

# Anti-Ribosomal-P Antibody Association with Neuropsychiatric Lupus in Sudanese Patients Attending Rheumatology Clinic in Omdurman Military Hospital

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**Purpose:** To assess and establish the relationship between neuropsychiatric systemic lupus erythematosus (NPSLE) involvement and serological biomarkers like antiribosomal-P antibodies.

**Patients and Methods:** This is an analytical cross-sectional hospital-based study conducted on patients attending Omdurman Military Hospital from July 2019 to December 2019. A total of 90 patients were enrolled, 30 of whom had NPSLE compared with 60 SLE patients without NPSLE. SLE diagnosis was established based on the revised SLICC criteria (presence of at least 4 criteria) for SLE classification, with neuropsychiatric manifestations defined based on the ACR nomenclature. The immunological examination results have been performed by (ELISA immune-enzymatic method, immunofluorescence, and Western immunoblotting test). SPSS v 21.0 software was utilised for data analysis.

**Results:** NPSLE patients exhibited +ve ANA in 96.7% vs 75% in non-NPSLE (P-value = 0.008), antiribosomal-P antibodies (46.7% vs 20%; P-value = 0.0001), anti-nucleosome antibodies (26.7% vs 5%; P-value = 0.005), and anti-histones antibodies (40% vs 20%; P-value = 0.04). ANA antibodies were significantly associated with neurological manifestations as ANA antibodies were common in epilepsy (n = 9; 91%) and stroke (n = 8; 27.6%) (P-value < 0.001).

**Conclusion:** Neuropsychiatric manifestation of systemic lupus erythematosus exhibits variable clinical manifestations. Neuropsychiatric manifestations of SLE are strongly associated with the anti-ribosomal P antibody presence and can be employed as a powerful diagnostic tool.

**Keywords:** SLE, neuropsychiatric, ANA, anti-ribosomal-P antibodies, anti-histone antibodies

## Introduction

One of the highest globally prevalent autoimmune diseases is systemic lupus erythematosus (SLE), which predominantly afflicts females of childbearing age, leading to significant morbidity burden and mortality. A primary concern regarding SLE is its fluctuating course and unpredictable flares leading to a relapse-remitting pattern. The principal aetiology behind SLE development is unknown; however, it is possibly multifactorial, including environmental factors, medications and hormonal and other factors collectively causing dysregulation of the immune system and consequently leading to autoantibodies production and precipitation in almost all body organs.<sup>1</sup> The clinical presentation complexity of SLE makes its recognition and diagnosis challenging to define, mandating the utilisation of classification criteria to identify and differentiate relatively akin patients' groups.<sup>2</sup> Hence, the American College of Rheumatology (ACR) SLE

classification criteria and its revised version in the late nineties were globally applied and consequently improved our insight about the disease.<sup>3</sup> This improvement was evident in routine clinical practice by demonstrating several explicit skin manifestations and utilising immunological tests like complement levels (C3 & C4) and anti-B2Glycoprotein I (Anti-B2GPI) antibodies. Furthermore, mucocutaneous and several other organ involvements were better understood, warranting modifications to the classification criteria employed.<sup>4</sup> Consequently, the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria 2012 was launched, addressing several considerations.<sup>5</sup> The newer criteria included mucocutaneous and neuropsychiatric manifestations, extra antiphospholipid antibody tests, hypocomplementemia, and refinement of criteria definitions. SLE diagnosis is established by the presence of at least one immunologic and clinical criteria or biopsy-proven nephritis consistent with SLE and the presence of antinuclear antibodies (ANA) or anti-double-stranded DNA (dsDNA) antibodies. When comparing both criteria, the SLICC criteria had lower specificity but raised sensitivity than the ACR criteria.<sup>5,6</sup>

Furthermore, in 2019, the EULAR/ACR classification criteria for SLE were introduced. It included ten domains, each weighted 2 to 10; seven clinical (Cutaneous, Serosal, Haematologic, Renal Neuropsychiatric, Musculoskeletal, and Constitutional) as well as three immunologic (SLE-specific antibodies, antiphospholipid antibodies, and complement proteins). A positive ANA is a requisite entry criterion and cumulative weighted criterion subsequently. Upon assessing the three criteria, the EULAR/ACR criteria achieved the highest specificity and sensitivity of 93.4% and 96.1% as compared to 93% and 82.8% and 83.7% and 96.7% by revised ACR and SLICC criteria, respectively.<sup>3</sup>

