

Epidemiological Features, Clinical Manifestation and Laboratory Findings of Patients With Brucellosis

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Received: December 29, 2013; Accepted: January 15, 2014

Background: Brucellosis as a zoonotic infectious disease is endemic in Iran and due to the variation in clinical and laboratory findings, its diagnosis is often delayed.

Objectives: The aim of this study was to determine clinical and laboratory aspects of the disease in Khuzestan.

Patients and Methods: Medical records of 81 admitted patients with a diagnosis of brucellosis were reviewed. The study took place at Razi Hospital, a teaching hospital where infectious patients of Khuzestan are referred. Clinical and laboratory findings of patients were reviewed. Diagnosis of brucellosis was made by measuring Brucella antibodies in the presence of clinical findings suggestive of brucellosis. Wright and mercapto-ethanol (2 ME) with titers more than 1/80 were considered positive.

Results: The most common symptoms of the disease in this study were fever (85.2%), joint pain (72.9%), chills (42%) and sweating (37%). The most common signs in this study were arthritis (9.9%), tachycardia (6.2%) and tenderness in the lumbar spine (4.9%). Furthermore, the most common laboratory findings were normal white blood count (WBC) (94.82%), anemia (75.3%) and elevated erythrocyte sedimentation rate (ESR) (75.3%).

Conclusions: In the studied region, when dealing with patients complaining of fever, chills, sweating and joint pain associated with normal WBC count and anemia, brucellosis should be placed on top of the differential diagnosis list and patients should be examined for Brucella serological evaluation.

Keywords: Brucellosis; Signs and Symptoms; Brucella; Epidemiology

1. Background

Brucellosis is a bacterial disease which is transmitted directly or indirectly from infected animals to humans (1). The disease is distributed worldwide (2). Except for a few countries that have eradicated the organism from animal reservoirs, this disease exists in other countries. Brucellosis as a reemerging zoonosis causes high economic losses and severe debilitating human disease worldwide. Brucellosis remains an important public health problem in high endemic areas such as the Mediterranean, Middle East, Latin America and Asia (3). Human Brucellosis is caused by Brucella species. *Brucella melitensis* is the most common cause of symptomatic disease in humans. The main sources of these bacteria are sheep, goats and camels (1, 3). All brucella are bacilli or small coccobacilli, gram-negative, non-spore forming and non-encapsulated. In vivo Brucella behaves as an optional intracellular parasite. These organisms are sensitive to sunlight, ionizing radiation and medium

heat. They are killed by boiling and pasteurization, but have resistance against drying and freezing. Their resistance to drying causes the bacteria to survive in aerosols and facilitates their transport by air (1-3). Clinical presentation of brucellosis may be acute or chronic with insidious onset followed by an acute attack. Human brucellosis may present a broad spectrum of clinical manifestations and its complications with varying degrees. Its clinical manifestations and focal complications as symptoms and signs are often troublesome in making a clinical diagnosis (3). Brucellosis almost always causes fever, which may be accompanied by sweating profusely, especially at night. In endemic areas it may be difficult to differentiate brucellosis from other common causes of fever. Other symptoms include: apathy, fatigue, loss of appetite and weight loss. The most common symptoms are musculoskeletal pain and physical findings in the central and peripheral skeleton. In

Implication for health policy/practice/research/medical education:

The results of this study are useful in diagnosis of brucellosis as a major public health problem in Khuzestan, south-west of Iran.

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most cases there is focal manifestations (1, 3, 4). Since the clinical manifestations of brucellosis are not clear, diagnosis should be based on potential exposure, disease manifestation and supportive laboratory findings. Routine laboratory examinations are usually normal, although serum levels of liver enzymes and bilirubin may be increased. Leukocyte counts are usually normal or low with comparative lymphocytosis. Thrombocytopenia, disseminated intravascular coagulation associated with increased levels of fibrin degradation products may be created. Erythrocyte sedimentation rate (ESR) and polymerase chain reaction (PCR) levels are usually normal but may increase (1-3, 5-7). According to the headline of country, Wright and 2 mercapto-ethanol (2ME) tests with titers equal to 1/80 or more with clinical symptoms appearance have high diagnostic values (3, 5).

2. Objectives

Considering the prevalence of brucellosis in Iran and variation of its clinical manifestations and laboratory results, we conducted this study to identify the most prevalent aspects of laboratory and clinical forms of the disease (5, 8-12).

