Research article

Characteristic features of lupus patients with neuropsychiatric manifestations: a study from a single tertiary care center in Saudi Arabia

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Abstract

Objective: This was a study reporting Neuropsychiatric Systemic Lupus Erythematosus Events (NPSLE) in Saudi lupus patients.

Methods: A retrospective study for adult patients who attended rheumatology clinics at King Fahad Medical City between 2014 and 2020 and fulfilled the Systemic Lupus International Collaborating Clinics classification criteria (SLICC). NPSLE identified based on ACR 1999 nomenclature. The primary outcome is to identify the most common NPSLE while the secondary outcome is to find the association between NPSLE and other major organs and with the radiological features.

Results: One hundred and forty eight Systemic Lupus Erythematosus (SLE) patients participated in the study, One hundred and thirteen (76.4%) females and 35 (23.6%) males. Twenty one (14.2%) of our patients had NPSLE of whom 16 (76.2%) were female patients. The most frequently recorded event is seizure (42.9%) followed by stroke (23.8%). Psychosis was the most dominant psychiatric symptom (9.5%). Depression, headache, acute confusion, transverse myelitis, and peripheral neuropathy each presented by 4.8%. Lupus nephritis was diagnosed in 66.7% of patients with NPSLE while carditis was 28%. No significant association was found between aPL and anti-ds- DNA positivity and NPSLE. The most obvious abnormalities in imaging (MRI/ MRA/ MRV) were abnormal high signal intensity that was identified in 8 (57.1%) patients, infarction in 4 (28.6%) patients while vasculitic changes was in 3 (21.4%) patients.

Conclusions: NPSLE are reported prominently among female patients with seizure being the most common symptom followed by cerebrovascular accidents (CVA). The kidney is the most obvious major organ involved in patients with NPSLE followed by the heart. Abnormal signal intensity, infarction and vasculitis are the most noticeable lesions in imaging respectively.

Key words: Features, Characteristic, Lupus, Neuropsychiatric, Saudi patients

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic multi-system autoimmune disorder causing organ dysfunction via immune complex deposition. It usually affects young women with a ratio ranging from 4.3-13.6:1[1]. It can cause a wide array of manifestations ranging from mild disease to more severe phenotypes associated with organ-threatening conditions. Neuropsychiatric events (NPSLE) are considered one of the devastating features of SLE. Patients with NPSLE could have central or/and peripheral nervous systems involvement and different psychiatric syndromes[2]. Nineteen clinical syndromes had been identified according to American College of Rheumatology (ACR) nomenclature 1999[3].

The pathophysiology of NPSLE is complex and can arise as a result of small vessel disease due to antibodies such as anti-phospholipid (aPL) antibodies while others occur as a consequence of the severe inflammatory process causing damage of neuronal cells[4,5]. The diagnosis of NPSLE is dependent mainly on the clinical picture in collaboration with some serological and radiological investigations. Several studies have been done worldwide focusing on NPSLE manifestations[6]; however, scarcity of data about NPSLE in Saudi Arabia is prominent.

Materials and methods

This was a retrospective, descriptive case series study, which included all SLE patients who attended the Rheumatology Clinic, King Fahad Medical City (KFMC) between 2014 and 2020. All patients aged >14 years diagnosed with SLE based on Systemic Lupus International Collaboration Classification Criteria (SLICC) 2012 criteria were included.

Exclusion criteria included any patient diagnosed with metabolic derangement that could explain neurological manifestations and any patients with coexistence autoimmune conditions like Sjögren's syndrome, systemic sclerosis and others.

Descriptive statistics was used to assess the most common NPSLE with logistic regression analysis done to identify the strength of association. SPSS version 22, was the program used to assess the statistical analysis with chi-square used for the association, and p-value <0.05 considered significant.

