UMSHA Press

AJCMI
Avicenna Journal of Clinical Microbiology and Infection

Avicenna J Clin Microbiol Infect 2026;13(2):96-110. doi:10.34172/ajcmi.3809

http://ajcmi.umsha.ac.ir

Original Article

Epidemiological and Clinical Profiling of Brucellosis Relapse and Complication Syndromes: Insights from a Registry in Western Iran

Elham Abdoli[1,2], Seyed Hamid Hashemi[1,2], Mohammad Mahdi Majzoobi[1,2], Mojgan Mamani[1,2], Peyman Eini[1,2], Fatemeh Torkaman Asadi[1,2], Mohammad Yousef Alikhani[1,3], Erfan Ayubi[4], Eleheh Talebi Ghane[5], Zahra Shivapour[6], Ali Saadatmand[1], Maryam Farokhi[7], Sima Kazemi[1*]

[1]Infectious Disease Research Center, Avicenna Institute of Clinical Sciences, Hamadan University of Medical Sciences, Hamadan, Iran
[2]Department of Infectious Diseases, Hamadan University of Medical Sciences, Hamadan, Iran
[3]Department of Microbiology, Faculty of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[4]Cancer Research Center, Institute of Cancer, Avicenna Health Research Institute, Hamadan University of Medical Sciences, Hamadan, Iran
[5]Modeling of Noncommunicable Diseases Research Center, Institute of Health Sciences and Technologies, Hamadan University of Medical Sciences, Hamadan, Iran
[6]School of Public Health and Social Determinants of Health Research Center, Institute of Health Sciences and Technologies, Hamadan University of Medical Sciences, Hamadan, Iran
[7]Deputy of Research and Technology, Hamadan University of Medical Sciences, Hamadan, Iran

Article history:
Received: September 27, 2025
Revised: December 4, 2025
Accepted: December 14, 2025
ePublished: June 29, 2026

***Corresponding author:**
Sima Kazemi,
Email: Simakazemi67@gmail.com

Abstract

Introduction: Brucellosis manifests heterogeneously across endemic regions, with relapse and complication patterns remaining inadequately characterized. This study leverages a provincial registry to delineate syndrome-specific epidemiological and clinical profiles.

Methods: A prospective cohort analysis of 30 brucellosis cases confirmed by both serological testing and compatible clinical manifestations registered in Hamadan Province, Iran (2023–2024). Cases were stratified as Relapse-only (R) (16.67%), Complication-only (C) (70%), or Relapse-Complication Syndrome (RC) (13.33%). Multivariate non-parametric analyses compared demographics, exposures, clinical features, and laboratory parameters.

Results: Males predominated (66.7%), with mean age 48.9 ± 18.9 years. Complication-only patients were older (51.2 ± 16.8 vs. 44.4 ± 11.1 in relapse; $P = 0.895$). Occupational animal contact (80%) and unpasteurized dairy consumption (40%) were primary risks. Relapse-Complication Syndrome showed male predominance (75%) and concentrated age distribution (53–62 years). Musculoskeletal complications dominated (40% arthritis, 40% spondylitis), disproportionately affecting lumbar vertebrae (80%). Symptomatically, generalized pain (93.3%), fatigue (83.3%), and back pain (73.3%) were ubiquitous, while fever discriminated Relapse-Complication Syndrome (75% vs. 47.6% in complications; $P = 0.560$). Serology (Wright ≥ 1:80 in 90%) and inflammatory markers (ESR > 50mm/hr in 32%) showed no syndromic discrimination. Novel incidence patterns emerged: highest relapse in Famenin males (35.71/1000), complications in Tuyserkan males (57.14/1000), and Relapse-Complication in Bahar females (45.45/1000).

Conclusion: This registry-based syndromic stratification identifies distinct epidemiological phenotypes. The high complication burden despite treatment, geographic clustering, and dissociation between serology and clinical severity demand revised surveillance protocols and targeted prevention in agricultural communities.

Keywords: Brucellosis relapse, Zoonotic, Iran, Registry data

Please cite this article as follows: Abdoli E, Hashemi SH, Majzoobi MM, Mamani M, Eini P, Torkaman Asadi F, et al. Epidemiological and clinical profiling of brucellosis relapse and complication syndromes: insights from a registry in western Iran. Avicenna J Clin Microbiol Infect 2026;13(2):96-110. doi:10.34172/ajcmi.3809

Introduction

Brucella is a genus of small, Gram-negative bacteria that live primarily inside the cells of animals (1). Several species of *Brucella* can infect livestock such as cattle, sheep, goats, and pigs, and some of them are able to cause disease in humans (2). The illness they produce, known

as brucellosis, is a zoonotic infection meaning it can be transmitted from animals to people. *Brucella* bacteria are well adapted to survive in animal tissues and can persist for long periods in certain environments, making control of the disease challenging. Brucellosis occurs in many parts of the world, but its prevalence is highest in regions where livestock vaccination programs are incomplete or food safety measures are insufficient (2). Countries in the Mediterranean basin, the Middle East, parts of Africa, South America, and Asia continue to report significant numbers of cases each year (3).

Iran reporting endemic transmission (incidence: 26.5/100,000). In Iran, brucellosis is considered an endemic disease, affecting both rural and semi-rural populations (4). Among Iranian provinces, Hamadan has been repeatedly identified as one of the areas with a relatively high incidence, largely due to its agricultural activities, high density of small ruminants, and cultural practices surrounding animal husbandry and dairy consumption (5). Humans typically acquire brucellosis through direct contact with infected animals or animal products (6). The most common route is ingestion of unpasteurized milk or fresh dairy products such as cheese made from infected animals. *Brucella* can also enter the body through cuts or abrasions in the skin during the handling of animal carcasses, placentas, or other contaminated materials. Inhalation of airborne bacteria, especially in abattoirs or laboratories, is another recognized route of transmission. Person-to-person spread is extremely rare (7, 8). The effects of brucellosis extend beyond human health, placing a considerable economic burden on affected regions. In livestock, the disease causes reproductive problems such as abortions, stillbirths, and reduced fertility, leading to lower herd productivity (9). These losses reduce farmers' incomes and, on a national scale, decrease the supply of meat and dairy products. Governments also face significant costs related to diagnosis, treatment, public health campaigns, and livestock vaccination programs. In endemic areas, brucellosis can slow the growth of the agricultural sector, indirectly influencing food prices and rural economic stability (10).

The Hamadan Brucellosis Registry, established in one of Iran's leading livestock-producing regions, offers valuable insights into existing knowledge gaps. This study introduces a novel syndromic framework comprising Relapse-only, Complication-only, and Relapse-Complication Syndrome to characterize demographic and exposure determinants, define clinical and laboratory phenotypes, and map geographic heterogeneity in incidence. We propose that susceptibility to complications arises from the combined effects of treatment adherence, host-specific factors, and pathogen-related virulence.

Materials and Methods

This prospective cohort analysis, conducted between 2023 and 2024, draws on data from the Hamadan Provincial Brucellosis Registry, which encompasses residents across nine counties. A confirmed case was defined as the presence of compatible clinical symptoms together with a Wright agglutination titer of at least 1:160 (11-13). Relapse was defined as the reappearance of symptoms accompanied by seroconversion after documented clinical cure, while complications were identified as focal organ involvement such as articular, neurological, or genitourinary manifestations verified through imaging or biopsy. Patients were further stratified into three syndromic groups: Group R, representing relapse without complications; Group C, representing complications without a prior history of relapse; and Group RC, representing concurrent relapse and complications. Data collection followed a standardized protocol and included demographic information, occupation, and place of residence, as well as detailed clinical features, the type of complications observed, serologic test results (Wright, 2ME, Coombs Wright), inflammatory markers such as ESR and CRP, and a complete treatment history.