Table 1. Epidemiological Features of Patients With Brucellosis

Epidemiological Feature	Patients, No. (%) (n = 81)
Gender	
Male	48 (59.3)
Female	33 (40.7)
Age, y	
< 20	17 (21)
20 - 40	30 (37)
> 40	34 (42)
Occupation	
Shepherds/nomads	18 (22.2)
Farmers	10 (12.3)
House keepers	15 (18.5)
Shop keepers	10 (12.3)
Abattoirs workers	5 (6.1)
Veterinary students	5 (6.1)
Others/unknown	10 (12.3)
Travel history	6 (7.4)
Ingestion of high risk foods	47 (58)
Rural residency	48 (59.3)
Familiar history of brucellosis	6 (7.4)

Table 2. Clinical Manifestation in Patients with Brucellosis

Clinical Manifestation	Patients, No. (%) (n = 81)
Symptoms	
Fever	69 (85.2)
Chills	34 (42)
Joint pain	34 (42)
Sweating	31 (38.3)
Anorexia	30 (37)
Weight loss	26 (32.1)
Back pain	25 (30.9)
Headache	21 (25.9)
Weakness	20 (24.7)
Nausea and vomiting	18 (22.2)
Myalgia	17 (21)
Respiratory symptoms	14 (17.2)
Lameness/abnormal gait	12 (14.8)
Abdominal pain	12 (14.8)
Urinary symptoms	12 (14.8)
Drowsiness	5 (6.1)
Testicle pain	3 (3.7)
Anxiety	2 (2.5)
Vertigo	2 (2.5)
Signs	
Arthritis	8 (9.9)
Tachycardia	5 (6.1)
Vertebral tenderness	4 (4.9)
Lymphadenopathy	4 (4.9)
Signs of skin problems	4 (4.9)
Signs of pulmonary issues	4 (4.9)
Testicle tenderness	3 (3.7)
Splenomegaly	3 (3.7)
Muscle tenderness	3 (3.7)
Joint tenderness	2 (2.5)
Abdomen tenderness	2 (2.5)

Table 3. Laboratory Findings in Patients with Brucellosis ^{a,b}

Laboratory Findings	Patients, No. (%) (n = 81)
Anemia	61 (75.3)
Elevated ESR	61 (75.3)
Leukocytosis	15 (18.5)
Leucopenia	0
Thrombocytopenia	0
Positive CRP	0

^a Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

^b Anemia, Hb < 12 g/dL; Elevated ESR, ESR > 20; leukocytosis, WBC > 10000; Leukopenia, WBC < 4000; Thrombocytopenia, Platelet count < 150000.

3. Patients and Methods

Medical records of patients admitted with a diagnosis of brucellosis were reviewed. Duration of the study was 10 years (1998-2007). The study took place at Razi Hospital, Infectious Diseases Department, affiliated to Ahvaz Jundishapur University of Medical Sciences. Patients with differential diagnosis of brucellosis were included. Cases that corresponded to the country's definition of brucellosis were enrolled. Eighty-one patients were diagnosed based on brucellosis diagnostic criteria (3). The diagnostic criteria of the disease were Wright test (serum agglutination test) with titers $\geq 1:160$, 2 mercapto-ethanol (2 ME) $\geq 1:80$ and clinical signs and symptoms compatible with brucellosis. Epidemiological data, such as occupation, exposure to animals, animal gestational products (placenta), living with animals and ingestion of high risk foods (unpasteurized dairy products & uncooked meat) were derived from medical files. Clinical presentations including symptoms, signs and complications were extracted of medical files and regarded as symptoms and signs. Laboratory findings including complete blood count (CBC), white blood count (WBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were extracted from medical files. The data about epidemiological, clinical and laboratory characteristics were analyzed by descriptive-analytic statistical methods using the statistical package for social sciences (SPSS) version 16 software.

4. Results

Amongst all studied patients with the mean age of 38.1 years (range from 11 to 80 years), 48 (59.2%) were male and 33 (40.7%) were female. The most common epidemiological findings were rural residency (53.1%), high risk occupation (38.2%) and ingestion of high risk foods (30.8%). Other epidemiological data are shown in Table 1. The most common signs and symptoms were fever (85.2%), arthralgia/arthritis (42%), chills (42%) and sweating (38.3%). Other signs and symptoms are shown in Table 2. The vertebral joints were the most involved area (30.9%) and half of the patients had multiarticular involvement. Anemia, elevated erythrocyte sedimentation rate (ESR) and leukocytosis were observed in 75.3%, 75.3% and 18.5% of patients, respectively (Table 3). Other laboratory findings included thrombocyte count and C-reactive protein (CRP) as shown in Table 3. Other laboratory tests including biochemical tests such as bilirubin, renal function tests and electrolytes had results within the normal range.