Results

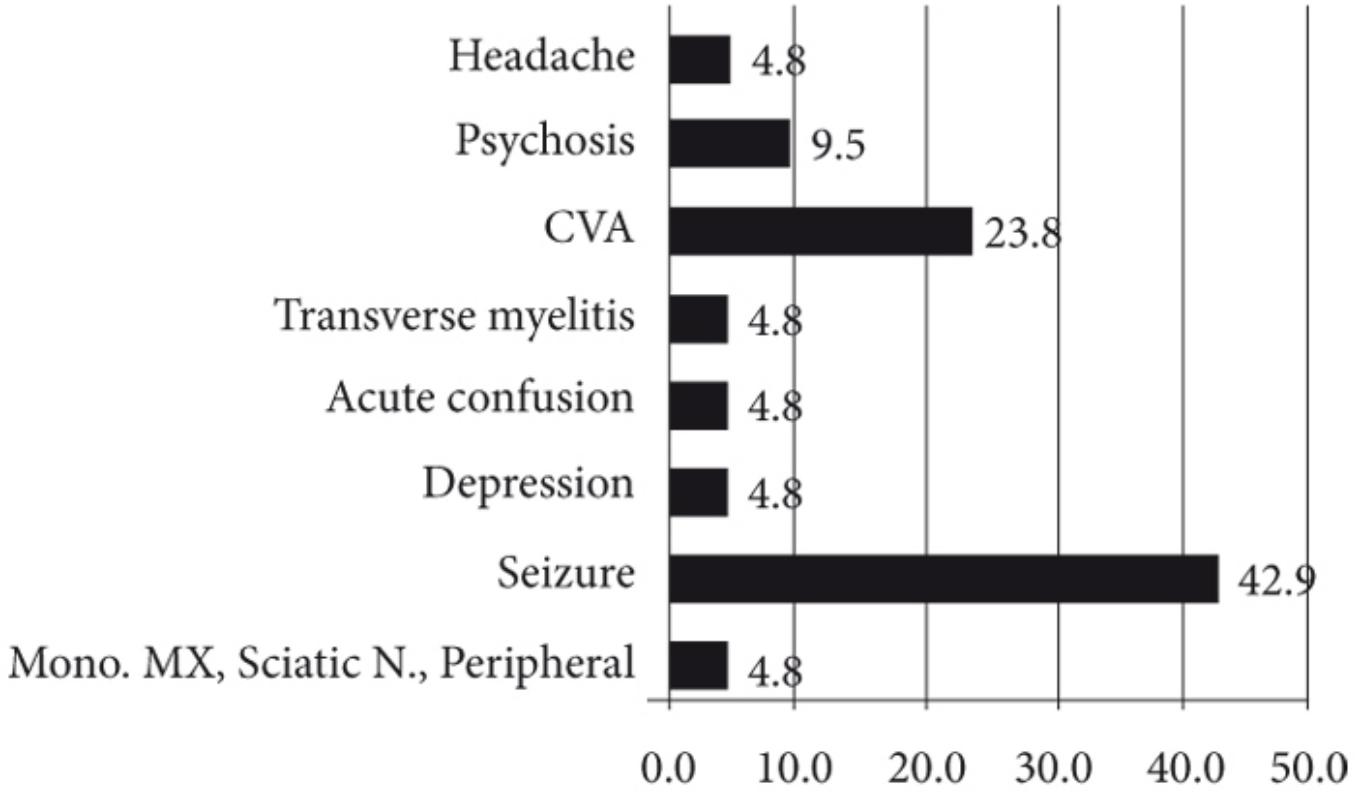
Of the 148 SLE patients diagnosed according to SLICC 2012 criteria, 21 patients were identified to have NPSLE. The prevalence of NPSLE in our study was 14.18%. Most of the patients were female 16 (76.2%) with a mean age of 34.7± 12.7 (range 17-58 years) (Table 1). The most common NPSLE seen among our patients was seizure that was reported in 9 (42.9%) patients followed by CVA in 5 (23.8%) patients. One (4.8%) patient presented with headache and another one (4.8%) presented with transverse myelitis. Four (19%) patients presented with diffuse neuropsychiatric manifestations, of whom 2 (9.5%) presented with psychosis, 1 (4.8%) with depression and 1 (4.8%) with acute confusional status. One (4.8%) patient presented with peripheral nervous system involvement in form of sciatic neuropathy (neuritis) (Figure 1).

Table 1: Distribution of neuropsychiatric events among Saudi lupus patients

Bio-demographic characteristics	Manifestations neurological only		Psychiatric only		Chi square tests	P-value
	No.	(%)	No.	(%)		
Gender						
Male	4	22.2	1	33.3	0.18	0.676**
Female	14	77.8	2	66.7		
Age (years)						
> 30	7	38.9	2	66.7		
31 – 40	5	27.8	0	0.0	1.29	0.523**
< 41	6	33.3	1	33.3		