Statistical Analysis

Non-parametric methods (Mann-Whitney U, Kruskal-Wallis) compared continuous variables; Fisher's exact test analyzed categorical data. Incidence rates calculated per 100,000 population using 2024 census data. Significance: $P < 0.05$. Analyses used Stata 17.0.

Ethical Approval

Hamadan University of Medical Sciences Ethics Committee (IR.HUMS.REC.1403.057).

Results

Demographic and Age Characteristics of Brucellosis Cases

During the study period (2023–2024), a total of 30 cases of brucellosis registered by in the software. The cohort demonstrated a clear male predominance, comprising 20 men (66.7%) and 10 women (33.3%). Patient ages ranged from 16 to 77 years, with an overall mean of 48.90 ± 18.90 years. Among males, the age range was 16–77 years with a mean age of 48.75 ± 15.19 years and a mean rank of 16.65. Female patients were aged 31–70 years, with a mean age of 49.20 ± 11.40 years and a mean rank of 15.20. Statistical analysis using the Mann–Whitney U test revealed no significant age difference between sexes ($P = 0.895$, $U = 97.00$), with a negligible effect size ($r = 0.03$).

Of the 30 registered patients, 5 patients had recurrence (16.67%), 21 patients had complications (70.00%), and 4 patients had both recurrence and complications (13.33%). (Table 1)

Age Distribution of Brucellosis Patients with Recurrence, Complications, or Both Recurrence and Complications, by Sex.

Based on the results of the Kruskal-Wallis test, no significant difference was observed in the age of patients with recurrence, complications, or both recurrence and complications among men (P-value = 0.560). The age range of men with complications (16-77 years) was wider

compared to men with recurrence (19-50 years) and both recurrence and complications (58-62 years). Men with both recurrence and complications had a narrower age range compared to the other two patient groups.

In men, the mean rank of age in patients with recurrence, complications, and both recurrence and complications increased (8.00, 10.23, and 13.50, respectively), indicating a higher age range in the group with both recurrence and complications compared to those with only complications or only recurrence.

Based on the results of the Kruskal-Wallis test, no significant difference was observed in the age of patients with recurrence, complications, or both recurrence and complications among women (P-value = 0.715). The age range in women with recurrence (31-60 years) and complications (37-70 years) was not available for those with both conditions. (Table 2)

In women, the mean rank of age in the group with both recurrence and complications was higher compared to those with only complications or only recurrence, indicating that patients with both recurrence and complications were older than those with only complications or only recurrence.

When comparing the age range of patients with final diagnoses between women and men, the age distribution was wider in men than in women. The minimum age in the group with both recurrence and complications was lower in men compared to women. The mean rank of age in the male group was higher than in the female group, indicating that the age of onset was higher in women compared to men.

No significant difference was observed in the age distribution of patients across the recurrence, complications, and both recurrence and complications groups.

Demographic and Geographic Patterns of Brucellosis

Table 1. Comparison of age distribution by sex

Sex	Male	Female	Total
Frequency	20	10	30
Age Range (years)	16–77	31–70	16–77
Mean Age ± SD (years)	48.75 ± 15.19	49.20 ± 11.40	48.90 ± 16.75
Mean Rank	16.65	15.20	-
Mann–Whitney U		97.00***	
P-value		0.895***	

***Non-parametric Kruskal-Wallis test

Recurrence and Complications

Among patients with recurrence, women (60%) had a higher frequency compared to men, while among those with recurrence and complication, men had a higher frequency compared to women (71.4% and 75%, respectively). In patients with recurrence, the highest frequency was observed in the 30–39-year age group (40.00%), whereas in patients with complications, the highest frequency occurred in the 70–79 and 50–59-year age groups (19.04% each). Among those with both recurrence and complication, half of the patients were in the 50–59-year age group and the other half in the 60–69-year age group. Overall, the highest frequency was in the 50–59-year age group (23.33%), and the lowest frequency was in the 10–19-year age group (6.67%).

Among patients with recurrence, the highest frequency was in rural residents (80.00% and 76.19%, respectively), while in patients with both recurrence and complication, the frequencies were equal between urban and rural residents. Among all registered patients, rural residents (73.33%) had a higher frequency compared to urban residents.

In patients with recurrence, the cities of Razan, Kabudarahang, Famenin, and Nahavand each had an equal distribution of one case. Among patients with complications, the highest frequency was from Kabudarahang and Razan, with 5 cases (23.81%), while 50% of patients with both recurrence and complication were from Asadabad, which had the highest frequency in this group. Overall, the highest frequency (20%) belonged to the cities of Razan and Kabudarahang. (Table 3)

Distribution of High-Risk Behaviors Based on Disease Status

The findings of this study revealed that among the 30 patients studied, 21 (70.00%) had complications, 5 (16.67%) had a relapse, and 4 (13.33%) experienced both relapse and complication.

Regarding occupational distribution, housewives (37.50%) had the highest frequency in the relapse group, while livestock farmers had the highest frequency in both the complication (50.00%) and relapse & complication (75.00%) groups.

The study indicated a significant association between contact with livestock and the disease, as 80% of all patients reported a history of contact. This rate was 80.00%, 80.95%, and 75.00% in the relapse, complication,

Table 2. The age distribution of brucellosis patients with recurrence, complication, and both recurrence and complication, by sex.

sex	Final Diagnosis	N	Min Age	Max Age	Mean Rank	P-value
Male	Relapse	2	19	50	8.00	0.560
	Complication	15	16	77	10.23	
	Relapse & Complication	3	58	62	13.50	
Female	Relapse	3	31	60	4.33	0.715
	Complication	6	37	70	5.92	
	Relapse & Complication	1	53	-	6.50	

***Non-parametric Kruskal-Wallis test

Table 3. The frequency distribution of demographic characteristics in patients with brucellosis presenting with recurrence, complication, and both recurrence and complication.

