significant difference in hospitalization rates between males and females. As evident from the table, the lowest and highest prevalence rate was related to *B. aborus* and *B. melitensis* (8.62 %) and *Brucella* spp. (32.68 %), respectively (Table 3). The study compared different subgroups based on *Brucella* species, including *B. melitensis*, *Brucella* spp., *B. aborus*, co-infection of *B. aborus* and *B. melitensis*, and an unspecified category labelled ND. In terms of sample size (NS), the highest number was found in the ND category with 153, followed by *Brucella* spp. with 21, *B. melitensis* with 13, and only 3 samples each for *B. aborus* and *B. aborus* and *B. melitensis* combined.

4. Discussion

The Middle East, with 17 countries, is a significant endemic region for human brucellosis [6]. The annual occurrence of brucellosis in Middle Eastern and Mediterranean regions ranges from 1 to 78 cases per 100,000 people [40]. This disease is not exclusive to the

Table 3
Meta-analysis prevalence of *Brucella* spp *(%)* in human based on occupation class, age and *Brucella* species subgroups.

Subgroups	Study	NS*	ES**	lower	Upper	Weight	Heterogeneity statistic	Degrees of freedom	P value	I^2
Occupation	General population	117	21.71	18.54	25.06	60.43	19706.92	116	0	99.41 %
	Livestock farmer	14	17.33	6.99	30.92	7.22	1301.02	13	0	99.00 %
	Laboratory worker	3	6.06	2.86	10.31	1.58	.	2	.	.%
	Slaughterers	3	11.96	6.05	19.47	1.56	.	2	.	.%
	Butcher	3	21.91	1.05	54.48	1.32	.	2	.	.%
	Rural communities	15	3.32	2.02	4.91	7.97	236.11	14	0	94.07 %
	NM***	14	34	20.42	49.07	7.39	2909.4	13	0	99.55 %
	Non-animal related works	1	33.33	25.86	41.48	0.52	.	0	.	.%
	Agriculture worker	4	26.87	0	76.2	2.03	642.09	3	0	99.53 %
	Veterinarians	4	14.95	4.71	29.33	2.05	59.91	3	0	94.99 %
	Abattoir worker	2	10.65	7.24	14.59	1.03	.	1	.	.%
	Blood Donors	1	0.43	0.33	0.55	0.54	.	0	.	.%
	Dairy factory worker	11	36.48	23.04	51.08	5.82	1411.08	10	0	99.29 %
	Non-permanent job in livestock farm	1	60.66	51.41	69.38	0.52	.	0	.	.%
Age (Year)	≥30	8	35.46	18.28	54.79	4.08	588.02	7	0	98.81 %
	30<	12	22.43	14.66	31.27	6.09	190.18	11	0	94.22 %
	ND	173	19.70	17.04	22.50	89.82	31949.64	172	0	99.46 %
Sample species	*B. melitensis*	13	25.61	10.54	44.45	6.77	1934.96	12	0	99.38 %
	Brucella spp.	21	32.68	21.59	44.83	10.98	2862.38	20	0	99.30 %
	B. aborus	3	19.71	10.57	30.66	1.42	.	2	.	.%
	B. aborus and B. melitensis	3	8.62	5.85	11.8	1.44	.	2	.	.%
	ND	153	18.82	16.16	21.64	79.38	27500.42	152	0	99.45 %

*Number of studies.
**Effect size or pooled prevalence.
***Not mentioned.

Middle East region but is widespread throughout other regions like India, Western Asia, Latin American, and Southern Europe countries [7,23,41]. The persistence of brucellosis in developing countries in the Middle East and Africa is influenced by several risk factors. These include a lack of coordinated efforts among policymakers, health officials, veterinary sectors, and farmers, which hampers effective control and prevention strategies. Other contributing factors are inadequate infrastructure for disease surveillance, limited access to diagnostic facilities, and insufficient public awareness and education about the disease. Additionally, socio-economic challenges, such as poverty and limited resources for healthcare and veterinary services, exacerbate the situation, allowing brucellosis to remain endemic in these regions [42].Animal brucellosis is thought to significantly impact humans in many places globally [21]. However, the exact number of human cases remains unknown, despite the disease being one of the oldest known. Many studies were excluded because they had unclear or incomplete descriptions of their design, or a design that was unlikely to produce unbiased estimates. Several studies on human infection in this study involved retrospective analysis of case series using hospital records. However, these studies often lacked a control group, which prevented the examination of infection risk variables. Other studies have examined the frequency of occurrence in high-risk subgroups such rural populations, butcher, abattoir worker, veterinarians, farmer or in patients who displayed symptoms consistent with infection, such as flu-like symptoms, including fever, sweating, osteoarthritis, and fatigue. Such research was excluded when the individuals were not selected probabilistically.