*Statistically significant at 0.05 **Statistically not significant

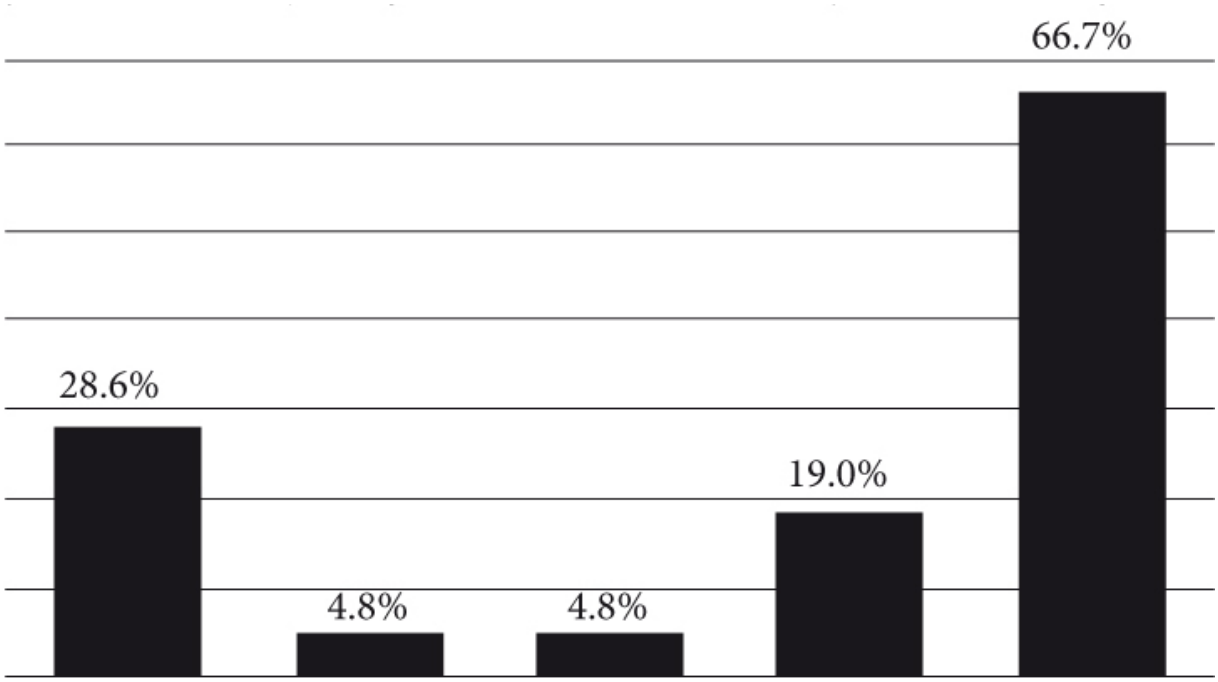
Figure 1: Most NPSLE patterns reported in Saudi lupus patients



(CVA: Cerebrovascular accident and MONO. MX: Mono-neuritis multiplex)

Major organs involvement were reported in 15 (71.4%) patients with NPSLE. Lupus nephritis was reported in 14 (66.7%) patients, heart involvements in 4 (19%) patients, pulmonary haemorrhage in 1 (4.8%) patient and colitis in 1 (4.8%) patient (Figure 2).

Figure 2: Other major organs affected concomitantly in patients diagnosed NPSLE



(Note: Many patients have two major organs involved simultaneously).*

Serological work-up: Anti double-stranded (ds-DNA) antibody levels were elevated in 18 patients with a mean value 165.9 ± 231.7 of whom, 13 patients were diagnosed with focal NPSLE, 4 patients with diffuse NPSLE and 1 patient was diagnosed with peripheral NPSLE. Table 2 summarizes laboratory values in our patients.

Table 2: Laboratory investigations among Saudi lupus patients diagnosed with NPSLE

Categorize		Type				chi-square	P-value
		Neurological only		Psychiatric only			
		No.	(%)	No.	(%)		
White blood cells (4-11)	Low	3	16.7	1	33.3	1.05	0.590**
	Normal	11	61.1	2	66.7		
	High	4	22.2	0	0.0		
Haemoglobin (11-18)	Low	10	55.6	2	66.7	0.13	0.719**
	Normal	8	44.4	1	33.3		
	High	0	0.0	0	0.0		
Platelet (155-435)	low	3	16.7	0	0.0	1.20	0.754**
	Normal	11	61.1	2	100.0		
	High	4	22.3	0	0.0		
Antibody double stranded-DNA (>25)	Normal	3	16.7	0	0.0	0.58	0.445**
	High	15	83.3	3	100.0		
Erythrocyte sedimentation rate (>20)	Normal	2	11.1	0	0.0	0.58	0.747**
	High	15	83.3	3	100.0		
	Not done	1	5.6	0	0.0		
C-Reactive protein (>3)	Normal	5	27.8	1	33.3	0.83	0.660**
	High	9	50.0	2	66.7		
	Not done	4	22.2	0	0.0		

* Statistically significant at 0.05 ** Not significant

Antiphospholipid (aPL) antibodies were requested in 17 patients with NPSLE. Lupus Anticoagulant (LA) was positive in six patients diagnosed with focal (NPSLE) events (four patients with CVA and two with seizure) and only one patient with diffuse NPSLE.

Out of the 21 patients, anti-cardiolipin (IgG) and anti - B2 glycoprotein (IgG) were elevated in three patients with focal NPSLE (two patients with seizure and one patient with CVA). The association between aPL antibodies and NPSLE could not be done due to the small number of patients.