Variable		Recurrence Frequency (%)	Complication Frequency (%)	Recurrence & Complication Frequency (%)	Total Frequency (%)
Final Diagnosis		5 (16.67)	21 (70.00)	4 (13.33)	30 (100)
	Yes	0 (0)	0 (0)	0 (0)	0 (0)
Pregnancy	No	3 (100)	6 (100)	1 (100)	10 (100)
	Total	3 (100)	6 (100)	1 (100)	10 (100)
	Male	2 (40)	15 (71.4)	3 (75.00)	20 (66.6)
Gender	Female	3 (60)	6 (28.6)	1 (25.00)	10 (33.3)
	Total	5 (100)	21 (100)	4 (100)	30 (100)
	10-19	0(0)	2(9.52)	0(0)	2(6.67)
	20-29	0(0)	2(9.52)	0(0)	2(6.67)
	30-39	2 (40.00)	3 (14.29)	0(0)	5 (16.67)
	40-49	1(20.00)	3 (14.29)	0(0)	4 (13.33)
	50-59	1(20.00)	4(19.40)	2 (50.00)	7 (23.33)
Age Group (years)	60-69	1(20.00)	3 (14.29)	2 (50.00)	6 (20.00)
	70-79	0(0)	4 (19.04)	0(0)	4 (13.33)
	80-89	0(0)	0(0)	0(0)	0(0)
	Range	31-60	16-77	53-62	16-77
	Mean (SD)	44.40 (11.05)	48.19(18.90)	58.25 (3.86)	-
	Mean Rank	12.20	15.26	20.88	-
			***P*-value: 0.331**		
	Urban	1 (20.00)	5 (23.81)	2 (40.00)	8 (26.67)
Place of Residence	Rural	4 (80.00)	16 (76.19)	2 (40.00)	22 (73.33)
	Total	5 (100)	21 (100)	4 (100)	30 (100)
	Asadabad	0 (0)	0 (0)	2 (50.00)	2 (6.7)
	Bahar	0 (0)	2 (9.52)	1 (25.00)	3 (10.00)
	Tuyserkan	0 (0)	3 (14.29)	1 (25.00)	4 (13.3)
	Razan	1 (20.00)	5 (23.81)	0 (0)	6(20.00)
	Kabudarahang	1 (20.00)	5 (23.81)	0 (0)	6(20.00)
County of Residence	Famenin	1 (20.00)	0 (0)	0 (0)	1 (3.3)
	Malayer	1 (20.00)	0 (0)	0 (0)	1 (3.3)
	Nahavand	0 (0)	1 (4.76)	0 (0)	1 (3.3)
	Hamadan	0 (0)	4 (19.05)	0 (0)	4 (13.3)
	Outside Hamadan Province	1 (20.00)	1 (4.76)	0 (0)	2 (6.7)
	Total	5 (100)	21 (100)	4 (100)	30 (100)

***Non-parametric Kruskal-Wallis test

and relapse & complication groups, respectively.

Furthermore, 40% of all patients consumed unpasteurized local dairy products, with the highest frequency of consumption (47.62%) observed in the complication group. Among the local dairy products, local milk (91.67%) and local cheese (41.67%) were the most commonly consumed by the patients. (Table 4)

History of Brucellosis Infection and Treatment in Patients with Relapse and Complications

The analysis of the patients' history of brucellosis revealed that all patients in the relapse group (100%) and half of the patients (50.00%) in the relapse & complication group had a previous history of brucellosis. Overall, a history of brucellosis was reported in 40.00% of the registered patients.

Among those with a history of previous infection, the vast majority (83.33%) had experienced the disease once, while 16.67% had been infected twice.

Regarding treatment status at the time of registration, 33.33% of all patients were under treatment for brucellosis. The highest frequency of patients undergoing treatment was observed in the relapse & complication group (75.00%). (Table 5)

Frequency and Distribution of Clinical Symptoms in Patients with Relapse, Complication, and Relapse with Complication

In the examination of clinical symptoms, generalized body pain, fatigue, and back pain were the most frequent

Table 4. Distribution of High-Risk Behaviors in Patients with Relapse, Complication, and Relapse & Complication of Brucellosis

Variable		Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
Final Diagnosis		5 (16.67)	21 (70)	4 (13.33)	30 (100)
Occupation	Farmer	1 (12.50)	1 (5.00)	0 (0)	2 (6.90)
	Livestock Farmer	1 (20.00)	10 (50.00)	3 (75.00)	14 (48.28)
	Butcher	0 (0)	0 (0)	0 (0)	0 (0)
	Slaughterhouse Worker	0 (0)	1 (5.00)	0 (0)	1 (3.45)
	Vaccinator/Veterinarian	0 (0)	0 (0)	0 (0)	0 (0)
	Housewife	3 (37.50)	5 (25.00)	0 (0)	8 (27.59)
	Other	0 (0)	3 (15.00)	1 (25.00)	4 (13.79)
	Total	5 (100)	20(100)	4 (100)	29 (100)
Contact with Livestock	Yes	4 (80.00)	17 (80.95)	3 (75.00)	24 (80.00)
	No	1 (20.00)	(05/19)4	1 (25.00)	6 (20.00)
	Total	5 (100)	21 (100)	4 (100)	30 (100)
Use of Local Dairy	Yes	1 (20.00)	(62/47)10	1 (25.00)	12 (40.00)
	No	4 (80.00)	(38/52)11	3 (75.00)	18 (60.00)
	Total	5 (100)	21 (100)	4 (100)	30 (100)
Subtypes of Local Dairy (Cream (Sarshir)	Yes	0 (0)	0 (0)	0 (0)	0 (0)
	No	1 (100)	10 (100)	1 (0)	12 (100)
	Total	1 (100)	10 (100)	0 (0)	12 (100)
Milk	Yes	1 (50.00)	9 (90.00)	1 (25.00)	11 (91.67)
	No	0 (0)	1 (10.00)	0 (0)	1 (8.33)
	Total	1 (100)	10 (100)	1 (100)	12 (100)
Traditional Ice Cream	Yes	0 (0)	0 (0)	0 (0)	0 (0)
	No	1 (100)	10 (100)	1 (100)	12 (100)
	Total	1 (100)	10 (100)	1 (100)	12 (100)
Cheese	Yes	0 (0)	5 (50.00)	0 (0)	5 (41.67)
	No	1 (100)	5 (50.00)	1 (100)	7 (48.33)
	Total	1 (100)	10 (100)	1 (100)	12 (100)
Traditional Cream	Yes	0 (0)	0 (0)	0 (0)	0 (0)
	No	1 (100)	10 (100)	1 (100)	12 (100)
	Total	1 (100)	10 (100)	1 (100)	12 (100)

*The assumptions of the chi-square test are not met.

Table 5. Distribution of relapse, complication, and relapse & complication based on the history of brucellosis infection

Variable	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
Final Diagnosis	5 (16.67)	21 (70.00)	4 (13.33)	30 (100)
History of Brucellosis				
Yes	5 (100)	5 (23.81)	2 (50.00)	12 (40.00)
No	0 (0)	16 (76.19)	2 (50.00)	18 (60.00)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Number of Brucellosis Episodes				
1 time	5 (100)	3 (60.00)	2 (50.00)	10 (83.33)
2 times	0 (0)	2 (40.00)	0 (0)	2 (16.67)
Total	5 (100)	5 (100)	2 (100)	12 (100)
Under Treatment for Brucellosis				
Yes	3 (60.00)	4 (19.05)	3 (75.00)	10 (33.33)
No	2 (40.00)	17 (80.95)	1 (25.00)	20 (66.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)

*The assumptions of the chi-square test are not met.

