Psychiatric disorders and MRI brain findings in patients with systemic lupus erythematosus and Behcet’s disease: A cross sectional study

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ABSTRACT

Introduction: Neuropsychiatric systemic lupus erythematosus (NPSLE) shows some similarities to neuro Behçet’s disease (NBD).

Aim of the work: to investigate and compare the psychiatric manifestations in a cohort of patients of systemic lupus erythematosus (SLE) versus Behcet’s Disease (BD). Also, a comparison of MRI brain findings in SLE patients and BD patients presented with psychiatric disorders was done. Finally, we correlate these manifestations with disease activity indices of the patients.

Patient and Method: The study included 50 patients of SLE, 34 patients of Behcet’s disease (BD) and 44 healthy volunteers as a control group. All patients were subjected to psychiatric interview to diagnose any psychiatric disorders clinically. MRI brain was done for SLE patients and BD patients presented with psychiatric disorders. Overall clinical assessment and disease activity of SLE and BD were evaluated.

Results: Psychiatric disorders were detected in 28 (56%) of SLE patients which were significantly more prevalent than psychiatric disorders that were detected in 9 (26.47%) of BD patients. Psychiatric disorders in healthy volunteers were significantly less prevalent than either SLE patients or BD patients. MRI brain of SLE patients presented with psychiatric disorders commonly showed cerebral white matter abnormalities while in BD patients presented with psychiatric disorders commonly showed brain stem lesions.

Conclusion: (1) High prevalence of psychiatric disorders in SLE and BD with a higher significant prevalence in SLE. (2) Evident MRI brain findings in SLE and BD patients presented with psychiatric disorders.

Keywords: Psychiatric disorders; Systemic Lupus Erythematosus; Behcet’s disease; MRI brain.

INTRODUCTION

Neuropsychiatric systemic lupus erythematosus (NPSLE) shows some similarities to neuro Behçet’s disease (NBD) and both conditions have some analogous clinical features and they are both pathologically associated cerebral vasculopathy.

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease that can affect any part of the body. As occurs in other autoimmune diseases, the immune system attacks the body cells and tissue, resulting in inflammation and tissue damage. In the course of SLE, a variety of neuropsychiatric disturbances is reported, with prevalence rates ranging from 17% to 75%. Psychiatric manifestations of SLE include depression, anxiety, cognitive deficits, psychosis and mania. Immuno-logic and cerebral imagery research suggests that psychiatric disorders are related to vasculitis and non-inflammatory vasculopathy of the small cerebral blood vessels. A common MRI brain finding in patients with SLE is cerebral white matter abnormality.

Behçet’s disease (BD) is a multi-system inflammatory disorder dominated clinically by recurrent oral and genital ulceration, uveitis, and erythema nodosum. The disease tends to wax and wane. BD is a vasculitis, affecting vessels of different types, sizes, and localizations. Although the cause of BD is unknown, autoimmune, infectious, and genetic causes have been suspected. Environmental factors, such as microbial in-
Infections, are also suspected to be factors that contribute to the development of BD. Central nervous system (CNS) involvement can be either parenchymal or non-parenchymal. Parenchymal involvement primarily affects the brainstem, spinal cord, and cerebral hemispheres. Nonparenchymal involvement includes intracranial hypertension, aseptic meningitis, cranial neuropathy, and cerebrovascular disorders such as dural sinus thrombosis, arterial dissection, occlusion, and aneurysm. The prevalence of psychological symptoms was remarkable in the patients with BD. The psychological symptoms in BD could be aggravated by the illness itself or by the immunosuppressive drugs used during the treatment course. Psychiatric reactions to BD may include anxiety, insomnia, manic/depressive episodes and psychosis. The characteristic MRI brain lesion in parenchymal involvement of BD is an upper brainstem lesion that extends into the thalamus and basal ganglia on one side.

**AIM OF THE WORK**

The purpose of this study is to investigate and compare the psychiatric manifestations in a cohort of patients with SLE versus BD and to correlate these manifestations with disease activity indexes of the patients. Likewise, a comparison of MRI brain findings in SLE patients and BD patients presented with psychiatric disorders has been carefully analyzed.