Among the Middle Eastern countries included in the analysis, varying rates of prevalence *Brucella* spp. were observed. The reported seroprevalence varied greatly from country to country, and even among regions of the same country. The combined prevalence rate of brucellosis among patients exhibiting symptoms and high-risk populations was reported at 20.45 % across various studies. Oman, Palestine, Lebanon, Jordan, and Kuwait reported relatively higher rates of prevalence, ranging from 27.87 % to 57.09 %. These findings suggest a significant presence of *Brucella* spp. in these regions, which is consistent with previous studies. In Oman, the disease was most common in men (56 %), then women (44 %). Most positive cases were Omani nationals, likely due to higher contact with sick animals on private farms [43]. The isolation, identification, and molecular characterization of *B. melitensis* in a cow (spillover), a non-preferred host, was the most intriguing finding in this study that led to increase human brucellosis in this regions [44]. The majority of patients had consumed raw dairy products [45]. Another study found that the high increase in human brucellosis in the Palestine was due to inadequate disease control and surveillance [46]. According to our results, the higher prevalence rate was reported among the age group 11–20 years (29 %) and in males (57.1 %). Different studies also were reported more cases in April, May, and June. Out of these, 62.7 % had contact with animals, and over 30 % had at least one affected family member [46].

Iran and Saudi Arabia had prevalence rates of 18.21 % and 17.83 % respectively. Despite Iran having a relatively large number of studies on brucellosis, the prevalence rate falls below that of some neighbouring countries. This could be due to differences in livestock practices, healthcare infrastructure, or other factors [47]. Comparing these prevalence rates with other regional studies, it is clear that some Middle Eastern countries have a notably higher burden of *Brucella* spp. infections, indicating a need for targeted prevention and control strategies in these areas. The prevalence rate of human brucellosis in Türkiye, as indicated by the reported prevalence rates of 15.03 %, aligns with prevalence rates seen in other Middle Eastern countries. This suggests a significant burden of the disease within the country. In a study conducted in Türkiye, all human isolates were determined to be of *B. melitensis* origin and antibiotic sensitivity testing was performed. Accordingly, it was determined that all isolates were sensitive to the antibiotics Streptomycin, doxycycline, ciprofloxacin, gentamicin, and trimethoprim/sulfamethoxazole [48].Several factors may contribute to the prevalence rate of brucellosis in Türkiye. The agricultural nature of many regions in the country, where livestock farming is common, increases the risk of exposure to *Brucella*-infected animals. Additionally, consumption of unpasteurized dairy products, which can harbor the bacteria, may further contribute to transmission. The Ministry of Agriculture and Forestry in Türkiye initiated a conjunctival mass vaccination program in 2012, aiming to combat a specific disease. Data from the Turkish Ministry of Health's official page, spanning from 2008 to 2017, provides valuable insights into the effectiveness of this vaccination effort on the number of human cases [49].

Our meta-analysis findings showed a prevalence rate of 71.43 % for brucellosis in Qatar, highlight the significant burden of this disease in the region. These prevalence rates highlight the severity of the problem and the substantial impact on public health in Qatar. The high prevalence rate observed in Qatar can be attributed to the specific target population in the studies [50,51]. In two studies, the population included individuals with symptoms resembling brucellosis who underwent culturing. This targeted approach likely contributed to the higher prevalence rates reported in these studies. While the high prevalence rate is concerning, it's essential to consider the context of the studies and the population they focused on. The findings emphasize the importance of targeted screening and diagnostic efforts for brucellosis, especially in regions like Qatar where the disease burden appears to be notably high among symptomatic individuals. The finding indicates that after Qatar, the highest prevalence rate of human brucellosis was observed in Kuwait (57.09 %). However, this report is based on a single article presenting data from 1836 patients between January 2000 and December 2001. In this study, any patient with a provisional diagnosis of fever or brucellosis underwent testing for brucellosis diagnosis [52]. The lowest prevalence rate of human brucellosis among Middle Eastern countries was reported in Yemen, based on findings from three studies [53,54]. However, a Yemeni review article stated that the seroprevalence of human brucellosis in Yemen ranged from 0.3 % to 32.3 % [55]. Further investigation into the factors contributing to this accurate prevalence rate in Yemen is recommended and could provide valuable insights for public health strategies aimed at reducing the prevalence rate of brucellosis in the country.

