

The Incidence of Depression is one of the Neurological Manifestations in Patients with Brucellosis

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ABSTRACT

Introduction: Brucellosis is a multi-aspect and complicated ailment that may present a wide range of clinical appearances. The main objective of this study was to determine depression as a neuropsychiatric sign in patients with brucellosis. One hundred with depression in the case group and 100 patients without depressive symptoms in the control group were selected and included. The Hamilton Depression Rating Scale (HDRS) was used to assess the severity of depression. Serological, Wright and Coombs-Light tests were performed on all subjects.

Result: The wright test was positive in 14% of the case group and 3% in the control group. Also, the coombs wright test was positive in 22% of the case group and was positive in 3% of the control group. In the case group, the average score of HDRS in patients with a positive wright test was 31 ± 4.47 , and in patients with a negative wright, the test was 3.11 ± 58.61 ($P = 0.001$), and the average score of HDRS in patients with positive Coombs wright test was 26.18 ± 7.56 , and in patients with negative wright, coombs were obtained 10.94 ± 3.07 ($P = 0.001$).

Conclusion: The present study results showed that the positive rate of the wright and coombs wright test was higher in patients with depression. The positive rate of serological tests was higher in patients with higher Hamilton scores.

INTRODUCTION

Brucellosis is the most common and multi-aspect zoonotic infection in the world. Commonly, it infects animals such as sheep and goats as the primary host, and in most cases, humans are the secondary host [1]. Brucellosis is a multi-aspect disease with several clinical manifestations as well as hematologic system, reticuloendothelial system, Central Nervous System (CNS), genitourinary system, cardiopulmonary system, and psychiatric ailments [2]. In addition, *Brucella* spp are facultative intracellular bacteria that have the ability to avoid the killing mechanism and proliferate within the macrophages, similar to other intracellular pathogens. After infecting the host, the pathogen becomes sequestered within the cells of the reticuloendothelial system [3]. Some psychiatric disorders resulting from *Brucellosis* have been described, such as psychosis, depression, nightmares, amnesia, and agitation, as well as some infrequent symptoms comprising confusion, and headache [4]. These problems may appear in the chronic phase or acute stage of brucellosis. Depression, is one of the main problems of brucellosis, affecting infected people [2,3]. The clinical picture of brucellosis is very

different. The statistics mentioned in various studies on the frequency of clinical symptoms are diverse, including fever from 6.66% to 8.92% and arthritis from 3 to 83% [5,6]. Several virulence factors such as Lipopolysaccharide (LPS), superoxide dismutase, catalase, and type IV secretion system (T4SS) are essential in brucella pathogenesis. Figure 1 presented a schematic illustration of brucella pathogenesis.

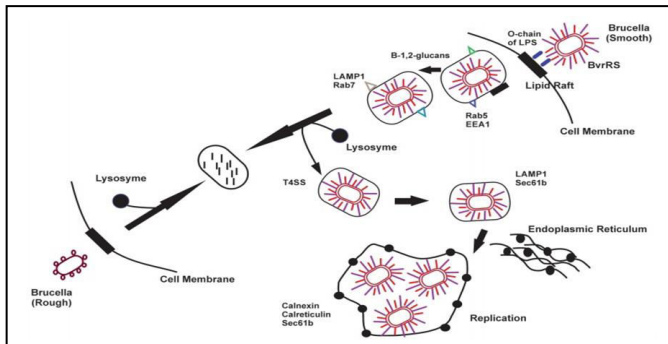


Figure 1: Schematic illustration of brucella pathogenesis [7].

Infectious diseases can play a critical role in the pathophysiology of the neurodegenerative and behavioral neurological disorders [8]. Psychological symptoms can occur as a clinical manifestation of systemic infections and central nervous system infections. On the other hand, psychological stress can weaken the immune system [9]. In psychiatric scientific texts, patients with severe mental illness are more likely to suspect physical illness [10]. Even chronic infections can cause cognitive impairment, hypersensitivity, depression, insanity, and mental disorders with mild symptoms of delirium. It may be associated with various psychological symptoms. A variety of psychological symptoms can occur in febrile illnesses [11,12]. Since brucellosis is highly prevalent due to the old method of animal husbandry and the continued use of unpasteurized dairy products, this rate is relatively higher in northwestern Iran than in other parts of the country, so the diagnosis and treatment of diseases is of particular importance together with brucellosis. Given the high cost of treatment and rehabilitation for mental illness and the damage these patients cause to society and health systems, we decided to investigate *Brucella* serology in patients with schizophrenia and depression. The main goal of the present research work was to determine the frequency of brucellosis positive serology in depressed

serial patients referred to Razi Hospital psychiatric clinic in Tabriz. Also, this study aimed to investigate the relationship between serological titer and Hamilton Depression Rating Scale score in depressed serial patients referred to the psychiatric clinic of Razi Hospital in Tabriz.