Furthermore, neuropsychiatric manifestations could be the presenting symptom of systemic lupus erythematosus.<sup>7</sup> These manifestations range from mild to severe, requiring high clinical suspicion to recognise and diagnose early.<sup>7</sup> The common presentations include anxiety, mood disorders, cognitive deterioration and others. However, the unpredictable patterns in the presentation of NPSLE and the frequent encounters with atypical or delayed characteristic laboratory findings make NPSLE very challenging even in a current era of enormous technological advancement.<sup>8</sup> Thus, recognising a biomarker to aid early diagnosis is crucial as it will impact outcomes and reduce comorbidities associated with such a devastating disease.<sup>9</sup> In 1985, anti-ribosomal P antibodies were recognised, with ongoing studies emphasising their prognostic value and implications. These autoantibodies occur exclusively in SLE.<sup>9</sup> However, several studies have highlighted a potential direct association between anti-ribosomal P antibodies and NPSLE, although no clear-cut decision was concluded.<sup>8</sup> In this current study, we emphasise the correlation between neuropsychiatric systemic lupus erythematosus (NPSLE) involvement and serological biomarkers like antiribosomal-P antibodies.

## Materials and Methods

### Participants

This is an analytical case-control hospital-based study conducted in the rheumatology clinic at Omdurman Military Hospital in Sudan from July 2019 to December 2019. We included all patients with systemic lupus erythematosus who demonstrated neuropsychiatric manifestations and fulfilled the ACR (NPSLE) criteria. In contrast, our control group included SLE patients with no NP manifestations fulfilling a minimum of 4 criteria of the revised ACR classification for SLE. Patients with neuropsychiatric disorders other than SLE and patients with other coexistent connective tissue diseases were excluded. Both case and control group patients were randomly selected and matched by age, sex, and level of education.

### Ethical Consideration

Ethical approval was obtained from Sudan Medical Specialisation Board (SMSB) under approval no. QA-9176. Approval acceptance to the hospital authority was given. Patients were counselled about the purpose of the study. The study complied with the tenets of the Declaration of Helsinki. Written and verbal consent were obtained from patients. Data was used anonymously using identity numbers instead of names to protect the patient's identity and kept securely and in a separate file. No reference to any individual participant was made in the study reports. Subject identities were known only by the study staff.

## Data Collection Tools and Methods

We used an interview questionnaire as a data collection tool; data from files and records of patients were obtained, and a complete medical history and clinical examination were conducted on all patients. SLE diagnosis was established upon the presence of at least 4 of the 11 revised SLICC criteria.<sup>5</sup> The nomenclature of ACR was used to define neuropsychiatric manifestations. Standard laboratory examinations were performed, and the immunological examination was performed by (ELISA immune-enzymatic method, immunofluorescence, and Western immunoblotting test).

## Data Analysis

The collected data was entered and encoded in SPSS (SPSS v.21.0) datasheet. The data were analysed and presented in tables and figures. Chi-square test/Fisher exact test was used to assess the associations between continuous and categorical data, with a P-value considered significant if less than 0.05. Adjusted P-value ( $P_{adj}$ ) was also calculated via the Chow–Denning test as required.

## Results

### Characteristics of the Patients

The overall recruitment in this study included 90 SLE patients, 30 patients with neuropsychiatric SLE (NPSLE) and 60 non-neuropsychiatric SLE (non-NPSLE). NPSLE patients' mean age was  $36.6 \pm 12.3$  years, and non-NPSLE was  $37.3 \pm 12.5$  years. All the NPSLE patients ( $n = 30$ ; 100%) and 55 (91.7%) of non-NPSLE were females (Table 1).