According to various studies in our analysis, the prevalence rate of human brucellosis among 2459 children under the age of 14 in the Middle East was found to be 3.2 %. The consumption of dairy milk and close contact with infected animals emerged as the primary important risk factors. The identified risk factors highlight areas for targeted prevention strategies. This suggests the need for public health initiatives to educate families and communities about the risks associated with these factors and promote practices to reduce exposure among children, ultimately aiming to lower the prevalence rate of brucellosis in this vulnerable population. Our analysis further reported that out of 1034 pregnant women studied, 6.5 % tested positive for brucellosis. This finding underscores the importance of screening for brucellosis during pregnancy, as it affects a notable proportion of expecting mothers. Brucellosis can have serious implications for both the mother and child and probably increases the risk of intra-uterine fetal death and prematurity, highlighting the need for heightened awareness and preventive measures among healthcare providers and pregnant women [56–58]. However, we were unable to locate sufficient data on human brucellosis in Bahrain, Cyprus, Israel, and the United Arab Emirates (UAE) that met the criteria for inclusion in the meta-analysis. This discovery is significant and reinforces the idea that brucellosis is prevalent, at least in all Middle Eastern countries. Further investigation into the factors contributing to the high prevalence rate in Kuwait, Qatar, Bahrain, Cyprus, Israel, and the United Arab Emirates could provide valuable insights for public health interventions aimed at reducing the prevalence rate of brucellosis in the country.

The prevalence rate of human brucellosis varied significantly across different methods of detection, as shown by our finding in this study. Our analysis showed that the Brucellacapt had the highest estimated prevalence rate at 44.04 %. Brucellacapt offers advantages such as high sensitivity, specificity, and rapid results, but it also comes with the risk of false positives, limitations in early detection, requirement for laboratory facilities, cost considerations, and the need for skilled interpretation of results [59]. Brucellacapt is more sensitive and typically demonstrates greater titers compared to the Coombs test. However, its specificity somewhat reduces when titers below 1/320 are utilized [59]. However, the SAT was the most commonly used method for detecting human brucellosis in Middle Eastern countries. The popularity of this method in the Middle East could be attributed to its well-established history of use, reliability, and relatively low cost compared to other diagnostic techniques. Additionally, SAT does not require sophisticated laboratory equipment, making it more accessible in resource-limited settings commonly found in the region [60]. Its simplicity and effectiveness in detecting *Brucella* antibodies make it a preferred choice for many healthcare facilities in the Middle East. However, ELISA was the second most commonly used method for detecting human brucellosis in Middle Eastern countries. The popularity of this method in the Middle East can be attributed to its high sensitivity and specificity, allowing for accurate detection of *Brucella* antibodies. Additionally, ELISA is relatively easy to perform, requires minimal equipment, and provides rapid results, making it a convenient choice for healthcare facilities in the region. Its ability to handle a large number of samples efficiently and its compatibility with automated systems also contribute to its popularity in Middle Eastern countries [61]. Other methods such as 2-ME, Coombs test, culture, RBPT, and PCR tests have been used less frequently than ELISA and SAT in studies in the Middle East. The reasons for their lower usage in the region may include factors such as higher cost, complexity of procedures, and the need for specialized equipment or expertise. Additionally, ELISA and SAT are well-established and widely accepted methods with proven reliability for brucellosis detection, which could contribute to their preference over other less common tests. Our results also suggest that while there is a difference in the estimated prevalence rate of brucellosis between males, and females group, there is also considerable heterogeneity across studies within each subgroup. This could be due to differences in study populations, methodologies, or other factors. In Uganda and Saudi Arabia, studies found that the prevalence rate of brucellosis was higher in males compared to females [62,63]. However, in Hamadan Province, Iran, the rate of brucellosis was reported to be higher in females [64].

The data from this study indicate that *B. melitensis* and *B. abortus* were the most commonly found *Brucella* species from human brucellosis in most Middle Eastern nations. The frequent detection of *B. melitensis* in cattle in the Middle East prompts inquiries on the involvement of cattle in disease persistence and spread, warranting additional research. Furthermore, it emphasizes the role of mixing large and small ruminants, which is common in many Middle Eastern countries [65,66]. The presence of *B. abortus* in humans exclusively in Iran, Egypt, and Iraq may be due to transfer from cattle to humans prior to its eradication from the country following the implementation of a vaccination campaign.

The study findings identified the primary risk factors associated with human seropositivity to *Brucella* spp. as consumption of contaminated milk and dairy products and close contact with animals. It has been revealed that the combination of high-risk behaviors, inadequate understanding of the disease, and the lack of effective prevention efforts leads to the persistence of the disease in the area [22]. Our finding highlights that those working in temporary farming positions are at a higher risk of contracting the disease. This can be attributed to several factors such as limited training and awareness, inadequate protective measures for temporary or seasonal workers, limited healthcare access, living conditions in close quarters or temporary accommodations on or near the farm, handling of infected animals [21,67]. Furthermore, workers in dairy factories have a significant prevalence rate of brucellosis. This highlights the risk associated with working in environments where dairy products are processed. It could be due to the nature of their work environment and the potential for exposure to *Brucella* bacteria.

