

# Different Clinical Presentations of Brucellosis

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## Abstract

**Background:** Brucellosis is one of the important multi-organ zoonotic infectious diseases. The forms of the clinical course of brucellosis in humans are acute, sub-acute and chronic.

**Objectives:** The present study aimed to retrospectively analyze the clinical characteristics and complications in the clinical forms of human brucellosis in Iran.

**Patients and Methods:** The population included 957 patients admitted in the infectious diseases clinic affiliated to Babol University of Medical Sciences, Babol, Iran, within the past two decades. Data for the patients were obtained and documented in questionnaires. Patients were divided into three groups according to their history, symptoms and clinical presentation time: acute (0 - 2 months), sub-acute (3 - 12 months), and chronic (> 1 year).

**Results:** Most of the patients (73.8%) were in the acute stages of brucellosis, 22.6% had sub-acute brucellosis and 3.7% had chronic brucellosis. The most frequently observed symptoms were arthralgia (71%), sweating (66.7%), fever (57.2%) and backache (39.3%). The most common complication was arthritis (13.2%) in this study.

**Conclusions:** This infection was observed with a diversity of clinical manifestations. Therefore, diagnostic difficulty because of the various clinical presentations and the way to find undiagnosed complications should be investigated in the differential diagnosis of other diseases.

**Keywords:** Brucellosis, Signs and Symptoms, Iran

## 1. Background

Brucellosis is one of the important multi-organ zoonotic diseases with annually more than 500,000 new cases worldwide (1). The epidemiological zone of this infection includes the Arabian Peninsula, Mediterranean basin, Indochina, some parts of central Asia and south America (2). In the endemic regions, many cases occur in females. Consumption of non-pasteurized dairy such as soft cheese, butter, ice cream is the most usual transmission manner of this infection (3). Yogurt and hard cheese have a lower risk than others due to lactic fermentation. The main complaints of the infected patients are fever, chills, night sweats, myalgia, anorexia, headache, joint pain and heart attacks (4, 5). The main symptom of brucellosis is fever with unknown origin; therefore, it can be misdiagnosed with similar pathologies such as all of fevers of unknown origin that may be caused by infectious diseases, malignancies, collagen vascular diseases including tuberculosis, malaria, rheumatic fever and leishmaniasis (6). The forms of the clinical course of brucellosis in humans are acute, sub-acute and chronic (7). To detect patients with the disease, medical history should be taken, and biochemical, hematological and serological

test should be performed. In addition, microbiological tests such as *Brucella* spp. isolation, and molecular tests should also be done. Among serologic tests, standard agglutination test (SAT), 2-mercaptoethanol (2ME) test and Coombs test are routine. Infected patients are cured after more appropriate treatments, of course after months.

## 2. Objectives

The main important purpose of brucellosis treatment was to decline the involvement and signs of the disease. Irrespective of the suitable treatment, some patients have relapse of the disease symptoms since these bacteria are intracellular and can survive within macrophages. These confidants may cause chronic and relapse infection (8). The present study aimed to retrospectively analyze the clinical characteristics and complications in the clinical forms of human brucellosis.

## 3. Patients and Methods

The current study included patients diagnosed with brucellosis at the infectious diseases clinic affiliated to

Babol University of Medical Sciences, Babol, Iran, within the past two decades. The files of the patients were retrospectively evaluated. All demographic characteristics such as age, gender, residency, risk factors and clinical manifestations of all admitted patients with brucellosis were exploited from their files and recorded in the questionnaires. The diagnosis of brucellosis was confirmed by representing standard agglutination test (SAT)  $\geq 1.320$  and 2-mercaptoethanol (2-ME)  $\geq 1.80$  for the patients with clinical signs and symptoms compatible with those of brucellosis. Patients were divided into three groups according to their history, symptoms and clinical presentation time: acute (0 - 2 months), sub-acute (3 - 12 months) and chronic ( $> 1$  year) (9).