Table 6. Frequency distribution of relapse, complication, and relapse & complication of brucellosis according to clinical symptoms

Clinical Symptom	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
Final Diagnosis	5 (16.67)	21 (70.00)	4 (13.33)	30 (100)
Fever				
Yes	3 (60.00)	10 (47.62)	3 (75.00)	16 (53.33)
No	2 (40.00)	11 (52.38)	1 (25.00)	14 (46.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Chills				
Yes	3 (60.00)	7 (33.33)	2 (50.00)	12 (40.00)
No	2 (40.00)	17 (80.95)	2 (50.00)	18 (60.00)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Fatigue				
Yes	5 (100)	16 (76.19)	4 (100)	25 (83.33)
No	0 (0)	5 (23.81)	0 (0)	5 (16.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Sweating				
Yes	0 (0)	8 (38.10)	0 (0)	8 (26.67)
No	5 (100)	13 (61.90)	4 (100)	22 (73.33)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Weight Loss				
Yes	0 (0)	4 (19.05)	1 (25.00)	5 (16.67)
No	5 (100)	17 (80.95)	3 (75.00)	25 (83.33)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Anorexia				
Yes	3 (60.00)	6 (28.57)	3 (75.00)	12 (40.00)
No	2 (40.00)	15 (71.43)	1 (25.00)	18 (60.00)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Headache				
Yes	2 (40.00)	1 (4.76)	1 (25.00)	4 (13.33)
No	3 (60.00)	20 (95.24)	3 (75.00)	26 (86.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Generalized body pain				
Yes	5 (100)	19 (90.48)	4 (100)	28 (93.33)
No	0 (0)	2 (9.52)	0 (0)	2 (6.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Back pain				
Yes	5 (100)	13 (61.90)	4 (100)	22 (73.33)
No	0 (0)	8 (38.10)	0 (0)	8 (26.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Arthralgia (Joint pain)				
Yes	1 (20.00)	14 (66.67)	3 (75.00)	18 (60.00)
No	4 (80.00)	7 (33.33)	1 (25.00)	12 (40.00)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Abdominal pain				
Yes	0 (0)	0 (0)	0 (0)	0 (0)
No	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Testicular pain (Men)				
Yes	0 (0)	3 (20.00)	1 (33.33)	4 (20.00)
No	2 (100)	12 (80.00)	2 (66.67)	16 (80.00)
Total	2 (100)	15 (100)	3 (100)	20 (100)

Table 6. Continued.

Clinical Symptom	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
Cough				
Yes	1 (20.00)	0 (0)	0 (0)	1 (3.33)
No	4 (80.00)	21 (100)	4 (100)	29 (96.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
Behavioral disorders				
Yes	0 (0)	0 (0)	0 (0)	0 (0)
No	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)

*The assumptions of the chi-square test are not met.

overall, with prevalence rates of 93.33%, 83.33%, and 73.33%, respectively. Conversely, abdominal pain and behavioral disorders had the lowest frequency (0%).

Among patients with relapse, fatigue, generalized body pain, and back pain were the most common symptoms, each with a frequency of 100%. In patients with complications, generalized body pain (90.48%) and fatigue (76.19%) were the most prevalent. For patients experiencing both relapse and complication, fatigue, generalized body pain, and fever were the most frequent symptoms, with rates of 100%, 100%, and 75%, respectively. (Table 6)

Correlation of Initial Symptom Duration with Subsequent Relapse and Complications

In patients with relapse, the number of days from symptom onset was greater than in the other two groups. The mean rank in all three groups of patients was close to the minimum value of the range, indicating that the concentration of the number of days affected is focused within short-term periods. (Table 7)

Distribution of Physical Examination Findings in Patients with Relapse, Complication, and Relapse with Complication

Joint swelling and vertebral tenderness had the highest frequency (23.33%). Lymphadenopathy, hepatomegaly, splenomegaly, rash, and jaundice were not observed in any of the patients. (Table 8)

Types and Frequency of Specific Complications in Brucellosis Patients

Arthritis and spondylitis were the most frequent complications investigated (40.00%). Among patients with arthritis, all had knee arthritis, and 80% of patients with spondylitis had lumbar spondylitis.

Endocarditis (involved valve), pneumonia, pyelonephritis, abdominal abscesses (liver, spleen), acute psychosis, chronic brucellosis, cerebral or peripheral vascular thrombosis, and hepatitis were not observed in any of the patients. No significant difference was found in the incidence of complications between patients with complication and those with relapse & complication. (Table 9)

3.10. Comparative Analysis of Laboratory Parameters in Brucellosis Patients with Relapse, Complication, and Relapse with Complication

In the diagnostic tests for brucellosis (Wright and Coombs Wright), at least 80% of patients had a titer of 1:80 for the Wright test and 50% for the Coombs Wright test across all groups diagnosed with relapse, complication, and relapse & complication. For the 2ME diagnostic test, 60% of patients with relapse had a titer less than 1:80, while 71.43% and 75% had a titer above 1:80 in the complication and relapse & complication groups, respectively.

The highest frequency of ESR test results fell within the 20–50 range. At least 75% of patients in each group had an ESR value below 100. The range of values for this test was 7–115. The range for patients with relapse was 11–50, which was narrower compared to the other two groups.

CRP was positive in 61.11% of cases, with the highest frequency of positive tests observed in patients with complications (80%). The range of CRP values was 1–65, with a shorter range observed in the complication group.

Over 96% of WBC test results fell between 4,000 and 10,000. The range of WBC values was 4,300–10,600, with patients in the relapse group exhibiting higher values compared to the other two groups.

60% of patients were anemic. The frequency of anemia was higher in patients diagnosed with relapse (80%) compared to the other two groups.

The mean rank for the AST liver test was lower in patients with complications (12.34) compared to the other two groups (17.90 for relapse and 18.00 for relapse & complication), indicating lower AST levels in this group of patients.

The mean rank for the ALT liver test was higher in patients with relapse (16.20) compared to the other two groups (13.42 for complications and 14.00 for relapse & complication), indicating higher ALT levels in this group of patients.

The mean ranks for the ALKP liver test in patients with relapse, complications, and relapse & complication were 7.50, 11.27, and 18.00, respectively, indicating the lowest, higher, and highest levels in these groups.

No statistically significant differences were observed in

Table 7. Distribution of Relapse, Complication, and Relapse with Complication based on the Duration of Symptom Onset

	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
	5 (16.67)	21 (70.00)	4 (13.33)	30 (100)
Minimum	20	7	12	7
Maximum	4380	365	90	4380
Mean (SD)	912.00 (1939.03)	64.14 (78.96)	38.00 (35.44)	201.96 (792.09)
Mean Rank	17.70	15.50	12.75	
	***	*P-value* = 0.700	Chi-square = 0.713	

***Non-parametric Kruskal-Wallis test

any of the tests among patients with relapse, complication, and relapse & complication. (Table 10)

3.11. Geographic and Gender-Based Variation in the Incidence of Relapse and Complications of Brucellosis

The highest incidence of relapse was in men from Famenin County (35.71 per thousand). The highest frequency of complication was in men from Tuyserkan County (57.14 per thousand). The highest frequency of relapse with complication was in women from Bahar County (45.45 per thousand). (Table 11)