5. Conclusion

This analysis sheds light on the concerning prevalence rate of human brucellosis in Middle Eastern countries, highlighting various risk factors and the need for targeted prevention strategies. The analysis of recorded human brucellosis cases in Middle Eastern countries revealed varying rates of prevalence of *Brucella* spp., with some countries like Oman, Palestine, Lebanon, Jordan, and Kuwait reporting higher prevalence rates. Factors such as consumption of raw dairy products, close contact with infected animals, handling and processing raw infected milk, airborne transmission, accidental inoculation and lack of awareness are the main causes of human brucellosis. Different diagnostic methods were used across studies, with Brucellacapt and SAT being commonly employed in the Middle East due to their reliability and accessibility. The study also highlighted occupational risks, with temporary farmers and dairy factory workers showing significant rates of prevalence. It is crucial to increase awareness level at the points of occupations and implement integrated preventive strategies in these settings to reduce the prevalence rate of the disease. In conclusion, this analysis emphasizes the need for continued surveillance, education, and targeted interventions to combat human brucellosis in Middle Eastern countries. Understanding the prevalence rate, risk factors, and effective diagnostic methods is crucial for public health efforts aimed at reducing the impact of this disease on individuals and communities in the region.

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Data availability statement

All data and materials used in the present systematic review are available from the corresponding author.

CRediT authorship contribution statement

Maryam Dadar: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Ja'far Al-Khaza'leh:** Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Yadolah Fakhri:** Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation. **Kadir Akar:** Writing – original draft, Visualization, Validation, Supervision. **Shahzad Ali:** Writing – original draft, Visualization, Validation, Software. **Youcef Shahali:** Writing – original draft, Visualization, Validation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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References

[1] M.J. Corbel, Brucellosis: an overview, Emerg. Infect. Dis. 3 (2) (1997) 213, https://doi.org/10.3201/eid0302.970219.
[2] M. Dadar, S.S. Omar, Y. Shahali, Y. Fakhri, J. Godfroid, A.M. Khaneghah, The prevalence of camel brucellosis and associated risk factors: a global meta-epidemiological study, Qual. Assur. Saf. Crops Foods 14 (3) (2022) 55–93, https://doi.org/10.15586/qas.v14i3.1088.
[3] E.E. Moreno, E.A. Middlebrook, P. Altamirano-Silva, S. Al Dahouk, G.F. Araj, V. Arce-Gorvel, Á. Arenas-Gamboa, J. Ariza, E. Barquero-Calvo, G. Battelli, If you're not confused, you're not paying attention: Ochrobactrum is not *Brucella*, J. Clin. Microbiol. 61 (8) (2023) e00438, https://doi.org/10.1128/jcm.00438-23, 23.
[4] K. Holzer, L.E. Hoelzle, G. Wareth, Genetic comparison of Brucella spp. and Ochrobactrum spp. erroneously included into the genus *Brucella* confirms separate genera, Ger. J. Vet. Res. 3 (1) (2023) 31–37, https://doi.org/10.51585/gjvr.2023.1.0050.
[5] J. Godfroid, S. Al Dahouk, G. Pappas, F. Roth, G. Matope, J. Muma, T. Marcotty, D. Pfeiffer, E. Skjerve, A "One Health" surveillance and control of brucellosis in developing countries: moving away from improvisation, Comp. Immunol. Microbiol. Infect. Dis. 36 (3) (2012) 241–248, https://doi.org/10.1016/j.cimid.2012.09.001.
[6] G. Pappas, Z. Memish, Brucellosis in the Middle East: a persistent medical, socioeconomic and political issue, J. Chemother. 19 (3) (2007) 243–248, https://doi.org/10.1179/joc.2007.19.3.243.
[7] G. Pappas, P. Papadimitriou, N. Akritidis, L. Christou, E.V. Tsianos, The new global map of human brucellosis, Lancet Infect. Dis. 6 (2) (2006) 91–99, https://doi.org/10.1016/S1473-3099(06)70382-6.
[8] A.S. Dean, L. Crump, H. Greter, J. Hattendorf, E. Schelling, J. Zinsstag, Clinical manifestations of human brucellosis: a systematic review and meta-analysis, PLoS Negl. Trop. Dis. 6 (12) (2012) e1929, https://doi.org/10.1371/journal.pntd.0001929.
[9] P.C. Baldi, G.H. Giambartolomei, Pathogenesis and pathobiology of zoonotic brucellosis in humans, Rev. Sci. Tech. 32 (1) (2013) 117–125, https://doi.org/10.20506/rst.32.1.2192.
[10] Y.Z. Demiroğlu, T. Turunç, H. Alişkan, Ş. Çolakoğlu, H. Arslan, Brucellosis: retrospective evaluation of the clinical, laboratory and epidemiological features of 151 cases, Mikrobiyol. Bul. 41 (4) (2007) 517–527.
[11] S. Guler, O.F. Kokoglu, H. Ucmak, M. Gul, S. Ozden, F. Ozkan, Human brucellosis in Turkey: different clinical presentations, J. Infect. Dev. Ctries. 8 (5) (2014) 581–588, https://doi.org/10.3855/jidc.3510.
[12] T.M. Peery, L.F. Belter, Brucellosis and heart disease: II. Fatal brucellosis: a review of the literature and report of new cases, Am. J. Pathol. 36 (6) (1960) 673.
[13] E.J. Young, M.R. Hasanjani Roushan, S. Shafae, R.M. Genta, S.L. Taylor, Liver histology of acute brucellosis caused by *Brucella melitensis*, Hum. Pathol. 45 (10) (2014) 2023–2028, https://doi.org/10.1016/j.humpath.2014.07.007.
[14] A.E.M. Eltorai, S.S. Naqvi, A. Seetharam, B.A. Brea, C. Simon, Recent developments in the treatment of spinal epidural abscesses, Orthop. Rev. 9 (2) (2017) 7010, https://doi.org/10.4081/or.2017.7010.
[15] E. Giannitsioti, A. Papadopoulos, P. Nikou, S. Athanasia, A. Kelekis, N. Economopoulos, A. Drakou, P. Papagelopoulos, O. Papakonstantinou, V. Sakka, A. Fragou, G. Koukos, K. Kanellakopoulou, H. Giamarellou, Long-term triple-antibiotic treatment against brucellar vertebral osteomyelitis, Int. J. Antimicrob. Agents 40 (1) (2012) 91–93, https://doi.org/10.1016/j.ijantimicag.2012.03.018.
[16] M. Dadar, R. Tiwari, K. Sharun, K. Dhama, Importance of brucellosis control programs of livestock on the improvement of one health, Vet. Q. 41 (1) (2021) 137–151, https://doi.org/10.1080/01652176.2021.1894501.

