



Investigating the Epidemiologic, Laboratory, and Clinical Features of Brucellosis Patients Hospitalized in the North of Iran During 2009 - 2014

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Abstract

Background: Brucellosis is a zoonosis with diverse clinical manifestations. This study investigated the epidemiological, laboratory, and clinical features of brucellosis.

Methods: In a cross-sectional survey, we evaluated brucellosis patients who referred to Razi hospital, a referral center for infectious diseases in Mazandaran province (north of Iran), from 21 March 2009 to 20 March 2014. Factors such as age, sex, clinical signs, and laboratory findings were extracted from their medical records.

Results: 219 patients with a mean age of 41.6 ± 16.9 years were enrolled including 86 women (39.27%) and 133 men (60.73%). 191 participants (87.2%) had used local dairy products. 174 (79.4%) were suffering from non-focal brucellosis and 45 patients (20.6%) from focal brucellosis. The rates of referral per season were 23.7, 33.8, 23.3, and 19.2 percent in the spring, summer, autumn, and winter, respectively ($P = 0.006$). In terms of job, 76 patients (34.7%) were in business/market-related jobs, 64 (29.2%) were homemakers, and 49 (22.4%) were in dairy jobs. The relationship between jobs and disease was significant ($P = 0.003$). The most common chief complaint of patients was fever and chills (31.1%).

Conclusions: Based on the findings, factors such as fever, chills, back pain, myalgia, anemia, and abnormal ESR were associated with brucellosis.

Keywords: Brucellosis, Epidemiology, Clinical

1. Background

Brucellosis is a common zoonosis that is transmitted to humans through cattle, sheep, or goats (1). Brucellosis is widespread around the globe, especially in the Mediterranean region and the Middle East (2). Brucellosis is endemic in Iran with an annual incidence of 225 cases per hundred thousand people; in the Mazandaran province, it has been reported 114 cases per hundred thousand people (3). The disease is observed in farmers, herders, and veterinarians who have occupational exposure. The laboratory staff and other people who deal with cultures and infectious samples of dairy products and others who consume dairies, especially unpasteurized cheeses and milk, are at risk of the disease (1). The clinical manifestation of brucellosis is very diverse, mostly including nonspecific fever, night sweats, fatigue, myalgia, arthralgia, myalgia, weight loss, loss of appetite, and hepatosplenomegaly.

Given the high prevalence of brucellosis in our region

and different clinical and laboratory manifestations in previous studies, this study was designed to determine the epidemiologic, laboratory, and clinical features of brucellosis in the north of Iran.

2. Methods

This was a cross-sectional study. The inclusion criteria included all patients who were hospitalized between 21 March 2009 and 20 March 2014 due to *Brucella* infection (according to the national protocol based on clinical evidence, the titre of 1:80 in Wright tests and 1:40 in 2ME positive) in Razi hospital of Qaemshahr city, the referral center for infectious diseases in Mazandaran province (north of Iran). The exclusion criteria included the absence of *Brucella* and the presence of kidney or liver disease.

The following criteria were defined: anemia as a hemoglobin level below 13 in men and 12 in women, leukopenia as a reduction in white blood cells (WBC) in

circulation below 4500 cells/mcL, leukocytosis, as an increase in WBC in circulation over than 10,000 cells/mcL, thrombocytopenia as a reduction in platelet count below 150,000/mcL, hypokalemia as a potassium level below 3.3 mg/dL, hyperkalemia as a potassium level over 5.5 mg/dL, hyponatremia as a sodium level below 135 mg/dL, hypernatremia as a sodium level above 145 mg/dl, and the abnormal erythrocyte sedimentation rate (ESR) as ESR above age divided by two for men and age plus 10 divided by two for women. Also, the creatinine level more than 1.5 mg/dL, AST < 5 or 40 < U/L, ALT < 7, or 56 < U/L, and ALP < 45 or < 115 U/L were considered abnormal (1). For most patients, a test was requested. Nevertheless, in cases where more than one test was requested, the most abnormal values were used.

We designed an information form to be used for collecting information and variables such as age, sex, clinical symptoms, and laboratory findings such as hemoglobin levels, WBC count, platelet count, potassium level, sodium level, ESR, AST, ALT, and ALP.