The mean SLE duration was  $4.7 \pm 3.3$  years, and 19 (64%) had an SLE duration of fewer than five years. Also, the mean NPSLE duration was  $3.4 \pm 2.6$  years; 22 (73.3%) patients had an NPSLE duration of fewer than five years, and the remaining 8 (27%) patients had a duration of 5–10 years.

### Clinical Presentations

Cutaneous clinical presentations, hair loss (80% vs 56.7%; P-value = 0.024) and oral ulcer (73.3% vs 46.7%; P-value = 0.014) were significantly common among NPSLE patients more than non-NPSLE patients (Table 2).

### Neuropsychiatric Manifestations

Headache ( $n = 26$ ; 86.7%) and confusion ( $n = 16$ ; 53.3%) were the major CNS-related clinical presentations, and excessive anxiety was the main psychiatric-related presentation in 14 (46.7%) patients. The Mini-Mental State Examination scale (MMSE) was used to assess cognitive function; 18 (60%) patients were normal, while 12 (40%) were borderline. The clinical examinations showed that NPSLE patients more likely to have cranial nerve palsy (13.3% vs 1.7%; P-value = 0.041), limb weakness (33.3% vs 0%; P-value = 0.000), sensory loss (23.3% vs 1.7%; P-value = 0.002) and abnormal gait (20% vs 0%; P-value = 0.001) more than non-NPSLE patients (Table 3) patients had borderline findings and 12 (20%) patients were normal (Table 2).

**Table 1** The Sociodemographic Characteristics of NPSLE and Non-NPSLE Groups

Variable		NPSLE (N=30)	SLE (N=60)	P-value
<b>Age (Year)</b>	<b>Mean <math>\pm</math> SD</b>	<b>36.6<math>\pm</math>12.3</b>	<b>37.3<math>\pm</math>12.5</b>	0.608
	<20	2 (6.7%)	3 (5.0%)	
	20–40	18 (60.0%)	30 (50.0%)	
	41–60	10 (33.3%)	25 (41.7%)	
	>60	0 (0.0%)	2 (3.3%)	
<b>Gender</b>	Female	30 (100.0%)	55 (91.7%)	0.124
	Male	0 (0.0%)	5 (8.3%)	

**Table 2** The Clinical Presentations of NPSLE and Non-NPSLE Groups

		<b>NPSLE (N=30)</b>	<b>SLE (N=60)</b>	<b>P-value</b>
<b>SBP; Median (mini-max)</b>		120 (100–170)	120 (100–150)	0.646
<b>DBP; Median (mini-max)</b>		80 (60–110)	80 (60–100)	0.882
<b>Fever</b>		22 (73.3%)	40 (66.7%)	0.347
<b>Skin rash</b>	Malar	11 (36.7%)	21 (35.0%)	0.628
	Discoid	4 (13.3%)	8 (13.3%)	
	Photosensitivity	4 (13.3%)	14 (23.3%)	
	All	2 (6.7%)	1 (1.7%)	
<b>Hair loss</b>		24 (80.0%)	34 (56.7%)	0.024*
<b>Oral ulcer</b>		22 (73.3%)	28 (46.7%)	0.014*
<b>Enlarge lymph nodes</b>		0 (0.0%)	1 (1.7%)	0.667
<b>Pericardial rub</b>		0 (0.0%)	2 (3.3%)	0.442
<b>Abnormal heart sound</b>		2 (6.7%)	2 (3.3%)	0.407
<b>Pleural rub</b>		1 (3.3%)	4 (6.7%)	0.457
<b>Pleural effusion</b>		1 (3.3%)	8 (13.3%)	0.130
<b>Cranial nerve palsy</b>		4 (13.3%)	1 (1.7%)	0.041*
<b>Limb weakness</b>		10 (33.3%)	0 (0.0%)	0.001*^
<b>Weakness with repetitive testing</b>		1 (3.3%)	0 (0.0%)	0.333
<b>Sensory loss</b>		7 (23.3%)	1 (1.7%)	0.002*^
<b>Abnormal gait</b>		6 (20.0%)	0 (0.0%)	0.001*^

Notes: \*P-value is sig (<0.05). ^Adjusted P-value <0.05.