4. Discussion:

This prospective registry-based cohort study from Western Iran provides a novel syndromic stratification of human brucellosis, delineating the epidemiological, clinical, and geographical characteristics of Relapse-only (R), Complication-only (C), and Relapse-Complication Syndrome (RC) groups. Our findings reveal critical insights that align with, yet also challenge, existing literature on brucellosis in both endemic and non-endemic regions. The significant male predominance (66.7%) and high rate of occupational exposure (80%) observed in our cohort are consistent with previous studies from Iran and other endemic regions. Keramat et al. similarly identified male gender and livestock contact as major risk factors in brucellosis transmission in Iran (14) while a global meta-analysis confirmed these patterns across multiple endemic countries (15).The mean age of our cohort (48.9 years) is notably higher than that reported in studies from Mediterranean countries where younger populations are typically affected (16). This finding possibly reflects an aging agricultural workforce in Hamadan province and aligns with reports from other Middle Eastern countries experiencing similar demographic shifts (17). The high complication burden (83.33% of our cohort) represents a particularly alarming finding. This rate exceeds those reported in many previous studies, including earlier reviews of brucellosis complications in Iran (18) and the 60-70% rates reported from other endemic regions (19). The musculoskeletal predominance (40% arthritis, 40% spondylitis) with a strong lumbar spine preference (80% of spondylitis cases) aligns with the well-established tropism of Brucella species for the axial skeleton. This pattern is consistent with international reports (20) (21), though our higher spondylitis rates may reflect differences in diagnostic intensity or strain virulence. A particularly intriguing finding was the demographic pattern of the Relapse-Complication Syndrome (RC) group, which showed a concentrated age distribution (53-62 years) and high male predominance (75%). This pattern differs from the more uniform relapse demographics reported by Hashemi et al. in the same region (22) and contrasts with international reports (23) .The distinct clinical presentation of this group, characterized by universal fatigue and generalized pain with high fever rates (75%), suggests a potentially different pathophysiological mechanism that merits specific attention. The higher proportion of females in the relapse-only group (60%) compared to the complication-only group (28.6%), though not statistically significant, presents an interesting paradox. This pattern may reflect gender-specific differences in healthcare-seeking behavior, treatment adherence, or immunological responses. These findings partially align with analyses from Turkey by Buzgan et al. (24) but contrast with reports from Peru (25), highlighting the importance of regional and cultural factors. The persistent high rate of unpasteurized dairy consumption (40%) despite extensive public health campaigns underscores the deep-rooted cultural practices in the region, a challenge consistent with reports from traditional societies in Mexico (26) and Kenya (27).However, the equally important role of occupational exposure (80% of cases) reinforces the need for combined agricultural and public health interventions. Perhaps our most significant finding is the profound dissociation between serological titers and clinical severity. The uniform elevation of Wright titers ($\geq$1:80 in 90% of cases) across all clinical syndromes challenges the conventional wisdom of using serological cutoffs as severity markers. This finding contradicts some earlier studies but aligns with the growing body of evidence, including work by Araj et al.(28) from Lebanon and Mantur et al. from India (29), suggesting that antibody titers may reflect exposure history rather than disease activity. The

Table 8. Distribution of Relapse, Complication, and Relapse with Complication based on Clinical Findings

Clinical Findings	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
	5 (16.67)	21 (70.00)	4 (13.33)	30 (100)
Joint Swelling				
Present	0 (0)	7 (33.33)	0 (0)	7 (23.33)
Absent	5 (100)	14 (66.67)	4 (100)	23 (76.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			
Splenomegaly				
Present	0 (0)	0 (0)	0 (0)	0 (0)
Absent	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			
Vertebral Tenderness				
Present	0 (0)	7 (33.33)	0 (0)	7 (23.33)
Absent	5 (100)	14 (66.67)	4 (100)	23 (76.67)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			
Orchitis (in males)				
Present	0 (0)	3 (20.00)	0 (0)	3 (15.00)
Absent	2 (100)	12 (80.00)	3 (100)	17 (85.00)
Total	2 (100)	15 (100)	3 (100)	20 (100)
	*			
Rash				
Present	0 (0)	0 (0)	0 (0)	0 (0)
Absent	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			
Lymphadenopathy				
Present	0 (0)	0 (0)	0 (0)	0 (0)
Absent	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			
Hepatomegaly				
Present	0 (0)	0 (0)	0 (0)	0 (0)
Absent	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			
Jaundice				
Present	0 (0)	0 (0)	0 (0)	0 (0)
Absent	5 (100)	21 (100)	4 (100)	30 (100)
Total	5 (100)	21 (100)	4 (100)	30 (100)
	*			

*The assumptions of the chi-square test are not met.

Table 9. Frequency Distribution of Patients with Complication and Relapse & Complication of Brucellosis by Type of Complication

Final Diagnosis	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
	21 (84.00)	4 (16.00)	25 (100)
Arthritis			
Present	8 (38.10)	2 (50.00)	10 (40.00)
Absent	13 (61.90)	2 (50.00)	15 (60.00)
Total	21 (100)	4 (100)	25 (100)
	**	*P* value=0.532	
Knee			
Present	8 (100)	2 (100)	10 (100)
Absent	0 (0)	0 (0)	0 (0)
Total	8 (100)	2 (100)	10 (100)
	*		
Hip			
Present	0 (0)	0 (0)	0 (0)
Absent	8 (100)	2 (100)	10 (100)
Total	8 (100)	2 (100)	10 (100)
	*		
Shoulder			
Present	0 (0)	0 (0)	0 (0)
Absent	8 (100)	2 (100)	10 (100)
Total	8 (100)	2 (100)	10 (100)
	*		
Wrist			
Present	0 (0)	0 (0)	0 (0)
Absent	8 (100)	2 (100)	10 (100)
Total	8 (100)	2 (100)	10 (100)
	*		
Ankle			
Present	0 (0)	1 (50.00)	1 (10.00)
Absent	8 (100)	1 (50.00)	9 (90.00)
Total	8 (100)	2 (100)	10 (100)
	*		
Elbow			
Present	0 (0)	0 (0)	0 (0)
Absent	8 (100)	2 (100)	10 (100)
Total	8 (100)	2 (100)	10 (100)
	*		
Sacroiliitis			
Present	2 (9.52)	0 (0)	2 (8.00)
Absent	19 (90.48)	4 (100)	23 (92.00)
Total	21 (100)	4 (100)	25 (100)
	**	*P* value=1.00	
Sacroiliitis			
Unilateral	1 (50.00)	0 (0)	1 (50.00)
Bilateral	1 (50.00)	0 (0)	1 (50.00)
Total	2 (100)	0 (0)	2 (100)
	*		
Spondylitis			
Present	8 (38.10)	2 (50.00)	10 (40.00)
Absent	13 (61.90)	2 (50.00)	15 (60.00)
Total	21 (100)	4 (100)	25 (100)
	**	*P* value=0.532	
Spondylitis (Cervical)			
Present	0 (0)	0 (0)	0 (0)
Absent	8 (100)	2 (100)	10 (100)
Total	8 (100)	2 (100)	10 (100)
	*		
Spondylitis (Thoracic)			
Present	3 (37.50)	0 (0)	3 (30.00)
Absent	5 (62.50)	2 (100)	7 (70.00)
Total	8 (100)	2 (100)	10 (100)
	*		
Spondylitis (Lumbar)			
Present	6 (75.00)	2 (100)	8 (80.00)
Absent	2 (25.00)	0 (0)	2 (20.00)
Total	8 (100)	2 (100)	10 (100)
	*		
Spondylitis (Sacral)			
Present	2 (25.00)	0 (0)	2 (20.00)
Absent	6 (75.00)	2 (100)	8 (80.00)
Total	8 (100)	2 (100)	10 (100)
	*		
Endocarditis (Involved Valve)			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Epididymo-orchitis (Males only)			
Present	3 (20.00)	0 (0)	3 (16.67)
Absent	12 (80.00)	3 (100)	15 (83.33)
Total	15 (100)	3 (100)	18 (100)
	*		
Testicular Abscess (Males only)			
Present	1 (6.67)	1 (33.33)	2 (11.11)
Absent	14 (93.33)	2 (66.67)	16 (88.89)
Total	15 (100)	3 (100)	18 (100)
	**	*P* value=0.31	
Neurobrucellosis			
Present	1 (4.76)	1 (25.00)	2 (8.00)
Absent	20 (95.24)	3 (75.00)	23 (92.00)
Total	21 (100)	4 (100)	25 (100)
	**	*P* value=0.30	

Table 9. Continued.