[17] E. Georgi, M.C. Walter, M.-T. Pfalzgraf, B.H. Northoff, L.M. Holdt, H.C. Scholz, L. Zoeller, S. Zange, M.H. Antwerpen, Whole genome sequencing of *Brucella melitensis* isolated from 57 patients in Germany reveals high diversity in strains from Middle East, PLoS One 12 (4) (2017) e0175425, https://doi.org/10.1371/journal.pone.0175425.

[18] B.G. Mantur, A.S. Akki, S.S. Mangalgi, S.V. Patil, R.H. Gobbur, B.V. Peerapur, Childhood Brucellosis - a microbiological, epidemiological and clinical study, J. Trop. Pediatr. 50 (3) (2004) 153–157, https://doi.org/10.1093/tropej/50.3.153.

[19] M. Dadar, Y. Shahali, A.M. Whatmore, Human brucellosis caused by raw dairy products: a review on the occurrence, major risk factors and prevention, Int. J. Food Microbiol. (2019), https://doi.org/10.1016/j.ijfoodmicro.2018.12.009.

[20] C.G. Laine, V.E. Johnson, H.M. Scott, A.M. Arenas-Gamboa, Global estimate of human brucellosis incidence, Emerg. Infect. Dis. 29 (9) (2023) 1789, https://doi.org/10.3201/eid2909.230052.

[21] K. Franc, R. Krecek, B. Häsler, A. Arenas-Gamboa, Brucellosis remains a neglected disease in the developing world: a call for interdisciplinary action, BMC Publ. Health 18 (1) (2018) 1–9, https://doi.org/10.1186/s12889-017-5016-y.

[22] I.I. Musallam, M.N. Abo-Shehada, Y.M. Hegazy, H.R. Holt, F.J. Guitian, Systematic review of brucellosis in the Middle East: disease frequency in ruminants and humans and risk factors for human infection, Epidemiol. Infect. 144 (4) (2016) 671 85, https://doi.org/10.1017/S0950268815002575.

[23] M. Gwida, S. Al Dahouk, F. Melzer, U. Rösler, H. Neubauer, H. Tomaso, Brucellosis - regionally emerging zoonotic disease? Croat. Med. J. 51 (4) (2010) 289–295, https://doi.org/10.3325/cmj.2010.51.289.

[24] H. Ozl, B. Cevik, M. Atasever, M. Sarialioglu, B. Polat, Investigation of meat species adulteration in beef-based meat products via real-time PCR in Türkiye, Qual. Assur. Saf. Crops Foods 15 (4) (2023), https://doi.org/10.15586/qas.v15i4.1374.

[25] F. Mehak, M.Y. Quddoos, S. Mahmood, S. Mukhtar, S. Selim, S.K. Al Jaouni, M.S. Almuhayawi, M.A. Elawad, N. Almutairi, A.A.E. Hamdoon, Emerging zoonotic viral diseases and preventive strategies with Islamic perspectives of halal foods, Ital. J. Food Saf 36 (1) (2024) 142–156, https://doi.org/10.15586/ijfs.v36i1.2404.