Diagnosis of musculoskeletal system complications was determined by the finding of swelling, effusion and limitation of motion in an involved joint and was confirmed by X-ray in the prone position. Moreover, spondylitis was diagnosed using magnetic resonance imaging (MRI). Genitourinary system involvement was diagnosed by finding swelling and tenderness of scrotal skin, testis and epididymis, with confirmation by sonography.

Endocarditis was diagnosed by elevation of anemia, cardiac murmur, and was confirmed by the detection of vegetations using echocardiography. Central nervous system (CNS) involvement was made by considering the presence of SAT positivity and abnormal findings obtained from cerebrospinal fluid (CSF) analyses ( $> 10$  leukocyte/mm<sup>3</sup>, protein  $> 45$  mg/dL, glucose  $< 2/3$  of the blood glucose level). The SPSS ver. 17.0 was used for the statistical analysis of data.

#### 4. Results

Overall, 957 patients with brucellosis were included in the study, 706 (73.8%) cases were acute, 216 (22.6%) sub-acute, and 35 (3.7%) were chronic. Among the patients 535 (55.9%) were male and 422 (44.1%) were female with the mean age of  $34 \pm 16.9$  years (rang: 1 - 90). In terms of gender distribution, involvement with acute form of brucellosis regarding other clinical forms, occurs significantly in males 418 (59.2%) more than females 288 (40.8%) ( $P=0.003$ ).

Most of the patients, 421 (44.1%), were 21 - 40 years. While 238 (24.9%) case were  $< 20$  years, 221 (23.1%) were 41 - 60 years and 77 (7.9%) patients were older than 60 years; therefore, age differences between the groups and all stages of disease were significant ( $P=0.001$ ).

More patients were from rural, 705 (73.8%), than the urban, 250 (26.2%), areas. Significant relationships were found between clinical forms of the disease and frequency of occupational exposure or risk factors in brucellosis ( $P=0.01$ ). The most common clinical manifestations were

arthralgia, sweating, fever and backache in 679 (71%), 638 (66.7%), 547 (57.2%) and 376 (39.3%) cases, respectively. Between clinical features, only fever and backache had significant association with clinical forms.

The most frequent involvement was arthritis with 126 cases (13.2%), gastrointestinal complications 57 (6%), splenomegaly 49 (5.1%), sacroiliitis 46 (4.8%) and spondylitis with 44 (4.6%) cases. Complications were observed at all stages of infection but arthritis; spondylitis were significantly observed in patients with acute disease ( $P=0.03$ ,  $P=0.001$ ) respectively. Focal organs involvement such as epididymo-orchitis and respiratory system were presented in 40 (4.2%) and 22 (2.3%) of the cases respectively. Surprisingly, osteomyelitis, bursitis, cellulitis, CNS and skin involvements were not observed in chronic form of the disease.

#### 5. Discussion

Brucellosis is a public health problem that can cause severe significant disability and complications (10). According to the annual report of world health organization (WHO), Iran is an endemic region (11). Brucellosis can occur in both genders and any age group (12). In the current study, 535 (55.9%) of the patients were male and 422 (44.1%) were female with a mean age of  $34 \pm 16.9$  years which was similar to some other studies (13). In some studies, the female ratio was reported more than that of the male (14). Overall, the prevalence of brucellosis can occur at any age but is common in adults and young people (15). In the current study the most common age group was 21 - 40 years, 421 patients (44.1%), which was similar to other studies (16). Of this age group 312 (44.2%) were acute, 95 (44.2%) sub-acute and 14 (40%) were chronic. These results show how age range reflects socio-economic and cultural status of this infection in an endemic area. Some studies reported older mean age groups usually working on farms with dairy production; therefore, brucellosis is more frequently occurs in this age group (17).

The current study results were similar to some studies presenting that brucellosis was still endemic in rural areas, but rare in urban areas (18). In the north of Iran, the rate of population involved in this infection in rural areas is more than that of the urban areas. In recent years human brucellosis cases have spread from rural to urban regions (19). A recent study found an overall 247 (25.8%) of patients in high risk occupational groups. Many previous studies overlooked some of these important at risk occupational groups (20).