Cerebrospinal fluid (CSF) analysis: CSF was performed in 5 patients and only one showed abnormal results with high White Blood Cells (WBC), low glucose, and high total protein.

Imaging finding: Brain MRI/MRA/MRV were done in 14 (66.6%) patients. Eight patients 57.1% revealed abnormal high signal intensity , 28.6% had stroke while vasculitis was reported in 21.4%, Table 3 includes details about radiological findings.

Table 3: Radiological findings noticed commonly in our patients diagnosed with NPSLE

Imaging		No.	(%)
Brain image type	CT	5	23.8
	MRI	14	66.7
	Not done	2	9.5
	Total	21	100.0
Brain CT (n=5)	Multiple old cerebellar infarction	1	20.0
	Normal	3	60.0
	Subacute stroke (frontal)	1	20.0
	Total	5	100.0
Brain MRI (n=14)	Normal	2	14.3
	Abnormal high signal intensity	8	57.1
	Infraction	4	28.6
	Vasculitis changes	3	21.4
	Brain volume loss	4	28.6
	Sinus occlusion	2	14.3

(Note : For MRI findings , some patients have two concomitant abnormalities and the number represents the frequency of each abnormality in images)*.

Discussion

NPSLE are serious manifestations of lupus that affect patients' quality of life and could impair the prognosis. Several studies have been done worldwide to recognize NPSLE events, but the data about Saudi population are very scarce[7]. This study aimed to identify the NPSLE events among Saudi lupus patients.

The prevalence of NPSLE is highly variable between different studies from 10-90%[8,9]. The prevalence rate of NPSLE among our patients was 14.2%. Medhat *et al*[10] reported the prevalence rate of NPSLE in Egyptian patients was 33.5%. While in another study done in Iran by Haghighi et *al*[11] NPSLE was reported in 11.3%. Moreover, another study conducted by Shamaila[12] in Pakistan reported NPSLE in 84% of lupus patients. This variation in different reports could be explained by different demographic data and the criteria that used to recognize these events.

In this study, the most common neuropsychiatric lupus events was seizure followed by CVA while headache, acute confusional status and transverse myelitis were less frequently recorded. The most noticed psychiatric manifestations were psychosis followed by depression. Peripheral neuropathy was documented in one case in this study. Alsomaily et *al*[6] who conducted their study in southern region of Saudi Arabia reported headache then followed by CVA as the most encountered neuropsychiatric events. However, a study done in China by Zhang *et al*[13] found seizures followed by acute confusional state then CVA as the most prominent symptoms. Depression disorder was not seen frequently among our patients and this could be related to defect in the screening methods of patients presented to the clinic of rheumatology. Interestingly, a multi- center study performed in Saudi Arabia showed a high prevalence of depression in lupus patients[14]. The diversity between different studies in the most frequent NPSLE is related to many contributors including; different approaches followed by rheumatologists to screen for these symptoms. Several challenges are faced by practitioners to differentiate between primary symptoms from lupus related manifestations[15]. Additionally, the pathological aspects responsible for occurrence of NPSLE are dependent mainly on either inflammatory process or thrombotic or both[16,17]. The relationship between aPL and NPSLE was identified in some studies[18], however this association was not significant in our patients diagnosed with NPSLE. The association between aPL and NPSLE is not clear as NPSLE are very heterogeneous manifestations. The aPL has been associated with development of some NPSLE like CVA but not all other NPSLE[19]. Lack of significant association between aPL and NPSLE in our study could be related to small sample size or could be related to diffuse immune - mediated inflammatory process causing damage of different organs including nervous tissues[20].

The radiological findings in the MRI brain of the patients diagnosed with NPSLE are highly variable. Among our patients, the most prominent radiological abnormality noticed is the abnormal high signal intensity followed by picture of stroke then vasculitis. Our findings are similar to the abnormalities noticed in a study performed in Japan which showed hyper-signal intensity is the most obvious lesion[21].

This study had several limitations. Firstly, the sample size was small and it would have been advisable if it was done as a multi-center study to include a larger number of patients. Secondly, it was a retrospective study so, the possibility of the selection bias affecting the results cannot be ruled out. Thirdly, some variables were missed such as details about the treatment, treatment's duration and the outcomes. To confirm these findings, a large sample size study, multicenter and prospective study should be conducted.

Conclusions

NPSLE are seen in 14.18% of Saudi patients diagnosed with lupus. NPSLE are more obviously reported among female patients. The most common NPSLE attacks are seizure followed by CVA while psychosis was the most obvious psychiatric syndrome. The study found no association between anti ds-DNA antibodies and aPL and NPSLE. MRI brain can be helpful and abnormal high signal intensity is predominantly noticed.

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