After collecting information, data were entered SPSS version 21 software and the descriptive analysis was run. Quantitative and qualitative values were examined using t-test and chi-square, respectively, and the significance level was set at a P value below 0.05.

3. Results

In total, 219 patients with a mean age of 41.6 ± 16.9 (12 - 87) years were enrolled, among whom there were 86 females (39.27%) and 133 males (60.73%). The mean age was 46.3 ± 16.6 and 37.3 ± 17.2 for women and men, respectively ($P < 0.001$). 174 (79.4%) patients were suffering from non-focal brucellosis and 45 patients (20.6%) were diagnosed with focal brucellosis including 17 cases (37.8%) of spondylitis, 10 cases (22.2%) of arthritis, 7 cases (15.6%) of epididymo orchitis, 4 cases (8.9%) of sacroiliitis, 2 cases (4.4%) of neuro-brucellosis, 2 cases (4.4%) of osteomyelitis, and 1 case (2.2%) of each of endocarditis, hepatitis, and thrombophlebitis of the lower extremities. Based on the statistical analysis, the type of detection in both sexes had no significant difference ($P = 0.546$).

The rates of referral per season were 23.7, 33.8, 23.3, and 19.2 percent in the spring, summer, autumn, and winter, respectively ($P = 0.006$). In terms of location of residence, 78 patients (35.6%) were living in cities and 141 patients (64.4%) in rural areas ($P = 0.260$). Of 219 participants, 85 (38.8%) mentioned animal contact. 191 (87.2%) patients had used local dairy products. In 20 participants (9.1%), including 15 non-focal and five focal brucellosis patients, the history of brucellosis in their family was positive.

The majority of clinical signs and symptoms included chills (78.5%), fever (58.4%), decreased appetite (44.7%), and

sweating (42.5%) (Table 1). The highest chief complaints were fever and chills (31.1%), back pain (22.4%), myalgia cases (5.5%), inflation of Testis (2.7%), and fever and laminitis (1.8%).

Table 1. Clinical Manifestations of Patients with Brucellosis

Signs and Symptoms	No. (%)
Fever	128 (58.4)
Sweating	93 (42)
Myalgia	12 (5.5)
Arthralgia	11 (5)
Back ache	49 (22.4)
Weight Loss	79 (36.1)
Cough	30 (13.7)
Headache	5 (2.3)
Arthritis	27 (12.3)
Splenomegaly	30 (13.7)
Orchitis	8 (3.6)
Hepatomegaly	11 (5)
Lymphadenopathy	7 (3.2)
Chills	172 (78.5)
Rash	2 (1)
Lethargy	82 (37.4)
Loss of appetite	98 (44.7)
Nausea	28 (12.8)
Vomit	20 (9.1)
stomach pain	28 (12.8)
Diarrhea	4 (1.9)
Constipation	11 (5)
Scrotal pain	6 (2.7)
Dysuria	21 (9.6)
Urinary frequency	15 (6.8)
Limb paresthesia	4 (1.9)

Of 219 patients, 172 (78.6%) were hospitalized for 6 days or less and 47 (21.4%) for more than 6 days; in the latter group, there were 12 people with more than 12 days hospitalization period. About 70% of the patients were anemic. 88.2% of the patients had abnormal ALP (Table 2).

4. Discussion

Although brucellosis is controlled in many developed countries, it remains a major problem for the health system in developing countries including the Mediterranean and the Middle East countries (4). In our study, 39% of the

Table 2. Laboratory Findings of Patients with Brucellosis

Finding	No. (%)
Anemia	151 (69.58)
Leukopenia	29 (13.6)
Leukocytosis	29 (13.6)
Thrombocytopenia	9 (4.1)
Abnormal ESR	122 (55.7)
Abnormal creatinine	3 (1.4)
Hypokalemia	2 (1)
Hyperkalemia	11 (5)
Hyponatremia	12 (5.5)
Hypernatremia	2 (1)
Hematuria	7 (3.2)
Pyuria	14 (6.4)
Abnormal AST	47 (21.5)
Abnormal ALT	35 (16)
Abnormal ALP	193 (88.2)

patients were female and 61% were male and the mean age was 41.6 ± 16.9 ; this study was similar to other studies in terms of age and gender of brucellosis patients (4-6).