[26] M.U. Farid, M.H. Jaspal, N. Luqman, B. Asghar, M. Ijaz, M.K. Yar, M.S.A. Taseer, Z. Iqbal, M.A. Naeem, J. Nasir, Age, sex, and chilling effects on goat meat, Ital. J. Food Saf 35 (4) (2023) 12–20, https://doi.org/10.15586/ijfs.v35i4.2195.

[27] S.B. Dong, D. Xiao, J.Y. Liu, H.M. Bi, Z.R. Zheng, L.D. Wang, X.W. Yang, G.Z. Tian, H.Y. Zhao, D.R. Piao, Z.F. Xing, H. Jiang, Fluorescence polarization assay improves the rapid detection of human brucellosis in China, Infect Dis Poverty10 (1) (2021) 46, https://doi.org/10.1186/s40249-021-00834-3.

[28] P. Gunaratnam, P. Massey, K. Eastwood, D. Durrhein, S. Graves, D. Coote, L. Fisher, Diagnosis and management of zoonoses - a tool for general practice, Aust. Fam. Physician 43 (3) (2014) 124–128.

[29] J.P. Higgins, S. Green, Cochrane handbook for systematic reviews of interventions, John Wiley & Sons (2011), https://doi.org/10.1002/9780470712184.

[30] A. Liberati, D.G. Altman, J. Tetzlaff, C. Mulrow, P.C. Gøtzsche, J.P. Ioannidis, M. Clarke, P.J. Devereaux, J. Kleijnen, D. Moher, The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration, PLoS Med. 6 (7) (2009) 15–25, https://doi.org/10.1371/journal.pmed.1000100.

[31] M. Dadar, Y. Fakhri, Y. Shahali, A.M. Khaneghah, Contamination of milk and dairy products by *Brucella* species: a global systematic review and meta-analysis, Food Res. Int. 128 (2020) 108775, https://doi.org/10.1016/j.foodres.2019.108775.

[32] M. Dadar, Y. Shahali, Y. Fakhri, J. Godfroid, The global epidemiology of *Brucella* infections in terrestrial wildlife: a meta-analysis, Transbound Emerg Dis 68 (2) (2021) 715–729, https://doi.org/10.1111/tbed.13735.

[33] Higgins, S. Thompson, Quantifying heterogeneity in a meta-analysis, Stat. Med. 21 (11) (2002) 1539–1558, https://doi.org/10.1002/sim.1186.

[34] X. Li, R. Jing, L. Wang, N. Wu, Z. Guo, Role of arbuscular mycorrhizal fungi in cadmium tolerance in rice (Oryza sativa L): a meta-analysis, Qual. Assur. Saf. Crops Foods 15 (2) (2023) 59–70, https://doi.org/10.15586/qas.v15i2.1182.

[35] Z. Tian, R. Li, J. Wei, W. Huai, J. Xia, H. Jiang, Y. Xiong, Y. Chen, Efficacy and safety of Shaoyao Gancao Tang for restless leg syndrome: a systematic review and meta-analysis, Qual. Assur. Saf. Crops Foods 15 (1) (2023) 169–181, https://doi.org/10.15586/qas.v15i1.1245.

[36] P. Gao, W. Liang, Q. Zhao, H. Li, L. Guan, D. Li, Effects of vitamins A, C, and D and zinc on urinary tract infections: a systematic review and meta-analysis, Qual. Assur. Saf. Crops Foods 15 (3) (2023) 88–95, https://doi.org/10.15586/qas.v15i3.1292.

[37] H. Huang, M. Liu, H. Liu, H. Wan, F. Wu, Laser-assisted delivery of vitamin c or vitamin c plus growth factors in the treatment of chloasma in women: a systematic review and meta-analysis, Qual. Assur. Saf. Crops Foods 14 (3) (2022) 156–164, https://doi.org/10.15586/qas.v14i3.1082.

[38] T.D. Stanley, S.B. Jarrell, Meta-Regression analysis: a quantitative method of literature surveys, J. Econ. Surv. 3 (2) (1989) 161–170, https://doi.org/10.1111/j.1467-6419.1989.tb00064.x.

[39] D. Jackson, J. Bowden, R. Baker, Approximate confidence intervals for moment-based estimators of the between-study variance in random effects meta-analysis, Res. Synth. Methods 6 (4) (2015) 372–382, https://doi.org/10.1002/jrsm.1162.

[40] A. Seimenis, G.F. Araj, I. Moriyón, D. Tabbaa, Brucellosis prevention and control in the Mediterranean & Middle East regions _ a guidance towards approaching the targets, J. Med. Liban. 67 (1) (2019) 52–61.