Final Diagnosis	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
Pneumonia			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Pyelonephritis			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Abdominal Abscess (Liver, Spleen)			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Acute Psychosis			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Chronic Brucellosis			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Cerebral or Peripheral Vascular Thrombosis			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		
Hepatitis			
Present	0 (0)	0 (0)	0 (0)
Absent	21 (100)	4 (100)	25 (100)
Total	21 (100)	4 (100)	25 (100)
	*		

*The assumptions of the chi-square test are not met.

superior performance of CRP in discriminating active disease supports the evolving paradigm toward using acute phase reactants for monitoring, as proposed in international guidelines (30). The geospatial analysis revealed distinct incidence hotspots that correspond to previously mapped agricultural patterns (31) and provide unprecedented granularity for targeting interventions. The specific clustering of relapse cases in Famenin, complications in Tuyserkan, and RC syndrome in Bahar suggests local variations in circulating strains, veterinary control measures, or healthcare access. Such spatial heterogeneity has been recognized as crucial for control, as demonstrated in studies from China by Liang et al. (32) and Argentina by Samartino et al. (33) . The high rate of treatment failure and complication development despite appropriate therapy (33.33% of patients were under treatment at registration) raises important questions about current therapeutic protocols. This finding resonates with concerns raised by prior research (34) regarding the adequacy of standard regimens. The particularly high treatment rate in the RC group (75%) suggests either more severe disease requiring prolonged therapy or possible development of secondary resistance, a phenomenon previously documented in relapsed cases (35). Several limitations warrant acknowledgment. The modest sample size, for which no *a priori* power calculation was performed, limits subgroup analyses and the statistical power to detect significant differences; consequently, the numerous non-significant *P*-values should be interpreted with caution as potential Type II errors. The absence of microbial genotyping prevents correlation of clinical syndromes with specific *Brucella* species or biovars and definitively distinguishing relapse from re-infection. Furthermore, we did not analyze the time from symptom onset to diagnosis and treatment, nor did we assess metrics of healthcare access (e.g., distance to care, health-seeking behavior), which precludes an evaluation of how these critical delays and disparities may contribute to the high complication burden, particularly among rural residents. Detailed data on the specific antimicrobial regimens and adherence for prior infections were also not analyzed, limiting our understanding of their role in relapse risk. Finally, as a registry study, it may be subject to ascertainment bias, particularly in complication diagnosis. Future research should integrate genomic epidemiology with detailed clinical phenotyping to unravel the complex host-pathogen interactions driving these distinct syndromic presentations.

Conclusion

This study reveals a high burden of complications and distinct relapse patterns in human brucellosis, which are not predicted by standard serological tests. The significant geographic clustering and demographic trends highlight the need for a revised public health strategy. We recommend implementing syndrome-specific surveillance, complication-focused therapies, and geo-targeted veterinary interventions in high-risk communities. Ultimately, integrating genomic data with clinical profiling is crucial to unravel the drivers of these severe disease outcomes.

Table 10. Frequency Distribution of Patients with Complication, Relapse, and Relapse & Complication of Brucellosis based on Laboratory Findings

Laboratory Test	Final Diagnosis	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
		5 (16.67)	21 (70.00)	4 (13.33)	30 (100)
Wright					
1:20		1 (20.00)	0 (0)	0 (0)	1 (3.33)
1:40		0 (0)	2 (9.52)	0 (0)	2 (6.67)
1:80		1 (20.00)	5 (23.81)	1 (25.00)	7 (23.33)
1:160		1 (20.00)	5 (23.81)	1 (25.00)	7 (23.33)
1:320		2 (40.00)	1 (4.76)	0 (0)	3 (10.00)
1:640		0 (0)	3 (14.29)	0 (0)	3 (10.00)
1:1280		0 (0)	3 (14.29)	2 (50.00)	5 (16.67)
≥1:2560		0 (0)	2 (9.52)	0 (0)	2 (6.67)
Total		5 (100)	21 (100)	4 (100)	30 (100)
Wright (Two groups based on titer 1:80)					
Less than 1:80		1 (20.00)	2 (9.52)	0 (0)	3 (10.00)
1:80 and higher		4 (80.00)	19 (90.48)	4 (100)	27 (90.00)
Total		5 (100)	21 (100)	4 (100)	30 (100)
	Fisher's Exact Test=1.20	*P*-value=0.675			
2ME					
1:20		2 (40.00)	2 (9.52)	0 (0)	4 (13.33)
1:40		1 (20.00)	4 (19.05)	1 (25.00)	6 (20.00)
1:80		0 (0)	7 (33.33)	0 (0)	7 (23.33)
1:160		2 (40.00)	1 (4.76)	0 (0)	3 (10.00)
1:320		0 (0)	3 (14.29)	1 (25.00)	4 (13.33)
1:640		0 (0)	2 (9.52)	1 (25.00)	3 (10.00)
1:1280		0 (0)	1 (4.76)	0 (0)	1 (3.33)
≥1:2560		0 (0)	1 (4.76)	1 (25.00)	2 (6.67)
Total		5 (100)	21 (100)	4 (100)	30 (100)
2ME (Two groups based on titer 1:80)					
Less than 1:80		3 (60.00)	6 (28.57)	1 (25.00)	10 (33.33)
1:80 and higher		2 (40.00)	15 (71.43)	3 (75.00)	20 (66.67)
Total		5 (100)	21 (100)	4 (100)	30 (100)
	Fisher's Exact Test=1.94	*P*-value=0.482			
Coombs Wright					
1:20		0 (0)	0 (0)	0 (0)	0 (0)
1:40		0 (0)	0 (0)	1 (50.00)	1 (8.33)
1:80		0 (0)	1 (12.50)	0 (0)	1 (8.33)
1:160		1 (50.00)	2 (25.00)	0 (0)	3 (25.00)
1:320		0 (0)	2 (25.00)	0 (0)	2 (16.67)
1:640		1 (50.00)	1 (12.50)	0 (0)	2 (16.67)
1:1280		0 (0)	0 (0)	0 (0)	0 (0)
≥1:2560		0 (0)	2 (25.00)	1 (50.00)	3 (25.00)
Total		2 (100)	8 (100)	2 (100)	12 (100)
Coombs Wright (Two groups based on titer 1:80)					
Less than 1:80		0 (0)	0 (0)	1 (50.00)	1 (8.33)
1:80 and higher		2 (100)	8 (100)	1 (50.00)	11 (91.67)
Total		2 (100)	8 (100)	2 (100)	12 (100)
	Fisher's Exact Test=4.07	*P*-value=0.333			

Table 10. Continued.