**Table 3** The Laboratory Investigations of NPSLE and Non-NPSLE Groups

<b>Investigation</b>		<b>NPSLE (N=30)</b>	<b>SLE (N=60)</b>	<b>P-value</b>
<b>Hemoglobin (g/dl);</b>	<b>M±SD</b>	11.4±2	13.5±1.6	0.02*
	<10	11 (36.7%)	9 (15.0%)	
	≥10	19 (63.3%)	51 (85.0%)	
<b>Leucocyte (c/Cumm);</b>	<b>M±SD</b>	9.7±3.5	7±3.1	0.012*
	<8000	14 (46.7%)	44 (73.3%)	
	≥8000	16 (53.3%)	16 (26.7%)	
<b>Lymphocyte count</b>	<b>M±SD</b>	2.4±0.9	2.1±0.7	0.137
<b>Platelets (10<sup>3</sup> c/Cumm)</b>	<140	6 (20.0%)	1 (1.7%)	0.005*
	≥140	24 (80.0%)	59 (98.3%)	
<b>CRP (positive)</b>		13 (43.3%)	30 (50.0%)	0.355

(Continued)

Table 3 (Continued).

Investigation		NPSLE (N=30)	SLE (N=60)	P-value
ESR (mm/hr);	<b>M±SD</b>	44.8±24	49.3±22.1	
	<30	11 (36.7%)	16 (26.7%)	0.087
	≥30	19 (63.3%)	44 (73.3%)	
C3	<b>M±SD</b>	60.7±26.1	62.2±22	
	<80	16 (69.6%)	26 (63.4%)	0.415
	80–160	7 (30.4%)	15 (36.6%)	
C4	<b>M±SD</b>	33.6±14.1	25.5±13.1	
	<16	3 (13.0%)	10 (24.4%)	0.528
	16–48	19 (82.6%)	30 (73.2%)	
	>48	1 (4.3%)	1 (2.4%)	
Blood glucose (mg/dl)	<b>M±SD</b>	116.3±33.6	117.1±18.3	
	<140	25 (83.3%)	57 (95.0%)	0.078
	≥140	5 (16.7%)	3 (5.0%)	
Albumin (g/dl)	<b>M±SD</b>	3.5±0.6	4.6±0.5	
	<3.5	11 (36.7%)	4 (11.6%)	0.008*
	≥3.5	19 (63.3%)	53 (88.3%)	
Urea	<b>M±SD</b>	32.7±14.2	30.7±12.3	
	<50	28 (93.3%)	58 (96.7%)	0.407
	≥50	2 (6.7%)	2 (3.3%)	
Creatinine (mg/dl)	<b>M±SD</b>	0.9±0.2	0.7±0.4	
	<1.5	27 (90.0%)	58 (96.7%)	0.204
	≥1.5	3 (10.0%)	2 (3.3%)	
Proteinuria		4 (13.3%)	9 (15.0%)	0.552
Urine cellular cast		2 (6.7%)	3 (5.0%)	0.543

Note: \*P-value is sig (<0.05).

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; C3/C4, complement.

## Laboratory Investigations

Hematological laboratory investigations showed that NSPLE patients were more prone to anemia than non-NSPLE patients (hemoglobin <10 g/dl) (36.7% vs 15%; P-value = 0.02) with hemoglobin means (11.4 ± 2 g/dl vs 13.5 ± 1.6 g/dl). NSPLE patients were more predisposed to have leukocytosis than non-NSPLE patients (leucocytes <8000 cell/Cumm) (53.3% vs 26.7%; P-value = 0.012) with leucocytes count means (9.7 ± 3.5 cell/Cumm vs 7 ± 3.1 cell/Cumm). In addition, thrombocytopenias were observed more in NSPLE patients than non-NSPLE patients (platelets <148\*10<sup>3</sup> cell/mm) (20% vs 1.7%; P-value = 0.005) with platelets count means (210\*10<sup>3</sup> ± 79.5 cell/mm vs 279\*10<sup>3</sup> ± 65 cell/mm). Inflammatory investigations included CRP (P-value = 0.335), ESR (P-value = 0.087), C3 complement levels (P-value = 0.415) and C4 complement levels (P-value = 0.528) were not significantly varying between both groups. Moreover, hypoalbuminemia was common among NPSLE than non-NPSLE patients (36.7% vs 11.6%;

P-value = 0.008). Nevertheless, blood glucose levels (P-value = 0.078), urea levels (P-value = 0.407), creatinine levels (P-value = 0.204), proteinuria (P-value = 0.552) and urine cellular cast (P-value = 0.543); all showing no significant differences between the NPSLE and non-NPSLE groups (Table 3).