[41] B.A.V. Cama, M. Ceccarelli, E.V. Rullo, F. Ferraiolo, I.A. Paolucci, D. Maranto, P. Mondello, M.R. Lo Presti Costantino, F. Marano, G. D'Andrea, V.D. Marco, G. Puglisi, M. Valenzise, G. D'Angelo, L. Mondello, G. Strano, F. Condorelli, D. Spicola, G.F. Pellicanò, G. Nunnari, Outbreak of *Brucella melitensis* infection in Eastern Sicily: risk factors, clinical characteristics and complication rate, New Microbiol. 42 (1) (2019) 43–48.

[42] A.F. Hikal, G. Wareth, A. Khan, Brucellosis: why is it eradicated from domestic livestock in the United States but not in the Nile River Basin countries? Ger. J. Microbiol. 3 (2023) 19–25, https://doi.org/10.51585/gjm.2023.2.0026.

[43] A. Al-Rawahi, The Epidemiology of Brucellosis in the, Murdoch University, Sultanate of Oman, 2015. https://core.ac.uk/download/pdf/77136278.pdf.

[44] Y. ElTahir, A.G. Al Toobi, W. Al-Marzooqi, O. Mahgoub, M. Jay, Y. Corde, H. Al Lawati, S. Bose, A. Al Hamrashdi, K. Al Kharousi, N. Al-Saqri, R. Al Busaidi, E. H. Johnson, Serological, cultural and molecular evidence of *Brucella melitensis* infection in goats in Al Jabal Al Akhdar, Sultanate of Oman, 4(3, Vet. Med. Sci. (2018) 190–205, https://doi.org/10.1002/vms3.103.

[45] K.S. Hassan, H. Schuster, A. Al-Rawahi, A. Balkhair, Clinical presentations of brucellosis over a four-year period at sultan qaboos university hospital and armed forces hospital, muscat, Oman, Sultan Qaboos Univ, Med. J. 21 (2) (2021) e282 e288, https://doi.org/10.18295/squmj.2021.21.02.018.

[46] A. Amro, B. Mansoor, O. Hamarsheh, D. Hjaija, Recent trends in human brucellosis in the West Bank, Palestine, Int. J. Infect. Dis. 106 (2021) 308–313, https://doi.org/10.1016/j.ijid.2021.04.037.

[47] M. Dadar, Y. Shahali, Y. Fakhri, Brucellosis in Iranian livestock: a meta-epidemiological study, Microb. Pathog. 155 (2021) 104921, https://doi.org/10.1016/j.micpath.2021.104921.

[48] E. Celik, T. Kayman, F. Buyuk, A.G. Saglam, S. Abay, M. Akar, E. Karakaya, C.E.B. Bozlak, M.R. Coskun, E. Buyuk, The canonical *Brucella* species-host dependency is changing, however, the antibiotic susceptibility profiles remain unchanged, Microb. Pathog. 182 (2023) 106261, https://doi.org/10.1016/j.micpath.2023.106261.

[49] K. Akar, O. Erganis, Evaluation of the genetic profiles of Brucella melitensis strain from Turkey using multilocus variable number tandem repeat analysis (MLVA) and multilocus sequence typing (MLST) techniques, Vet. Mic. 269 (2022) 109423, https://doi.org/10.1016/j.vetmic.2022.109423.

[50] A.I. Rahil, M. Othman, W. Ibrahim, M.Y. Mohamed, Brucellosis in Qatar: a retrospective cohort study, Qatar Med. J. 2014 (1) (2014) 4, https://doi.org/10.5339/qmj.2014.4.

[51] I. Varikkodan, V.A. Naushad, N.K. Purayil, M. Zahid, J. Sirajudeen, N. Ambra, A.M. Mohammed, J. Trivedi, S.P. Kandalam, P. Joseph, Demographic characteristics, laboratory features and complications in 346 cases of brucellosis: a retrospective study from Qatar, IJID regions 10 (2024) 18–23, https://doi.org/10.1016/j.ijregi.2023.11.007.

[52] T. Dimitrov, D. Panigrahi, M. Emara, F. Awni, R. Passadilla, Seroepidemiological and microbiological study of brucellosis in Kuwait, Med. Princ. Pract. 13 (4) (2004) 215–219, https://doi.org/10.1159/000078319.

[53] A.M. Al Haddad, A.K. Al Madhagi, A.A. Talab, H.A. Al Shamahy, The prevalence of human brucellosis in three selected areas in Al-Dala'a governorate, Yemen, Faculty Sci. Bull. 25 (2013) 61–71.