METHODS AND MATERIAL

The present study is descriptive-analytical. The sample consisted of 100 outpatients referred to a psychiatric clinic in Razi Hospital in Tabriz diagnosed with depression. The control group also included 100 normal individuals without depression who were selected for comparison. In this study, the diagnosis of depression by a psychiatrist was considered as an inclusion study. Exclusion criteria in this study also included: Vaccination for *Vibrio cholera*, *Tularemia*, *Typhoid*, *Butcher*, *Veterinary*, and *Livestock*. The study method was as follows: the study sample consisted of 100 outpatients referred to a psychiatric clinic in Razi Hospital in Tabriz examined for depression. The control group also included normal, non-depressed individuals selected for comparison. All patients diagnosed with depression were referred to the psychiatric clinic at Razi Hospital as outpatients. Sampling was random and tested for *Brucella* serology (Cooms and Coombs-Light test) using standard tubes during the first visit after a psychiatric diagnosis. The Hamilton Depression Rating Scale (HDRS) was used to assess the severity of depression. HDRS is a multiple-item questionnaire used to provide an indication of depression, and as a guide to evaluate recovery.

STATISTICAL ANALYSIS

All data were analyzed using SPSS22 statistical software. Descriptive statistical methods (frequency, percentage, mean standard deviation) were used for statistical analysis. Chi-square test was used to compare the qualitative findings. One-way ANOVA and non-parametric Cross Cal Wallis test, as well as Independent t test were used to compare quantitative findings between groups. A p value of less than 0.05 was considered significant in this study.

RESULT

In this study, 200 people entered the study, of which 100 people in the group were depressed patients and 100 people in the control group were normal. In the case group, 54

patients (54%) were male and 46% (46%) were female, and in the control group, 50% were male and 50% were female. There was no significant difference between the two groups in terms of sex. The mean age deviation of patients in the case group was 36.28 ± 9.82 years and the maximum and minimum age of patients were 78 and 20 years, respectively. There was no statistically significant difference between the two groups in terms of age ($P=0.62$). Table 1 shows the data of both wright and coombs wright in positive and negative are statically significant $P \leq 0.05$.

Test	Control group	Case group	P-value
Wright	3% (+)	14% (+)	0.005
	97% (-)	86% (-)	
Coombs wright	3% (+)	22% (+)	0.001
	97% (-)	78% (-)	

The standard deviation ($SD = a$ quantity expressing by how much the members of a group differ from the mean value for the group) of the HDRS score of patients in the case group was 14.3 ± 7.72 with the highest and lowest scores of 36 and 8, respectively. In the control group, the standard deviation of the score was 0.0 ± 55.12 HDRS and the highest and lowest scores were 7 and 0. It was found that the HDRS score was significantly higher in patients in the case group.

	Case group	Control group	P-value
Depressed mood (sad, frustrated)	2/06 ± 0/73	0/13 ± 0/03	0/001
Feel guilty	0/07 ± 0/02	1/14 ± 0/58	0/001
Suicide (suicidal ideation)	0/69 ± 0/07	0/05 ± 0/02	0/001
Insomnia early	0/68 ± 0/67	0/11 ± 0/03	0/001
Insomnia middle	0/08 ± 0/02	0/46 ± 0/05	0/001
Insomnia late	0/56 ± 0/53	0/03 ± 0/01	0/001
Work and activities	0/92 ± 0/77	0/06 ± 0/02	0/001
Retardation: psychomotor	0/56 ± 0/05	0	0/001
Agitation	0/6 ± 0/06	0	0/001
Anxiety (psychological)	0/93 ± 0/86	0	0/001
Anxiety (Somatic)	0/58 ± 0/07	0/07 ± 0/02	0/001
Somatic symptoms (gastrointestinal)	0/38 ± 0/05	0	0/001

	Case group	Control group	P-value
Somatic symptoms general	0/28 ± 0/04	0	0/001
Genital symptoms	0/73 ± 0/44	0	0/001
Hypochondriasis	0/14 ± 0/04	0	0/001
Loss of weight	0/28 ± 0/04	0	0/001
Insight	0/12 ± 0/03	0	0/001
Daily changes	0/22 ± 0/04	0	0/001
Transfiguration of character and reality	0/16 ± 0/03	0	0/001
Paranoid symptoms	0/04 ± 0/01	0	0/001
Symptoms of obsessive-compulsive disorder	0/2 ± 0/05	0	0/001
Helplessness or despair	1 ± 0/06	0	0/001
Despair	0/9 ± 0/75	0	0/001
Feeling worthless	0/73 ± 0/56	0	0/001

As shown in Tables (1-3), P-value is 0/001 indicates that if the null hypothesis tested were indeed true, then there would be a one-in-1,000 chance of observing results at least as extreme.