Furthermore, ANA titres were more positive among NPSLE patients than in the non-NPSLE group (96.7% vs 75%; P-value = 0.008). Similarly, anti-ribosomal-p antibodies, anti-histones antibodies and anti-nucleosome antibodies were more positive among NPSLE group than non-NPSLE group (46.7% vs 20%; P-value = 0.001), (26.7% vs 5%; P-value = 0.005), (40% vs 20%; P-value = 0.04), respectively. Other ANA profile antibodies were not significantly varying between NPSLE and the control groups (Table 4). Additionally, anti-lupus antibodies (26.7% vs 1.7%; P-value = 0.001), anticoagulant antibodies (30% vs 3.3%; P-value = 0.001), and anticardiolipin antibodies (26.7% vs 0%; P-value = 0.001) were significantly more observed in NPSLE group than the non-NPSLE group.

ANA profile distribution regarding the neurological manifestations according to ACR criteria of NPSLE is shown in Table 5, in which ANA antibodies were significantly associated with neurological manifestations as ANA antibodies were common among epilepsy (n = 9; 91%) and stroke (n = 8; 27.6%) manifestations (P-value = 0.001). In addition, other antibodies in the ANA profile were not significantly differed between neurological manifestations (P-value >0.05).

**Table 4** The Other ANA Profile Antibodies among NPSLE and Non-NPSLE Groups

ANA Profile Antibodies	NPSLE (N=30)	SLE (N=60)	P-value
<b>ANA</b>	19 (96.7%)	45 (75%)	0.008*
<b>Anti-Sm Abs</b>	13 (43.3%)	22 (36.7%)	0.350
<b>Anti-dsDNA</b>	13 (43.3%)	19 (31.7%)	0.195
<b>Anti-histone</b>	12 (40%)	12 (20%)	0.04*
<b>Anti-nucleosome</b>	8 (26.7%)	3 (5%)	0.005* <sup>^</sup>
<b>Anti-ribosomal p</b>	14 (46.7%)	12 (20%)	0.001* <sup>^</sup>
<b>Anti RO52 Abs</b>	8 (26.7%)	17 (28.3%)	0.538
<b>Anti SS-B Abs</b>	9 (30.0%)	10 (16.7%)	0.119
<b>Anti PNCA Abs</b>	0 (0.0%)	2 (3.3%)	0.442
<b>Anti-Centromere B Abs</b>	2 (6.7%)	2 (3.3%)	0.407
<b>Anti SS-A Abs</b>	14 (46.7%)	18 (30.0%)	0.093

**Notes:** \*P-value is sig (<0.05), <sup>^</sup>Adjusted P-value <0.05.

**Abbreviations:** Anti-dsDNA, anti-double stranded DNA; Anti-CCP, anti-cyclic citrullinated peptide antibody; Anti-RNP, anti-ribonucleoprotein antibody; ANA, antinuclear antibody; AMA, anti-mitochondrial antibody, anticentromere B antibodies; SCL, antiscleroderma 70 antibodies; SMD1, Smith antibodies; anti-SS-A/Ro 60 KD, Sjögren anti-SS-A; anti-SS-A/Ro 52 KD, Sjögren anti-SS-B; ANCA, antineutrophil cytoplasm antibodies.