5. Discussion

Epidemiological findings of this study are consistent with previous studies (9, 10, 13-15). There were more male patients in comparison with female patients, which is consistent with all but one of the previous studies (9, 10, 16, 17). Alavi et al. reported more infection in females than in males among nomads living in the mountainous of

north Khuzestan (18). This variation could be due to the difference in their study design (hospital based vs. community based) and life style of nomads where women and girls are more vulnerable because they have more contact with livestock and dairy products (18). Most patients in this study were residents of villages that have been prepared in accordance with findings of other studies (5, 8-11). Villagers in the region of this study as well as other rural inhabitants are at higher risk of brucellosis in comparison with residents of big cities as they keep animals in their house and because of their nutritional habits. In this study, consumption of local dairy and other high risk food products was high in brucellosis patients; this result is consistent with other studies (3, 6, 9, 10, 13, 14). A significant number of patients in this study had animal related jobs. These findings are in agreement with a number of studies, but are not consistent with some other studies (2, 3, 6, 15, 19). In outpatient studies, jobs are more plentiful and less jobs in hospital studies. Although this study was done in the hospital, but was more frequent in patients with associated jobs. In conclusion, since our hospital is the only available hospital with an infectious disease specialty department in the region, most rural patients through the province are admitted to this hospital.

In our study, in many cases the disease was found in multiple family members. These findings are in agreement with the research of Haddadi et al. and Haj Abdolbaghi et al. (11, 20). It is recommended for screening to be performed for other family members who may have had a common food source or been in contact with other common infected sources (21). In this study, the most common symptoms of brucellosis were as fever, joint pain and sweating. These findings are largely similar to the findings of previous studies from other parts of Iran (5,8-12) and with the medical literature (3). In the present study, the most common signs were arthritis, tachycardia and tenderness in the lumbar spine. Arthritis prevalence rate was the same in other studies (4, 6, 12, 17, 22), yet other studies did not mention tachycardia and tenderness of the bones (16). The most common laboratory findings of our study were anemia, elevated ESR, normal WBC and platelet count. These results are in agreement with other studies (3, 5, 6, 17). Anemia was not common in the study by Haddadi et al. The reason for this difference is probably due to higher anemia in the general population of Khuzestan in contrast to the general population in the province of Tehran (11). Similar to other studies, elevated ESR is a common laboratory finding but with some fluctuation in its values (3, 5, 6, 23). It seems that the higher number of patients with elevated ESR in our study in comparison to the Hadadi study is due to differences in the definition of ESR cut off in the two studies. Haddadi and colleagues defined a value more than 50 as elevated ESR in their study whereas Majidpoor similar to our study defined a value of more than 20 as elevated ESR. Thus, our results indicate greater elevation of ESR than the report

by Hadadi et al., yet our ESR findings are approximately equal to that of Majidipoor (65% vs. 75%) (11, 23). The normal number of leukocytes found in this study has been confirmed by other studies and references (3, 5, 17). Normal platelet count found in this study is consistent with some previous articles (1, 14), yet differs from some other reports (5, 11). In the Haddadi et al. study, 48% of cases had thrombocytopenia (11). This study has two limitations, retrospective design and the long duration of the study. The restriction of study to the previous years is the main limitation of this study. The reason for these limitations is that brucellosis is at present an outpatient disease and the number of admitted patients per year is low. To reduce the effect of a small sample size, we reviewed the studies through a span of ten years. To minimize the bias of old studies, new patients in the recent five years were added. In conclusion, in the region of study, when dealing with patients complaining of fever, chills, sweating and joint pain associated with normal WBC count and anemia, brucellosis should be placed on top of the differential diagnosis list and patients should be examined for Brucella serological evaluation.

Acknowledgements

We greatly appreciate the staff of the Infectious Department of Razi Hospital and Infectious Diseases Research Center affiliated to Jundishapur University of Medical Sciences for their kind cooperation.

Author's Contributions

Sasan Mugahi: data collection and writing; Ruhangiz Nashibi: data collection and writing; Seyed Mohammad Alavi: final revision and primary design; Saeid Gharkholu: primary design and analysis; Kianoosh Najafi: writing.

Funding/Support

This study was funded by Jundishapur Infectious and Tropical Diseases Research Center.

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