

## Depressive disorder among brucellosis patients in Hamadan, Iran: A case-control study

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**Abstract: Objectives:** The aim of this study was to determine the prevalence of depressive disorder among brucellosis patient attending to the central university hospital in Hamadan, Iran. **Methods:** In this case-control study, the rate of depression was compared between 100 brucellosis patients as cases and 71 healthy controls. The depression was assessed with Zung Depression Scale and confirmed by a clinical psychologist. **Results:** The prevalence of depression in case and control group was 53% and 16.9%, respectively ( $P < 0.001$ ). **Conclusion:** Iran is an endemic region for *Brucella* infection and there is a high rate of depression among brucellosis patients. Physicians should pay more attention to behavioral disorders in high risk patients with unexplained neurologic symptoms to rule out the infectious nature of such diseases.

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### Introduction

Human brucellosis is the major zoonotic infectious diseases with a worldwide distribution and still remains as a serious public health problem in many countries, especially, where the animal health care programs are poor (1,2). Patients with *Brucella* infection may present various clinical features with involvement of all organs of the body including reticuloendothelial system, hematologic system, central nervous system (CNS), cardiopulmonary system and genitourinary system (1, 3, and 4).

The neurological involvement in this infectious disease has a variety manifestation and usually occurs without a background disease (5). These include encephalitis, meningoenephalitis, radiculitis, myelitis, peripheral and cranial neuropathies, subarachnoid haemorrhage and psychiatric appearance. Some psychiatric disorders consequent to *Brucella* infection have been reported such as depression, amnesia, psychosis, agitation, nightmares, personality disorder and euphoria as well as some rare symptoms including headache, confusion, and gait disorders (6-8). These complications may appear in the acute stage of brucellosis or, even later, during the chronic phase (5).

The depression has been showed as the most common finding of psychiatric disturbance among brucellosis patients (10). Although, depressive disorders and mental confusion are common in brucellosis, direct invasion of the CNS occurs in less than 5% of patients (9). However, studies indicated

that psychiatric disorders disappeared among neurobrucellosis patients after administration of only antibiotics with no antidepressant or antipsychotic therapy (6).

In Iran the incidence of brucellosis has increased in recent years because of its incomplete eradicating in animals. Hamadan province in the western part of the country has been shown with the highest incidence rate in Iran and it was 130 cases per 100,000 population (11). The aim of this study was to determine the prevalence of depressive disorder among brucellosis patient attending to the central university hospital in Hamadan, Iran.

### Methods

A case-control study was conducted and all consecutive patients with chronic brucellosis presenting to Farshchian Hospitan in Hamadan between October 2009 and September 2010 were included as cases. A case of brucellosis was defined by the presence of clinical symptoms of fever, fatigue, night sweats and myalgia confirmed by positive serologic tests (wright  $\geq 1:160$ , Coomb's test  $\geq 1:320$ , 2-mercapto ethanol  $\geq 1:80$ ). Patients presented at the acute stage of the disease (less than two months) were not eligible for enrolment.

Healthy controls were randomly selected from patient companions at the hospital. The individual controls were defined as persons who were free of brucellosis and/or without a diagnosis of fever of undetermined origin. Also, controls with a history of hospitalization within the preceding 1 month as

well as having a chronic disease influencing depression such as CNS disorders (including, but not limited to, stroke, Parkinson's disease, and head trauma), cardiovascular disease, cancer, diabetes, and autoimmune system diseases such as lupus were not included the study.

The study protocol was performed in accordance with the declaration of Helsinki and subsequent revisions and approved by ethics committee at Hamadan University of Medical Sciences. All participants were informed of the study purpose and gave their verbal consent. Also, an informed consent was obtained from participants before entering into the study.

Information on patients and controls was supplemented with data obtained by interview with study subjects using a standard questionnaire. A Persian-validated translation of the Zung Depression Scale (ZDS) was used to assess depressive symptoms. The ZDS is a 20-item questionnaire to assess depressive symptoms at the time of testing (12). Cases and controls were asked to answer the questions themselves or respond the interviewer if they were not able to read or write. In analysis and

reporting the patients, we did not consider severity of the depression and its diagnosis was confirmed by the consulting clinical psychologist if the ZDS indicated a depression condition.

Results are given as “means  $\pm$  standard deviation” for continuous variables and number (percent) for categorical variables. Bivariate associations were assessed using the chi-square test or Fisher's exact test. Statistical analyses were performed using SPSS v.18 (SPSS, Chicago, Illinois, USA) and a *P* value less than 0.05 was considered significant.