**Table 5** Distribution of ANA Profile Regard to the Neuropsychiatric Manifestations According to ACR Criteria of NPSLE

NPSLE	ANA	ASmAb	dsDNA	ARO54	ANsome	ARpAb	SS-B	AHA	Cent-B	SS-A
<b>Psychosis</b>	3 (10.30%)	2 (15.40%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	2 (18.20%)	1 (11.10%)	2 (16.70%)	0 (0.00%)	1 (7.10%)
<b>Anxiety</b>	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
<b>Stroke</b>	8 (27.60%)	4 (30.80%)	3 (23.10%)	4 (50.00%)	1 (12.50%)	2 (18.20%)	2 (22.20%)	1 (8.30%)	0 (0.00%)	4 (28.60%)
<b>Epilepsy</b>	9 (31.00%)	6 (46.20%)	6 (46.20%)	2 (25.00%)	2 (25.00%)	6 (54.50%)	5 (55.60%)	5 (41.70%)	1 (50.00%)	6 (42.90%)
<b>Headache</b>	4 (13.80%)	0 (0.00%)	2 (15.40%)	2 (25.00%)	1 (12.50%)	0 (0.00%)	1 (11.10%)	1 (8.30%)	0 (0.00%)	2 (14.30%)
<b>Demyelinating</b>	1 (3.40%)	1 (7.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (9.10%)	0 (0.00%)	1 (8.30%)	1 (50.00%)	0 (0.00%)
<b>MG</b>	1 (3.40%)	0 (0.00%)	1 (7.70%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
<b>Cerebrovascular</b>	1 (3.40%)	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (8.30%)	0 (0.00%)	0 (0.00%)
<b>Mood Disorders</b>	2 (6.90%)	0 (0.00%)	1 (7.70%)	0 (0.00%)	1 (12.50%)	0 (0.00%)	0 (0.00%)	1 (8.30%)	0 (0.00%)	1 (7.10%)
<b>P-value</b>	0.000*	0.202	0.423	0.569	0.456	0.149	0.7	0.331	0.074	0.733

**Note:** \*P-value is sig (<0.05).

## Discussion

Concomitant neuropsychiatric symptoms substantially impact the severity of SLE and the patient's quality of life, and the prognosis is relatively poor. Neuropsychiatric systemic lupus erythematosus symptoms may range from mild diffuse ones to acute life-threatening events. While the chief mechanism behind NPSLE is still primarily unravelled, various hypotheses have been identified, for instance, neurotoxicity and vasculopathy caused by antibodies and cytokines.<sup>10</sup> The current study is aimed to evaluate and correlate anti-ribosomal P antibodies among the Sudanese population demonstrating NPSLE manifestations.

The present study showed that all the patients with NPSLE were females ( $n = 30$ ; 100), with a mean age of  $36.6 \pm 12.3$  years. These findings are comparable to several previous studies; Mengdi et al found that 93% were females with a mean age of 33.<sup>11</sup> Also, Wei et al reported females in 90% of NPSLE with a mean age of  $35.2 \pm 13.7$ .<sup>7</sup> All these findings confirmed that NPSLE was common in young aged females.

In our study, 73.3% of the patients with NPSLE manifestations developed NP events as early as five years after SLE onset, similar to prior findings by Jönsen et al, Bertias et al, and Bernatsky et al.<sup>12–14</sup> This is presumably due to the insufficient control of the disease activity in the early stages of treatment. In our current study, 30 SLE patients demonstrated neuropsychiatric presentations, primarily epilepsy in 9 (30%) patients, stroke in 8 (26.7%) patients, and headache in 4 (13.3%) patients. Wei et al reported comparable outcomes, with epilepsy being the most common NP manifestation in 47% of NPSLE patients, followed by headache and psychosis.<sup>7</sup> Similarly, Zhou et al illustrated that epilepsy was the most frequent presentation in NPSLE patients seen in 35%.<sup>15</sup> Nevertheless, an Italian study by Antonella et al reported different manifestations in patients with NPSLE: cognitive impairment, mood disorders and stroke (52%, 27% and 24%), respectively.<sup>16</sup> However, among the Sudanese NPSLE patients, epilepsy was the most frequent NP presentation.