Laboratory Test	Final Diagnosis	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
ESR					
Less than 20		2 (50.00)	2 (11.76)	1 (25.00)	5 (20.00)
20-50		2 (50.00)	9 (52.94)	1 (25.00)	12 (48.00)
51-100		0 (0)	4 (23.53)	1 (25.00)	5 (20.00)
More than 100		0 (0)	2 (11.76)	1 (25.00)	3 (12.00)
Total		4 (100)	17 (100)	4 (100)	25 (100)
Unspecified		1	4	0	5
Frequency		4	17	4	25
Mean (SD)		26.50 (18.30)	51.37 (29.63)	70.00 (0)	52.25 (44.38)
Range		11-50	7-115	7-110	7-115
	***	Chi-square = 1.97	*P*-value = 0.390		
CRP					
Positive		1 (20.00)	8 (80.00)	1 (25.00)	11 (61.11)
Negative		4 (80.00)	2 (20.00)	2 (50.00)	7 (38.89)
Total		5 (100)	10 (100)	3 (100)	18 (100)
Unspecified		0	11	1	12
	*				
Frequency		0	7	2	9
Mean (SD)			17.71 (24.27)	6.52 (6.36)	15.22 (24.21)
Range			1-65	2-11	1-65
Mean Rank			4.93	5.25	
	***	Chi-square = 0.022	*P*-value = 0.882		
WBC					
4000-10000		5 (100)	20 (95.24)	4 (100)	29 (96.67)
More than 10000		0 (0)	1 (4.76)	0 (0)	1 (3.33)
Total		5 (100)	21 (100)	4 (100)	30 (100)
	*				
Frequency		5	19	4	28
Mean (SD)		7900.00 (1598.43)	6842.10 (1819.74)	6400 (1354.00)	6967.85 (1734.83)
Mean Rank		19.20	13.71	12.38	
Range		6100-10000	4300-10600	4800-8100	4300-10600
	***	Chi-square = 2.07	*P*-value = 0.354		
Hemoglobin					
Normal		1 (20.00)	9 (42.86)	2 (50.00)	12 (40.00)
Anemia		4 (80.00)	12 (57.14)	2 (50.00)	18 (60.00)
Total		5 (100)	21 (100)	4 (100)	30 (100)
	*				
Frequency		1	8	1	10
Mean (SD)		10.00 (0)	11.12 (1.67)	13.00 (0)	11.20 (1.64)
Range			8.40-13.60		8.40-13.60
Mean Rank		3.00	5.44	8.50	
	***	Chi-square = 1.6	*P*-value = 0.430		
Liver Tests					
AST					
Frequency		5 (18.52)	19 (70.37)	3 (11.11)	27 (100)
Mean (SD)		26.00 (11.48)	20.53 (11.73)	25.00 (10.53)	22.04 (11.40)
Range		17-40	12-32	17-37	17-37

Table 10. Continued.

Laboratory Test	Final Diagnosis	Relapse Frequency (%)	Complication Frequency (%)	Relapse & Complication Frequency (%)	Total Frequency (%)
Mean Rank		17.90	12.34	18.00	
	***	Chi-square=2.84	*P*-value=0.241		
ALT					
Frequency		5 (18.52)	19 (70.37)	3 (11.11)	27 (100)
Mean (SD)		33.20 (18.67)	30.05 (23.82)	26.33 (10.78)	30.04 (23.82)
Range		12-113	11-113	11-113	11-113
Mean Rank		16.20	13.42	14.00	
	***	Chi-square=0.486	*P*-value=0.784		
ALKP					
Frequency		4 (18.19)	15 (68.18)	3 (13.63)	22 (100)
Mean (SD)		162.75 (57.68)	225.22 (136.92)	347.67 (99.80)	230.56 (129.52)
Range		89-230	2-587	278-462	2-587
Mean Rank		7.50	11.27	18.00	
	***	Chi-square=4.560	*P*-value=0.103		
BILIRUBIN TOTAL					
Frequency		0 (0)	2 (100)	0 (0)	2 (100)
Mean (SD)			6.60 (36.77)		
Range			34-86		34-86
Bilirubin Direct					
Frequency		0 (0)	2 (100)	0 (0)	2 (100)
Mean (SD)			6.15 (8.27)		
Range			0-12		0-12

*: The assumptions of the Chi-square test were not met.
**: Fisher's Exact Test
***: Kruskal-Wallis Test

Table 11. Incidence Rate of Relapse, Complication, and Relapse with Complication by County and Sex

County	Male				Female			
	Relapse	Complication	Relapse & Comp.	Total	Relapse	Complication	Relapse & Comp.	Total
Asadabad	0	0	36.36	36.36	0	0	0	0
Bahar	0	12.20	0	12.20	0	22.73	22.73	45.45
Tuyserkan	0	57.14	28.57	85.71	0	28.57	0	28.57
Razan	0	28.17	0	28.17	15.15	15.15	0	30.30
Kabudarahang	5.54	21.62	0	27.03	0	14.08	0	14.08
Famenin	35.71	0	0	35.71	0	0	0	0
Malayer	0	0	0	0	28.21	0	0	28.21
Nahavand	8.40	0	0	8.40	0	0	0	0
Hamadan	0	24.39	0	24.39	0	15.38	0	15.38

Acknowledgments
The authors would like to thank Mr. Eshraghian and Mr. Hajilooi for their valuable collaboration on this study.

Authors' Contribution
Conceptualization: Elham Abdoli, Sima Kazemi, Mohammad Yousef Alikhani
Data curation: Elham Abdoli, Seyed Hamid Hashemi, Mohammad Mahdi Majzoobi, Mojgan Mamani, Peyman Eini , Fatemeh Torkaman Asadi, Maryam Farokhi , Ali Saadatmand
Formal analysis: Zahra Shivapour, Erfan Ayubi, Eleheh Talebi Ghane
Funding acquisition: Elham Abdoli
Investigation: Sima Kazemi, Elham Abdoli
Methodology: Zahra Shivapour, Erfan Ayubi
Project administration: Elham Abdoli
Resources: Sima Kazemi
Software: Zahra Shivapour
Supervision: Sima Kazemi, Elham Abdoli
Validation: Elham Abdoli, Mohammad Yousef Alikhani, Sima Kazemi
Visualization: Sima Kazemi
Writing–original draft: Sima Kazemi
Writing–review & editing: Sima Kazemi, Elham Abdoli

Competing Interests
The authors declare no conflict of interests.

Ethical Approval
The ethics committee of the Hamadan University of Medical Sciences approved the study protocol (Ethical approval code: IR.UMSHA.REC.1402.135). Ethical Review Board approved written consent taken from all the participants.

Funding
The Vice-chancellor of Research and Technology, Hamadan University of Medical Sciences, Hamadan, Iran supported

financially the study (Grant Number: 140209147897). The funding body had no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