## Results

A total of 100 cases and 71 controls were analyzed: 57 cases (57%) and 39 controls (54.9%) were male. The mean age was  $38 \pm 15.8$  (ranged from 14 to 72) years for cases and  $39.5 \pm 16.3$  (ranged from 14 to 76) years for controls. All cases and controls were Iranian; 77% of cases and 76.1% of controls lived in villages. There was no difference between cases and controls on the demographic data. (Table 1)

**Table 1- Demographic data and depression in two groups**

	Case n=100	Control n=71	P value
<b>Gender</b>			
Male	57 (57%)	39 (54.9%)	NS
Female	43 (43%)	32 (45.1%)	NS
<b>Age group</b>			
29 and less	33 (33%)	27 (38%)	NS
30-49	36 (36%)	29 (40.8%)	NS
50 and over	31 (31%)	15 (21.1%)	NS
<b>Mean age</b>	$38 \pm 15.8$	$39.5 \pm 16.3$	NS
<b>Location</b>			
Urban area	23 (23%)	17 (23.9%)	NS
Rural area	77 (77%)	54 (76.1%)	NS
<b>Depression</b>	53 (53%)	12 (16.9%)	<0.001

Table 2 shows the rate of depression in the two groups based on gender, age, and location. The prevalence of depression in case group was 53% vs. 16.9% in control group. There was a significant difference in the rate of depression between two groups ( $\chi^2=22.9$ ,  $P<0.001$ ). This difference remained significant in both genders, so among men 47.4% of cases vs. 17.9% of controls ( $\chi^2=8.7$ ,  $P=0.003$ ) and among women 60.5% of cases vs. 15.6% of controls ( $\chi^2=15.2$ ,  $P<0.001$ ) had a depressive disorder. Also,

this difference remained significant in all age groups ( $P<0.05$ ).

Among participants who lived in urban area, there was no difference between two groups in the rate of depression (43.5% of cases vs. 35.3% of controls). However, the rate of depression was significantly higher among cases who lived in rural area (55.8% of cases vs. 11.1% of controls;  $\chi^2=27.2$ ,  $P<0.001$ ).

**Table 2- Comparison of depression between cases and controls**

	Depression in cases n=53	Depression in controls n=12	p value
<b>Gender</b>			
Male	27 (47.4%)	7 (17.9%)	0.003
Female	26 (60.5%)	5 (15.6%)	<0.001
<b>Age group</b>			
29 and less	19 (57.6%)	6 (22.2%)	0.006
30-50	20 (55.6%)	4 (13.8%)	<0.001
51 and over	14 (45.2%)	2 (13.3%)	0.034
<b>Location</b>			
Urban area	10 (43.5%)	6 (35.3%)	NS
Rural area	43 (55.8%)	6 (11.1%)	<0.001

### Discussion

Brucellosis is a systemic infection that can involve any organ or organ system of the body. The disease has a variety of clinical features. It appears in the differential diagnosis of many infectious and noninfectious diseases. Although depression is a common complication of chronic brucellosis, there are little research data on this issue and data found in the literature are generally restricted to case reports or case series. This study conducted on 100 brucellosis patients and compared the prevalence of depression between these patients and a group of 71 healthy participants. Most of our patients were men with a mean age of about 38 years. Our findings suggest that the rate of depression may be as much as 53% higher in brucellosis patients than in normal population, in whom the prevalence of depression was indicated as about 17%. It highlights the high prevalence of depression in this infectious disease. Some other studies have reported a lower rate of depression in brucellosis. Shehata et al in a study on brucellosis patients showed that depression was seen in 7 of 27 (25.9%) patients (13). Gul et al conducted a pooled analysis based on primary data from 35 studies on brucellosis in Turkish medical practice (3). Totally, 187 neurobrucellosis was investigated and depression was found in 5% of cases. Eren et al compared 34 neurobrucellosis cases and 30 patients with brucellosis without neurological involvement (6). They found a mild depression among neurobrucellosis patients after the psychiatric examination and stated that the depression was in consequence of a general medical condition (neurobrucellosis). However, they found no depression among the brucellosis patients without neurologic involvement. The high rate of depression among our patients indicated that depressive disorder could not be related only to a neurological involvement as a special complication of neurobrucellosis. Although, depressive disorders could be directly due to destructive effect of *Brucella*

organism on CNS or indirectly as a result of cytokine or endotoxin on the neural tissue (5), the chronic nature of the disease as well as its long time treatment and its relative disability may aggravate this condition or even induce depression without any neurological involvement.

Another finding of our study was the higher rate of depression among patients resident in rural areas than their controls. However, there is no study on this field which compared the difference between rural and urban areas. Overall, the higher prevalence of depression among rural patients could be explained by occupational nature of the disease and its related disability as well as the high cost of diagnosis and treatment which are the major stressors for these patients. In fact, these stressors are a key source for onset of depression. It emphasizes the need for particular attention to mental health of the society, especially among those whose role in economic development cannot be negligible. Indeed, the negative impact of depressive disorders on economy is a consequence to the lack of manpower in the community, especially in rural areas. Also, coexistence of depression in the chronic condition of brucellosis can result in subsequent fail of treatment programs which may lead to more additional costs.

### Conclusion

There is a need for attention to the cognitive and behavioral changes in brucellosis patients, especially in endemic areas. Study of these conditions may help to facilitate the treatment of *Brucella* infection. Also, psychiatric consulting as well as administering the cognitive function tests in these patients may lead to determine the etiology of disorder and prevent wrong medications. It is recommended further investigations with greater study samples to identify the specific role of microorganism in development of depressive disorder in brucellosis with comparing to the rate of depression in other chronic diseases.

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