**PATIENTS AND METHODS**

**PATIENTS AND CONTROLS**

Fifty patients of SLE and 34 patients of BD and 44 control subjects with similar demographic characteristics were included in the study. All SLE patients had fulfilled American College of Rheumatology criteria for the classification of systemic lupus erythematosus, while BD patients had fulfilled the International Study Group for BD diagnostic criteria. The study was approved by the hospital ethical committee and a written informed consent was taken from all patients who agreed to contribute.

**PSYCHIATRIC ASSESSMENT**

All patients and control group were subjected to patient-based structured psychiatric interview and neuropsychological evaluation to diagnose clinically any psychiatric disorders. All subjects included in the study were asked to perform a series of neuropsychological test done by expert psychologist to detect depression, anxiety, cognitive impairment, mania or psychosis.

**1. HAMILTON DEPRESSION INVENTORY TO DETECT DEPRESSION**

It is a 23-item self report inventory that assesses depressive symptomatology for the previous 2 weeks. The administration time is 10-15 minutes. Scoring varies by item, with a total range of 0-73 and a score of 19 has been suggested as a cut off score when screening for depression.

**2. STATE-TRAIT ANXIETY SCALE TO DETECT ANXIETY**

It is a self-report and one of the widely used scales in a variety of research studies. The administration time is 20 minutes. It is a two 20-item scale and each item is scored on a 4-point scale and scores ≥ 20 indicate anxiety.

**3. MINI MENTAL STATE EXAMINATION TO DETECT COGNITIVE DYSFUNCTION**

The most common neurocognitive screening tool used to detect cognitive losses through a score (maximum score = 30) of the five areas of cognition, orientation, registration, attention and calculation, as well as recall and language. Scores < 24 suggest the presence of decline.

**4. MOOD DISORDER QUESTIONNAIRE TO DETECT MANIA**

It is a self-report questionnaire designed to screen for mania. The administration time is 5-10 minutes. It is a brief 13-item questionnaire in a yes/no format. The screen is considered positive when 7 or more symptoms have occurred.

**5. BRIEF PSYCHIATRIC RATING SCALE TO DETECT PSYCHOSIS (BPRS)**

BPRS remains one of the most widely used clinician-administered tools designed to assess overall psychopathology in patients with a major psychiatric disorder, particularly psychosis. It is administered in a semi-structured manner and it takes about 30 minutes to complete. It comprehends 24 items that can be scored from 1 (not present) to 7 (very severe). The total BPRS-E score is the sum of the scores for each of the 24 items.
BRAIN MAGNETIC RESONANCE IMAGING (MRI)

All SLE and BD patients presented with psychiatric disorders underwent brain MRI including T1-weighted images, T2-weighted images and fluid-attenuated inversion-recovery images (FLAIR) images. The MRI was performed using a 1.5 T MRI system (GE SIGMA Advantage version 4-8). The conventional spin echo pulse sequence with a TE of 20 ms and a TR of 400 ms was used to obtain the T1-weighted NR images. The fast spin echo pulse sequence with a TE of 90 ms and a TR of 2,500 ms was used to obtain the T2-weighted MR images. Contrast medium was administered to all SLE and BD patients presented with psychiatric disorders and this was followed by obtaining the axial/sagittal/coronal T1-weighted images. MRI were studied for: an abnormal T2-weighted image, infarct-like lesions (moderate to large, roughly wedge-shaped areas of abnormal high signal on the T2-weighted images and/or encephalomalacia involving the gray and white matter), parenchymal hemorrhage, and loss of brain volume or abnormal intracranial enhancement. The location of the brain lesion was addressed. Finally, the abnormal MRI findings were classified into two main categories: parenchymal (mainly located in upper brainstem thalamus and basal ganglia) and non-parenchymal (mainly venous sinus thrombosis).

DISEASE ACTIVITY MEASUREMENT

All the patients were subjected to disease activity measurement in the following manner:

* Overall clinical assessment and disease activity index of SLE patients: was done using the BILAG (British Isles Lupus Assessment Group) disease activity index\(^21\). It distinguishes activity in 8 organs or systems namely general, mucocutaneous, Central Nervous System, musculoskeletal, Cardio-Vascular System/respiratory, vasculitis, renal and haematological systems. It provides an accurate means of grading disease activity from the “most active” to “no evidence of disease activity currently”. Patients are classified to 5 grades:
  - Grade A “Active” the most active disease state requiring major immunosuppressive drug. A = 9 points.
  - Grade B “Beware” patients known to have active disease but is already on immunosuppressive therapy. B = 3 points.
  - Grade C “Contentment”, patients has relatively mild disease controlled by little specific therapy if any. C = 1 point.
  - Grade D “Discount”, there is no activity in this system now. D = 0 point.
  - Grade E “No Evidence”, of activity in this system now or previously. E = 0 point.