The primary transmission route of brucellosis is by the ingestion of unpasteurized dairy products in the endemic countries; whereas in the developed countries infection

**Table 1.** A Comparison of the Brucellosis Forms According to the Patient Characteristics<sup>a</sup>

| Characteristics                       | Total Patients (n = 957) | Acute (n = 706 (73.8)) | Sub-Acute (n = 216 (22.6)) | Chronic (n = 35 (3.7)) | P Value |
|---------------------------------------|--------------------------|------------------------|----------------------------|------------------------|---------|
| <b>Gender</b>                         |                          |                        |                            |                        | 0.003   |
| Male                                  | 535 (55.9)               | 418 (59.2)             | 100 (46.3)                 | 17 (48.6)              |         |
| Female                                | 422 (44.1)               | 288 (40.8)             | 116 (53.7)                 | 18 (51.4)              |         |
| <b>Residency</b>                      |                          |                        |                            |                        | 0.6     |
| Urban                                 | 250 (26.2)               | 180 (25.6)             | 59 (27.3)                  | 11 (31.4)              |         |
| Rural                                 | 705 (73.8)               | 524 (74.4)             | 157 (72.7)                 | 24 (68.6)              |         |
| <b>Age</b>                            |                          |                        |                            |                        | 0.000   |
| < 20                                  | 238 (24.9)               | 206 (29.2)             | 28 (13.1)                  | 4 (11.4)               |         |
| 21 - 40                               | 421 (44.1)               | 312 (44.2)             | 95 (44.2)                  | 14 (40)                |         |
| 41 - 60                               | 221 (23.1)               | 140 (19.9)             | 65 (30.4)                  | 16 (45.7)              |         |
| > 60                                  | 77 (7.9)                 | 50 (7)                 | 26 (12.1)                  | 1 (2.9)                |         |
| Mean age                              | 34 ± 16.9                | 32 ± 16.8              | 39 ± 16.4                  | 39 ± 13.2              |         |
| <b>Risk factors</b>                   | 439 (45.9)               | 342 (48.4)             | 78 (36.1)                  | 19 (54.3)              | 0.01    |
| <b>Occupational exposure</b>          | 247 (25.8)               | 195 (27.6)             | 40 (11.5)                  | 12 (34.3)              | 0.01    |
| <b>Fever</b>                          | 547 (57.2)               | 439 (62.2)             | 99 (45.8)                  | 9 (25.7)               | 0.000   |
| <b>Sweating</b>                       | 638 (66.7)               | 483 (68.4)             | 134 (62)                   | 21 (60)                | 0.1     |
| <b>Arthralgia</b>                     | 679 (71)                 | 499 (70.7)             | 153 (70.8)                 | 27 (77.1)              | 0.7     |
| <b>Backache</b>                       | 376 (39.3)               | 254 (36)               | 109 (50.5)                 | 13 (37.1)              | 0.001   |
| <b>Anorexia</b>                       | 32 (3.3)                 | 26 (3.7)               | 5 (2.3)                    | 1 (2.9)                | 0.6     |
| <b>Nausea and vomiting</b>            | 9 (0.9)                  | 8 (1.1)                | 1 (0.5)                    | 0                      | 0.5     |
| <b>Abdominal pain</b>                 | 16 (1.7)                 | 12 (1.7)               | 4 (1.9)                    | 0                      | 0.7     |
| <b>cellulitis</b>                     | 2 (0.2)                  | 2 (0.3)                | 0                          | 0                      | 0.7     |
| <b>bursitis</b>                       | 3 (0.3)                  | 2 (0.3)                | 1 (0.5)                    | 0                      | 0.8     |
| <b>Osteomyelitis</b>                  | 1 (0.1)                  | 0                      | 1 (0.5)                    | 0                      | 0.2     |
| <b>Sacroillitis</b>                   | 46 (4.8)                 | 37 (5.2)               | 9 (4.2)                    | 0                      | 0.3     |
| <b>Spondylitis</b>                    | 44 (4.6)                 | 20 (2.8)               | 22 (10.2)                  | 2 (5.7)                | 0.000   |
| <b>Arthritis</b>                      | 126 (13.2)               | 104 (14.7)             | 21 (9.7)                   | 1 (2.9)                | 0.03    |
| <b>polyarthritis</b>                  | 19 (2)                   | 12 (1.7)               | 5 (2.3)                    | 2 (5.7)                | 0.2     |
| <b>Epididymo-orchitis</b>             | 40 (4.2)                 | 33 (4.7)               | 7 (3.2)                    | 0                      | 0.2     |
| <b>Splenomegaly</b>                   | 49 (5.1)                 | 39 (5.5)               | 10 (4.6)                   | 0                      | 0.3     |
| <b>Skin involvement</b>               | 5 (0.5)                  | 5 (0.7)                | 0                          | 0                      | 0.4     |
| <b>Respiratory system involvement</b> | 22 (2.3)                 | 19 (2.7)               | 3 (1.4)                    | 0                      | 0.3     |
| <b>CNS involvement</b>                | 2 (0.2)                  | 1 (0.1)                | 1 (0.5)                    | 0                      | 0.6     |
| <b>GI complications</b>               | 57 (6)                   | 46 (6.5)               | 10 (4.6)                   | 1 (2.9)                | 0.4     |