[54] H.A. Al-Shamahy, C.J.M. Whitty, S.G. Wright, Risk factors for human brucellosis in Yemen: a case control study, Epidemiol. Infect. 125 (2) (2000) 309–313, https://doi.org/10.1017/S0950268899004458.
[55] S. Al-Arnoot, Q. Abdullah, S. Alkhyat, A. Almahbashi, M. Al-Nowihi, Human and animal brucellosis in Yemen, J. Hum. Virol. Retrovirol. 5 (4) (2017) 00162, https://doi.org/10.15406/jhvrv.2017.05.00162.
[56] M. Alsaif, K. Dabelah, R. Featherstone, J.L. Robinson, Consequences of brucellosis infection during pregnancy: a systematic review of the literature, Int. J. Infect. Dis. 73 (2018) 18–26, https://doi.org/10.1016/j.ijid.2018.05.023.
[57] A.M. Arenas-Gamboa, C.A. Rossetti, S.P. Chaki, D.G. Garcia-Gonzalez, L.G. Adams, T.A. Ficht, Human brucellosis and adverse pregnancy outcomes, Curr Trop Med Rep 3 (4) (2016) 164–172, https://doi.org/10.1007/s40475-016-0092-0.
[58] A. Inan, H. Erdem, N. Elaldi, S. Gulsun, M.K. Karahocagil, A.U. Pekok, M. Ulug, R. Tekin, M. Bosilkovski, S. Kaya, A. Haykir-Solay, T. Demirdal, S. Kaya, M. Sunnetcioglu, A. Sener, S. Tosun, E. Aydin, S. Ural, T. Yamazhan, M. Muhcu, E. Ayaslioglu, S. Bilgic-Atli, A. Erbay, P. Ergen, A. Kadanali, S. Sahin, E. Sahin-Horasan, A. Avci, Y. Cag, N.J. Beeching, Brucellosis in pregnancy: results of multicenter ID-IRI study, Eur. J. Clin. Microbiol. Infect. Dis. 38 (7) (2019) 1261–1268, https://doi.org/10.1007/s10096-019-03540-z.
[59] A. Orduna, A. Almaraz, A. Prado, M.P.n. Gutierrez, A. Garcia-Pascual, A. Duenas, M. Cuervo, R. Abad, B. Hernández, B. Lorenzo, Evaluation of an immunocapture-agglutination test (Brucellacapt) for serodiagnosis of human brucellosis, J. Clin. Mic. 38 (11) (2000) 4000–4005, https://doi.org/10.1128/JCM.38.11.4000-4005.2000.
[60] G. Di Bonaventura, S. Angeletti, A. Ianni, T. Petitti, G. Gherardi, Microbiological laboratory diagnosis of human brucellosis: an overview, Pathogens 10 (12) (2021) 1623, https://doi.org/10.3390/pathogens10121623.
[61] P. Yagupsky, P. Morata, J.D. Colmenero, Laboratory diagnosis of human brucellosis, Clin. Mic. Rev. 33 (1) (2019), https://doi.org/10.1128/CMR.00073-19, 10.1128/cmr. 00073-19.
[62] G. Tumwine, E. Matovu, J.D. Kabasa, D.O. Owiny, S. Majalija, Human brucellosis: sero-prevalence and associated risk factors in agro-pastoral communities of Kiboga District, Central Uganda, BMC Publ. Health 15 (2015) 1–8, https://doi.org/10.1186/s12889-015-2242-z.
[63] A.M. Alkahtani, M.M. Assiry, H.C. Chandramoorthy, A.M. Al-Hakami, M.E. Hamid, Sero-prevalence and risk factors of brucellosis among suspected febrile patients attending a referral hospital in southern Saudi Arabia (2014-2018), BMC Infect. Dis. (2020), https://doi.org/10.1186/s12879-020-4763-z.
[64] S. Nematollahi, E. Ayubi, M. Karami, S. Khazaei, M. Shojaeian, R. Zamani, K. Mansori, B. Gholamaliee, Epidemiological characteristics of human brucellosis in hamadan Province during 2009–2015: results from the national notifiable diseases surveillance system, Int. J. Infect. Dis. 61 (2017) 56–61, https://doi.org/10.1016/j.ijid.2017.06.002.
[65] M. Refai, Incidence and control of brucellosis in the Near East region, Vet. Mic. 90 (1–4) (2002) 81–110, https://doi.org/10.1016/S0378-1135(02)00248-1.
[66] F. Abnaroodheleh, A. Emadi, S. Dashtipour, T. Jamil, A.M. Khaneghah, M. Dadar, Shedding rate of *Brucella* spp. in the milk of seropositive and seronegative dairy cattle, Heliyon 9 (4) (2023) e15085, https://doi.org/10.1016/j.heliyon.2023.e15085.
[67] A.S. Dean, L. Crump, H. Greter, E. Schelling, J. Zinsstag, Global burden of human brucellosis: a systematic review of disease frequency, PLoS Negl. Trop. Dis. 6 (10) (2012) e1865, https://doi.org/10.1371/journal.pntd.0001865.