A global score can finally be calculated in the patients collecting the 8 system/organ score together.

* Iranian Behcets Disease Dynamic Activity Measure (IBDDAM)\(^22\): patient is evaluated on several weeks or months. Each attack is measured separately and given an index. The obtained indexes are added together and the total is divided by the number of months of the evaluated period. The final result is the mean disease activity index. One point is given for: oral ulcers (2 for more than 5 ulcers at a time), genital ulcers (one for each ulcer), pseudofolliculitis (2 for more than 10), erythema nodosum (2 if more than 5), arthralgia, superficial phlebitis and pathergy. Two points are given for phlebitis (each vessel), epididymitis, and mononarthritis. Three points for polyarthritis, mild CNS, and intestinal manifestations. Six points are given for large vessel thrombosis, moderate to sever intestinal lesions. Each inflammatory sign of the eye is given 1 to 4 points. If an attack does not heal in 1 month, the same point is given for each additional month.

STATISTICAL ANALYSIS

Comparison of the studied groups was done using the students T test. The Chi-squared test was used to compare categorical variables. Correlations between groups were evaluated using the Spearman test. Non-parametric Mann–Whitney U test was used for the comparison of variables between tested groups with and without psychiatric disorders. Pearson’s correlation analysis was used to investigate relation between SLE duration and psychiatric disorder. A probability value (P-value) less than 0.05 was considered significant.

Data were collected and tabulated using Microsoft excel version 7 (Microsoft Cooperation. NY, USA) and analyzed using SPSS for windows (Statistical Package for the Social Science, version II, SPSS, Inc, Chicago, IL, USA).

RESULTS

Table I demonstrates the Demographic and clinical characteristics of SLE and BD patients as well as con-
The study comprised 50 SLE patients; 44 female and 6 males with mean age of 29.5 (range: 18-42) years, and 34 BD patients with a mean age of 39.5 (range: 22-55) years, 18 female and 16 males. Disease duration of SLE patients was 7.5±2.3 with range of 6 months to 11 years. Disease duration of BD patients was 8.4±3.3 with range of 1 year to 13.5 years.

Corticosteroids medication in patients: approximate cumulative dose of corticosteroids and current daily dose of corticosteroids, for each patient were calculated. Cumulative corticosteroid dose in SLE patients was in range 0–98g, mean 18.55 ± 11.2g and current dose 0–45 mg, mean 12.4 ± 5.19mg. Cumulative corticosteroid dose in BD was in range 0–22g, mean 9.12 ± 3g and current dose 0–30 mg, mean 7.5 ± 2.5 mg.

Table II specifies the steroid dosage in SLE and BD patients in detailed manner. No significant difference in SLE and BD patients in steroid dosage in different categories (p <0.05).

Overall clinical assessment and disease activity index of SLE patients were done using the BILAG:
- Group (1): 12 patients with 0-3 points.
- Group (2): 10 patients with 4-6 points.
- Group (3): 12 patients with 7-12 points.
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- Group (5): 9 patients > 15 points.
- Iranian Behcet’s Disease Dynamic Activity Measure (IBDDAM): patients were evaluated monthly for 12 months without appointment failure for those 24 patients:
  - Group (1): 6 patients < 1 point.
  - Group (2): 7 patients with 1-3 points.
  - Group (3): 8 patients with 4-6 points.
  - Group (4): 5 patients with 7-12 points.
  - Group (5): 8 patients > 12 points.

CLINICAL AND PSYCHOMETRIC ASSESSMENT OF PSYCHIATRIC DISORDERS (FIGURE 1)

Psychiatric disorders were detected in 28 (56%) patients with SLE which were statistically significant compared to 9 (26.47%) patients with BD. Psychiatric disorders in each of SLE or BD patients were significantly more prevalent than that of control group (6 persons = 13.63%).

As shown in Figure 1 depression was more prevalent in SLE patients (19 patients =38%) compared to BD patient (7 patients =20.59%) in a statistically significant manner. In either SLE or BD patients the prevalence of depression is significantly higher than the control group (5 persons = 11.36%) (p<0.05).