Abbreviations: CNS, central nervous system; GI, gastrointestinal.

<sup>a</sup>Values are expressed as No. (%) or mean ± SD.

occurs mostly due to occupational exposure (21). Similar to other studies, the majority of patients, 439 (45.9%) cases, had risk factors such as history of consuming unpasteurized milk or milk products (22). In contrast to the current

study results about residency and risk factors, some experts showed that chronic brucellosis were from rural areas because of consumption of unpasteurized dairy products or contact with animals (9).

Brucellosis seems to affect human immune system and can cause acute, sub-acute and chronic clinical features. In the present study, 73.8%, 22.6% and 3.7% of the patients had the acute, sub-acute and chronic forms of the disease, respectively. But the study by Eini et al. presented that 24% of the patients had acute brucellosis, 70.8% were in sub-acute stages and 5.2% had chronic brucellosis (23). Acute form in different genders was compared (male: 59.2% vs. female: 40.8%). In another study by Keramat et al. 178 patients (58.9%) with acute brucellosis were male (13).

Most patients had brucellosis with the main clinical symptoms of being arthralgia, sweating, fever and backache; findings were similar to the results obtained by the others working in endemic regions (24). Moreover, typically cases with acute brucellosis present signs such as fever, fatigue, chills and sweating (25). In this study, 71% of the patients had arthralgia and in terms of clinical type, 70.7% had the acute form. The results of the current study were similar to those of the studies in other countries; and arthritis was the most common complications of brucellosis (22). On physical examination, sweating (66.7%) and fever (57.2%) were mostly observed in the acute form the disease. Another study identified a significant correlation between fever and the acute form of brucellosis (26). Similar to the study by Aygen et al. in which the most frequent symptoms were fever (63.2%), sweating (62.7%), arthralgia (59.1%) and back pain (58.5%) (27).

Brucellosis complications are a major medical problem in countries where the infection is still endemic. The prevalence of focal involvement has been reported to range from 20% to 40% in many studies (28). Arthritis occurred for the first time in the patients with the acute form. It was one of the main presented clinical features. In the current study, arthritis involvement was observed in 14.7%, 9.7% and 2.9% of the patients with acute, sub-acute and chronic brucellosis, respectively. Geyik et al. showed that sacroiliitis and polyarthritis were more frequent complications in acute cases (29). In a recent study, spondylitis occurred in 2.8%, 10.2% and 5.7% of the patients with acute, sub-acute and chronic disease, respectively.

According to Bodur et al. spondylitis was observed in 12 (46%) and 13 (50%) patients with acute and sub-acute brucellosis (30). Brucellosis is a common disease which may occur in different forms. In Iran, people should be taught to avoid consumption unpasteurized dairy products and contact with infected animals. This infection was observed with a diversity of clinical manifestations. Therefore, due to the various clinical presentations and undiagnosed complications, diagnosis of brucellosis is difficult. Hence, differential diagnosis of the infection should be investigated in the further studies.

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## Footnotes

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