Non-localized brucellosis was detected in 79.4% of patients in our study, while others were complicated with spondylitis, epididymo-orchitis, sacroiliitis, meningoencephalitis, osteomyelitis, arthritis, hepatitis, thrombophlebitis of the lower extremities, and endocarditis. In Roshan et al.'s study in 2004 in Babol, 31% of cases had a localized brucellosis (7). In a study by Najafi et al. in 2003 (8), about 8.7% of patients were complicated with epididymo orchitis while in this study, 3.2% of cases had this problem.

In our survey, 70% of patients were anemic. In addition, leukopenia and leukocytosis, each in 13%, thrombocytopenia in 4.1%, abnormal ESR in 56%, abnormal AST in 22%, abnormal ALT in 16%, and abnormal ALP in 88% of cases were observed. Various studies have presented different values. In a study by Karaman et al. in Turkey, anemia, leukopenia, and were reported in 28.6%, 13.9%, and 16% patients, respectively (9). Davoudi et al. reported a case of DVT in a 15-year-old boy with acute pain and swelling in his left thigh in June 2011, as a rare complication of Brucellosis (10). In a study by Fanni et al. in Tehran, anemia as 53%, leukopenia as 33%, and thrombocytopenia as 12% were reported (11). In an analysis conducted by Roshan et al. in Northern Iran, anemia in 15.1%, leukopenia in 3%, and abnormal ESR in 77.8% of patients were reported (7). In a study by Guler et al. in Turkey, leukopenia as 21.4%, anemia as 70%, thrombocytopenia as 23%, and pancytopenia were reported (12).

In our study, 23% of cases had jobs involving direct contact with animals and 87.2% had used local dairy products. Therefore, most of our patients had occupational exposure. In a study by Haddadi et al. in Tehran, 17.1% of patients had occupational exposure to livestock (13). In other studies, occupational exposure has been reported in 58.7%, 71%, 27%, and 32% of cases (7, 14). Therefore, although occupation is considered a risk factor, the disease is not necessarily transmitted occupationally in developing countries. However, the high percentage of using local dairy products both in our study and in other studies (15) suggests that the main route of transmission still remains the consumption of contaminated dairy products.

Most inflicted cases were observed in the spring and summer. Considering the spring and summer are the calving seasons with highest milk production in the cattle, the dairy production and contact with animals increase in this period. Thus, most of the cases were observed in the spring and summer. This is consistent with the findings of many previous studies (16, 17).

Most clinical signs and symptoms included chills, fever, loss of appetite, and sweating. In addition, the most common chief complaints included fever, chills, backache, and myalgia. In a 10-year clinical study on brucellosis patients in Macedonia, the most frequently observed symptoms were arthralgia, fever, and sweating and the most common signs were fever and hepatomegaly (18). In the Roushan's study, the most common complaints were fever and arthralgia (7).

For serological diagnosis of human brucellosis, Rose Bengal, Wright's Sero-agglutination, 2-ME, and antiglobulin Coombs tests are done as standard methods. Most patients with acute infection respond to all tests (19). In a study by Najafi et al. titled "Comparing the Serological Diagnostic value of ELISA and Wright tests in human brucellosis with positive PCR," a clinical and laboratory study was conducted on 59 patients suspected of brucellosis, the Wright test compared to ELISA had higher sensitivity, lower specificity, approximately equal positive predictive value, higher negative predictive value, and generally higher accuracy (20).

4.1. Conclusions and Recommendations

Clinical symptoms and laboratory parameters in our study included fever, chills, back pain, myalgia, anemia, and abnormal ESR. Our study showed that although occupation is considered a risk factor for brucellosis, the disease is not necessarily transmitted occupationally. The consumption of contaminated dairy products is still the main route of transmission of brucellosis. It is recommended to detect brucellosis by using standard laboratory

techniques and regarding clinical and epidemiologic information.

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