In the case group of patients with depression, it was found that the mean \pm standard deviation of HDRS score in patients with positive wright test was 31 ± 4.47 and in patients with negative wright test was 11.58 ± 3.61 which was significant in patients with the positive wright test. Also, in the patients of the case group, it was found that the mean \pm standard deviation of HDRS score in patients with positive Coombs wright test was 26.18 ± 7.56 and in the patients with negative coombs wright test was $10/94 \pm 3/07$. Tables 4 and 5 show the relationship between the severity of depression in depressed patients with the positive wright and coombs wright tests. Based on the results, it was found that patients with positive wright and coombs wright test showed higher severity of depression.

DISCUSSION

The relationship between infectious diseases and the incidence of neurological disorders has been shown in several studies. For example, in 2009, Rothbard et al. Studied the prevalence of metabolic syndrome and infectious diseases among the mental disorder. The results showed a direct and significant relationship between infectious diseases and neurological disorders [13]. Clinical, epidemiological and laboratory results showed in patients with Brucella additionally disorders such as arthralgia, weakness, headache, diarrhea and abdominal

pain are detectable [14]. To evaluate the occurrence of depressive disorder among brucellosis patient Zung Depression Scale was used in original work by Eini and co-worker. Finding revealed the prevalence of depression in case group was more than 53% [15]. In 2010, shehata et al. Conducted a neuropsychological study of patients with brucellosis. In this study, 27 patients with brucellosis were studied. The results of this study showed obvious neuropsychological involvement in 14 patients. This study showed that patients with brucellosis have severe cognitive impairment and score higher on depression [16]. In 2013, Montazeri et al. Reported a case report of brucellosis with meningoencephalitis. In this study, a young woman with symptoms of fever and psychosis was admitted with neuroimaging findings of meningoencephalitis. Brucella serology was reported to be positive for the patient. The patient was treated with doxycycline, rifampin and trimethoprim. This study suggests that the diagnosis of neurobrucellosis be presented as a differential diagnosis for patients with acute neurological symptoms or atypical psychosis [17]. In 1986, Annesley reported a case involving a 41-year-old woman with schizophrenia following chronic untreated brucellosis. The patient suffered from headache, nausea, dizziness and vomiting, sweating and weakness and lethargy following consumption of non-sterilized milk. The patient was hospitalized with a diagnosis of secondary schizophrenia. Bone marrow samples showed iron deficiency. After treatment with tetracycline and streptomycin, the patient's psychological and physical symptoms completely disappeared [18]. In 2015, Jafari et al evaluated the therapeutic effect of celecoxib in the treatment of depression caused by brucellosis. In this study, 40 Outpatients with a s Hamilton Depression Rating Scale score of $19 \leq$ were examined. This study showed that celecoxib is effective in treating depression caused by brucellosis [19]. Depression was assessed in children and adolescents with brucellosis without neurological involvement. A total of 120 children and adolescents were included in the study. The results showed that the incidence of depression was much higher in patients with brucellosis [20]. Findings revealed that the positive rate of wright and coombs wright tests in patients with depression was significantly higher than healthy individuals. In addition, the HDRS score for depressed patients who tested

positive for the light test was 47.4 31 31, the HDRS score for patients who tested positive for the Coombs light test was 56.7 18 18.26, and the HDRS for patients who were negative for Coombs wright and 61.58113.11 was significantly higher than the score 3.10. \pm was 94/07.

CONCLUSION

This study shows that HDRS has promising psychometric properties and is a good tool for identifying patients with depression. Awareness and treatment of depression in general practice aimed at improving patient outcomes and reducing medical costs is undoubtedly justified. In patients with brucellosis, neuropsychiatric disorders are very common in patients with and without overt neurological involvement (neurobrucellosis). Emotional and cognitive abnormalities can be observed in patients with neurobrucellosis. The use of such tests supports true incidence. The results of this study showed that the positive rates for the Wright and Coombs-Light tests were higher in patients with depression, and the positive rates for serological tests were higher in patients with Hamilton scores. In the other words, the percentage of brucellosis in depressed patients is higher than the normal and healthy people in the studied region. Attention should be paid to cognitive and behavioral changes in brucellosis patients, especially in endemic areas. Research into these disorders will help guide treatment for *brucella* infections. Psychiatric counseling and cognitive testing in these patients also help identify etiology. We suggest conducting further studies using larger study samples to identify specific roles of microbes in the development of depressive disorders in brucellosis compared to rates of depression in other regions.

ETHICAL CONSIDERATIONS

Written consent to participate in the study was obtained from all patients prior to the study. No additional cost was incurred on the patient and all required tests were provided through an approved study program. The patient's name and address were not listed anywhere, in which case full fidelity was maintained.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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