No significant difference in the prevalence of anxiety in SLE and BD patients (11 patients = 22% vs 8 patients =23.53% respectively). Also, in SLE and BD patients the prevalence of anxiety was significantly higher than control group (4 persons = 9.09%) (p>0.05).

Cognitive deficits were significantly high in SLE patients (23 patients = 46%) compared to BD patients (8 patients = 23.53%) and the frequency of cognitive deficits from either patients were notably higher than the control group (7 persons = 15.91%) (p <0.05).

Three SLE patients (6%) had mania compared to 2 BD patients (5.88%) with no statistical significant difference (p >0.05). No reported cases in control group had mania.

For psychosis, 2 SLE patients (4%) and 1 (2.94%) BD patients were affected, with no statistical significant difference (p >0.05). Mixed psychiatric disorders were detected in a statistically significant higher percentage in SLE patients compared to BD patients (21 =42% vs 8 = 20.59%) (p <0.05). Likewise, mixed psychiatric disorders were statistically more prevalent in SLE and BD patients compared to control group (3 persons = 6.82%) (>0.05).

Table III explains the effect of disease duration on psychiatric disorders of both SLE and BD patients. It shows that shorter duration of illness in SLE and BD patients is statistically correlated with anxiety disorders if compared with those without anxiety disorder. No significant correlation with depression, cognitive impairment, mania or psychosis.

For MRI of brain (Table IV), there was a statistically significant (p=0.05) frequency of abnormalities in BD patients presented with psychiatric manifestations (7/9 patients = 77.78%) than that in SLE patients (18/28 patients = 64.29%). Abnormal T2-weighted images were more common (p = 0.1) in BD patients (5/7 = 71.43%) than SLE patients presented with psychiatric manifestations (4/18 = 22.22%). MRI brain showed no abnormal findings in 10 SLE patients (35.71%) out of 28 and 2 BD patients (22.22%) out of

![Figure 1](image-url)

FIGURE 1 shows the prevalence of different psychiatric disorders in Systemic Lupus Erythematosus (SLE), Behcet’s Disease (BD) and control group.
Despite presentation with psychiatric manifestations with statistically insignificant difference in both groups (p= 0.06).

For location of the lesion in MRI (Table V), Cerebral white matter lesions on MRI were more frequently encountered in a significant ratio (p= 0.01) in SLE patients presented with psychiatric disorders (10 patients = 55.56%) than those of BD (1 = 14.29%) whereas the...
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Figure 3. (A, B) axial T2WI (C) axial FLAIR: 45 years old female with SLE show bilateral diffuse periventricular ischemic high signal (arrow) and infarct like lesions (filled arrows). No significant atrophy, no hemorrhage, no enhancement in T1 study (not shown).

Frequency of brain stem lesion tended to be statistically higher (p = 0.01) in BD patients presented with psychiatric disorders (4 patients = 57.14%) than those of SLE (4 patients = 22.22%). In BD we noticed that 6 (85.5%) patients had parenchymal lesion, while 1 (14.5%) patient had non-parenchymal lesion, with a significant difference (p = 0.05) (data not shown in the table). Figures 2 and 3 showed MRI findings in a patient with SLE with brain involvement and a patient with neuro-Behcet’s respectively.

Figure 2. (A) axial T2WI (B) axial FLAIR: 50 years old male patient with BD, show bifrontal atrophic changes with loss of volume (arrow) as well bilateral advanced periventricular ischemic high signal (filled arrow), no area of infarction, no hemorrhage, no enhancement in T1 study (not shown).
Correlation of psychiatric disorders with disease activity in both diseases yields a significant accumulation of patients with major psychiatric disorders like psychosis and mania in groups with more disease flares. Five SLE patients with mania and psychosis were of groups (4) and (5) of BILAG disease activity and 3 BD patients with mania and psychosis were of groups (4) and (5) of IBDDAM (p < 0.005). On the other hand, the groups with less disease activity in both SLE and BD such as groups (1), (2) and (3) BILAG of SLE and IBDDAM of BD showed significant accumulation of anxiety, depression and cognitive disorders (28 SLE patients and 9 BD patients) (p < 0.001).