References

1. Adem A, Duguma A. Characteristics and intracellular life of *Brucella* organism: a review. J Microb Biochem Technol. 2020;12(3):431. doi: 10.35248/1948-5948.20.12.431
2. Jawad SM. Brucellosis: infectious disease. In: Rodriguez-Morales AJ, ed. Current Topics in Zoonoses. IntechOpen; 2024. doi: 10.5772/intechopen.114141
3. Liu Z, Gao L, Wang M, Yuan M, Li Z. Long ignored but making a comeback: a worldwide epidemiological evolution of human brucellosis. Emerg Microbes Infect. 2024;13(1):2290839. doi: 10.1080/22221751.2023.2290839.
4. Dadar M, Alamian S, Zowghi E. Comprehensive study on human brucellosis seroprevalence and *Brucella* species distribution in Iran (1970-2023). Microb Pathog. 2025;198:107137. doi: 10.1016/j.micpath.2024.107137
5. Khazaei S, Solgi M, Goodarzi S, Khazaei L, Salehi I, Jenabi E. Epidemiology of human brucellosis in Nahavand county, Hamadan province, western Iran: an 8-year (2010-2017) registry-based analysis. Asian Biomed (Res Rev News). 2020;14(4):151-8. doi: 10.1515/abm-2020-0022
6. Corbel MJ. Brucellosis in Humans and Animals. World Health Organization; 2006.
7. Qureshi KA, Parvez A, Fahmy NA, Abdel Hady BH, Kumar S, Ganguly A, et al. Brucellosis: epidemiology, pathogenesis, diagnosis and treatment-a comprehensive review. Ann Med. 2023;55(2):2295398. doi: 10.1080/07853890.2023.2295398
8. Sharma V, Singh BB, Brookes VJ. Risk assessment of *Brucella* exposure through raw milk consumption in India: one health implications and control strategies. Vet Sci. 2025;12(5):465. doi: 10.3390/vetsci12050465
9. Lokamar PN, Kutwah MA, Atieli H, Gumo S, Ouma C. Socio-economic impacts of brucellosis on livestock production and reproduction performance in Koibatek and Marigat regions, Baringo county, Kenya. BMC Vet Res. 2020;16(1):61. doi: 10.1186/s12917-020-02283-w
10. McDermott J, Grace D, Zinsstag J. Economics of brucellosis impact and control in low-income countries. Rev Sci Tech. 2013;32(1):249-61. doi: 10.20506/rst.32.1.2197
11. Kazemi S, Saidijam M, Hashemi SH, Karami M, Vaisi-Raygani A, Alikhani MY. Analysis of IL-10 and IL-6 gene polymorphisms and their serum levels in patients with brucellosis: a case control study. Immunol Invest. 2016;45(2):107-15. doi: 10.3109/08820139.2015.1096285
12. Kazemi S, Vaisi-Raygani A, Keramat F, Saidijam M, Soltanian AR, Alahgholi-Hajibehzad M, et al. Evaluation of the relationship between IL-12, IL-13 and TNF-α gene polymorphisms with the susceptibility to brucellosis: a case control study. BMC Infect Dis. 2019;19(1):1036. doi: 10.1186/s12879-019-4678-8
13. Lashtoo Aghaee B, Alikhani MY, Kazemi S, Ahmadyousefi M, van Leeuwen WB, Nasaj M. Phage therapy: a targeted solution for brucellosis. Vector Borne Zoonotic Dis. 2025;25(12):713-21. doi: 10.1177/15303667251367519
14. Keramat F, Karami M, Alikhani MY, Bashirian S, Moghimbeigi A, Adabi M. Cohort profile: Famenin brucellosis cohort study. J Res Health Sci. 2019;19(3):e00453.
15. Dean AS, Crump L, Greter H, Hattendorf J, Schelling E, Zinsstag J. Clinical manifestations of human brucellosis: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2012;6(12):e1929. doi: 10.1371/journal.pntd.0001929
16. Abdeen A, Ali H, Bardenstein S, Blasco JM, Cardoso R, Corrêa De Sá MI, et al. Brucellosis in the Mediterranean Countries: History, Prevalence, Distribution, Current Situation and Attempts at Surveillance and Control. Office International des Épizooties (OIE); 2019.
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. Epidemiol Infect. 2016;144(4):671-85. doi: 10.1017/s0950268815002575
18. Adabi M, Gharekhani J, Saadatmand A, Shahbazi F. Seroprevalence of brucellosis in livestock in Iran: a meta-analysis. Comp Clin Path. 2024;33(1):175-82. doi: 10.1007/s00580-023-03543-5
19. Arslan M, Ertunç B, Düz ME, Menekşe E, Avci BY, Avci E, et al. Epidemiological, clinical, biochemical, and treatment characteristics of brucellosis cases in Turkey. J Infect Dev Ctries. 2024;18(7):1066-73. doi: 10.3855/jidc.18977
20. Colmenero JD, Ruiz-Mesa JD, Plata A, Bermúdez P, Martín-Rico P, Queipo-Ortuño MI, et al. Clinical findings, therapeutic approach, and outcome of brucellar vertebral osteomyelitis. Clin Infect Dis. 2008;46(3):426-33. doi: 10.1086/525266
21. AlQahtani H, Alzahrani F, Abalkhail G, Hithlayn HB, Ardah HI, Alsaedy A. Brucellar, pyogenic, and tuberculous spondylodiscitis at tertiary hospitals in Saudi Arabia: a comparative retrospective cohort study. Open Forum Infect Dis. 2023;10(9):ofad453. doi: 10.1093/ofid/ofad453
22. Hashemi SH, Keramat F, Ranjbar M, Mamani M, Farzam A, Jamal-Omidi S. Osteoarticular complications of brucellosis in Hamedan, an endemic area in the west of Iran. Int J Infect Dis. 2007;11(6):496-500. doi: 10.1016/j.ijid.2007.01.008
23. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. Lancet Infect Dis. 2006;6(2):91-9. doi: 10.1016/s1473-3099(06)70382-6
24. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, et al. Clinical manifestations and complications in 1028 cases of brucellosis: a retrospective evaluation and review of the literature. Int J Infect Dis. 2010;14(6):e469-78. doi: 10.1016/j.ijid.2009.06.031
25. Ramos-Ramírez LD, Saldaña-Ahuactzi Z, Morales-Lara L, Martínez-Laguna Y, Castañeda-Roldán EI. Isolation and identification of two *Brucella* species from a volcanic lake in Mexico. Curr Microbiol. 2020;77(11):3565-72. doi: 10.1007/s00284-020-02184-z
26. Lucero NE, Ayala SM, Escobar GI, Jacob NR. *Brucella* isolated in humans and animals in Latin America from 1968 to 2006. Epidemiol Infect. 2008;136(4):496-503. doi: 10.1017/s0950268807008795
27. Osoro EM, Munyua P, Omulo S, Ogola E, Ade F, Mbatha P, et al. Strong association between human and animal *Brucella* seropositivity in a linked study in Kenya, 2012-2013. Am J Trop Med Hyg. 2015;93(2):224-31. doi: 10.4269/ajtmh.15-0113
28. Araj GF, Azzam RA. Seroprevalence of *Brucella* antibodies among persons in high-risk occupation in Lebanon. Epidemiol Infect. 1996;117(2):281-8. doi: 10.1017/s095026880000145x
29. Mantur BG, Amarnath SK, Shinde RS. Review of clinical and laboratory features of human brucellosis. Indian J Med Microbiol. 2007;25(3):188-202. doi: 10.4103/0255-0857.34758
30. Mantur BG, Amarnath SK. Brucellosis in India - a review. J Biosci. 2008;33(4):539-47. doi: 10.1007/s12038-008-0072-1
31. Wilson N, Pedersen S. Inflammatory markers in clinical practice. Am J Respir Crit Care Med. 2000;162(2 Pt 2):S48-51. doi: 10.1164/ajrccm.162.supplement_1.maic-13
32. Liang PF, Zhao Y, Zhao JH, Pan DF, Guo ZQ. Human distribution and spatial-temporal clustering analysis of human brucellosis in China from 2012 to 2016. Infect Dis Poverty. 2020;9(1):142. doi: 10.1186/s40249-020-00754-8
33. Samartino LE. Brucellosis in Argentina. Vet Microbiol. 2002;90(1-4):71-80. doi: 10.1016/s0378-1135(02)00247-x
34. Solís García del Pozo J, Solera J. Systematic review and meta-analysis of randomized clinical trials in the treatment of human brucellosis. PLoS One. 2012;7(2):e32090. doi: 10.1371/journal.pone.0032090
35. Keramat F, Karami M, Mamani M, Saadatmand A, Hashemi SH, Alikhani MY, et al. Relapse and complications of brucellosis: findings of a disease quality registry. J Microbiol Infect Dis. 2023;13(3):155-64. doi: 10.5455/JMID.2023.v13.i3.8