Additionally, the current study demonstrated that patients with NPSLE significantly exhibited more severe cutaneous presentation (hair loss and oral ulceration), chest and cardiac presentations (breathing difficulty and rapid or irregular heartbeat), and central and peripheral nervous system-related clinical presentations, as well as psychiatric related clinical presentations. Nevertheless, on assessing adjusted P-value for clinical presentations, neurological symptoms were significantly ( $\text{adj}P\text{-value} < 0.05$ ) correlated with NPSLE. Although NPSLE diagnosis is not associated with a particular blood test, we observed that NPSLE patients tend to have anaemia, leucocytosis, thrombocytopenia, and hypoalbuminemia non-NPSLE patients ( $P < 0.05$ ), with similar results reported by Maria et al.<sup>16</sup>

Our present study showed that ANA was more positive among NPSLE patients than non-NPSLE patients (96.7% vs 75%;  $P\text{-value} = 0.008$ ). These results were in agreement with studies of Wei et al in China.<sup>7</sup> Although anti-nucleosome antibodies are probably better for predicting flares in quiescent Lupus, we observed in this study that anti-nucleosome antibodies were present among the NPSLE more than in the non-NPSLE group (26.7% vs 5%;  $P\text{-value} = 0.005$ ), and correspondingly  $\text{adj}P\text{-value}$  was  $< 0.05$ . These findings were similar to Dina et al, which might be explained by the recognised significant direct relationship between lupus disease severity and the level of anti-nucleosome antibodies.<sup>17,18</sup> Significantly, anti-histones antibodies were more positive among the NPSLE group than in the non-NPSLE group (40% vs 20%;  $P\text{-value} = 0.04$ ). Likewise, Parodi et al reported that anti-histones antibodies correlated with Alzheimer's, dementia and other neurological diseases.<sup>19</sup> Also, Xiao-Yun et al noticed that the anti-histone antibodies are significantly present in approximately 50% of patients with NPSLE compared with SLE.<sup>20</sup>

Furthermore, excitingly anti-ribosomal-p antibodies were positive among patients with NPSLE than non-NPSLE patients (46.7% vs 20%;  $P\text{-value} = 0.001$ ) in the current study, and significance level was further confirmed through  $\text{adj}P\text{-value}$  of  $< 0.05$ . These results were consistent with several studies reporting a direct correlation between neuropsychiatric manifestations in SLE and anti-ribosomal-p antibodies.<sup>8,21,22</sup>

Regard to the antiphospholipid antibodies (APA) profile, anti-lupus antibodies (26.7% vs 1.7%;  $P\text{-value} = 0.001$ ), anticoagulant antibodies (30% vs 3.3%;  $P\text{-value} = 0.001$ ), and anticardiolipin antibodies (26.7% vs 0%;  $P\text{-value} = 0.000$ ) were substantially noted in the NPSLE group than the non-NPSLE group. Comparably, Sciascia et al reported that antiphospholipid antibodies (Anti-Cardiolipin, Lupus anticoagulant, and anti- $\beta$ 2GP) were commonly seen in NPSLE patients.<sup>23</sup> Furthermore, De Groot et al observed that concurrent prevalence of antiphospholipid syndrome (APS) and SLE

is associated with a raised prothrombotic risk linked to anti- $\beta$ 2-glycoprotein presence.<sup>24</sup> Additionally, some studies have pointed out that NPSLE is more prevalent among APS patients.<sup>25</sup> Lastly, testing for APA in SLE patients is paramount since it is present in around 40% of these patients, and it has been linked with a raised likelihood of a future CNS manifestation.<sup>26</sup>

## Conclusion

Neuropsychiatric manifestation of systemic lupus erythematosus exhibits variable clinical manifestations; epilepsy is the common neuropsychiatric manifestation. Anti-ribosomal P antibodies are strongly correlated to SLE neuropsychiatric manifestations; thus, it can be employed as a powerful diagnostic tool. In addition, anti-phospholipid, anti-histone, and anti-nucleosome antibodies are linked to a certain extent with neuropsychiatric manifestations. ANA antibodies were significantly associated with neurological manifestations, particularly epilepsy. Other antibodies in the ANA profile were not significantly differed between neurological manifestations.

## Data Sharing Statement

The authors declare that all the data supporting the findings of this study are available within the article.

## Acknowledgments

Omdurman Military Hospital medical staff and admission office.

## Disclosure

All authors report no conflicts of interest in this work.

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