**DISCUSSION**

In our study, we addressed the different psychiatric disorders in both SLE and BD in a comparative way. Our results were comparable with other studies. We revealed that the prevalence of psychiatric disorders in SLE (56%) was higher than in BD (26.47%). Those figures were comparable with that of other studies. Kaplan and Sadock’s mentioned that 50 percent of patients with SLE show neuropsychiatric manifestation. Kakalami et al reported that neuropsychiatric involvement occurs in 10-20% of cases with BD. We revealed higher frequency of depression in SLE patients (38%) than BD patients (20.59%) in a statistically significant manner, which is consistent with the results of Cho et al who reported that a common feature in SLE patients was depression (32%) which was uncommon in BD patients. However, depression was more prevalent in SLE and BD than the general population (17%)33. Cohen et al stated that depression is the second most common psychiatric disorder in SLE, with a prevalence of almost 50%. Moreover, we reported that prevalence of cognitive dysfunction in SLE patients (46%) was higher than BD patients (23.53%). This was in agreement with the results of Denburg and Ainalia but it was contradictory with the results of Cho. He reported that cognitive dysfunction in BD patients was more frequent than in SLE patients (36.4%). A possible plausible explanation of this discrepancy was different cultures and tools of psychometric assessment in addition to the intermingling features of cognitive deficits that are considered a common feature of depression which is prevalent in SLE. In our study no statistical significant difference between the prevalence of anxiety disorder in SLE patients (22%) and BD patients (23.53%) was noted but in each disease, anxiety disorder is more prevalent than the general population (17.7%). We reported no significant difference of mania frequency in SLE patients (6%) and BD patients (5.88%). Berlit reported that mania is commonly occurs in SLE and also related to dose dependent corticosteroid therapy. Also, we noticed no significant difference in the prevalence of psychosis in SLE patients (4%) and BD patients (2.94%), which is similar to the results of other publications.

For the effect of disease duration on psychiatric disorders of both SLE and BD patients, we found that the duration of SLE and BD in patients with anxiety disorders was short if compared with those without anxiety disorders. This is consistent with the results of McCracken et al who relate this finding to the development of coping strategies with better social functioning.

MRI is a useful tool for detecting CNS lesions in patients suffering with SLE and Behçets disease. The present study revealed that MRI brain of BD patients presented with psychiatric disorders frequently showed abnormal T2-images (71.43%) than those of SLE patients (22.22%). In the current work we addressed that cerebral white matter involvement in brain MRI of SLE patients presented with psychiatric disorders (55.56%) were more frequent than those of BD patients (14.29%), while brain stem lesions were more encountered in BD patients presented with psychiatric disorders (57.14%) than those of SLE patients (22.22%). This findings is comparable with the results of Byung-Sik Cho et al who found that cerebral white matter abnormalities are more common in NPSLE (48%) than NBD (22.29%) whereas brain stem lesions on MRI are more common in NBD (55.6%) than NPSLE (20.2%).

Furthermore, we have tried to correlate disease activity scoring in both SLE and BD with psychiatric disorders taking severity in mind. Accordingly, we have divided psychiatric disorders into both divisions; namely anxiety, depression and cognitive disorders in one “pol e” and the “major psychiatric disorders” like mania and psychosis in another “pole”. Our results found a positive correlation between high disease activity scores in both diseases with major psychiatric disorders like mania and psychosis. Explanation may be linked to the more chance of cerebral vasculitis in higher disease activity score patients with higher propensity to have more aggressive psychiatric disorders. To our knowledge, no reports correlating disease acti-
vity measures in SLE and BD with psychiatric illness in both diseases. In this respect, a wide scale study with more stress on a cohort of higher disease activity score patients in both diseases may appear interesting.

Finally, a wider scale study may be recommended to address the effect of chronic pain, the impact of functional disability and socioeconomic status as well as the effect of medications -mainly steroid- in the psychiatric make up of SLE and BD patients.

We therefore conclude that there is a high prevalence of psychiatric disorders in both SLE and BD with a significant increase of prevalence in SLE. There is accumulation of patients with major psychiatric disorders like psychosis and mania in groups with more disease flares in both diseases. MRI is a useful tool for detecting CNS psychosis and mania in groups with more disease flares in both diseases. In this respect, a wide scale study with more stress on a cohort of higher disease activity score patients in both diseases may appear interesting.

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