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Pattern and prevalence of neuropsychiatric lupus: a retrospective study from a tertiary level hospital in Bangladesh

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Abstract

Background: Neuropsychiatric systemic lupus erythematosus (NPSLE) is well known for its varying presentations and poor outcomes, but little is evident about its distribution and characteristics among the Bangladeshi population. This study aimed to assess the pattern and prevalence of neuropsychiatric symptoms in female systemic lupus erythematosus (SLE) patients of Bangladesh. A retrospective study was conducted at a tertiary care hospital in Dhaka, Bangladesh, between January and December 2018. One hundred female SLE patients were included in the study purposively. Data were collected on sociodemographic and clinical characteristics of diagnosed SLE cases visiting the SLE clinic and indoor medicine department. Neuropsychiatric (NP) syndromes were defined according to the widely accepted American College of Rheumatology (ACR) nomenclature and case definitions.

Results: A total of 244 NP events were identified in fifty-five patients. Headache was the most frequent symptom (55%), followed by cognitive dysfunction (50%), anxiety (49%), psychosis (43%), seizure (23%), depression (17%), and cerebrovascular disease (ischemic type, 7%). The NP manifestations were more prevalent among urban residents (58.2%), younger patients (41.8%), and patients with graduate-level education (34.5%). Besides, young age at diagnosis ($p = 0.038$), Raynaud's phenomenon ($p = 0.015$), other organ involvement ($p < 0.001$), and time of NPSLE development ($p < 0.001$) were found to be significantly associated with the development of these manifestations.

Conclusion: NP damage is prevalent among Bangladeshi female SLE patients (55%) with headache and cognitive dysfunction being the most common symptoms. Routine screening for neuropsychiatric symptoms among suspected SLE cases and further evaluation with a larger population are warranted.

Keywords: Neuropsychiatric systemic lupus erythematosus, ACR criteria, Pattern, Prevalence, Bangladesh

Background

Systemic lupus erythematosus (SLE or lupus) is an idiopathic relapsing-remitting autoimmune condition affecting multiple systems of the body. At any given time, about 5 million people suffer from one form of lupus worldwide [1]. Females of childbearing age (between 15 and 45 years) are its prime targets with an additional predilection for Afro-Caribbean, Asian, North American, and Hispanic origins [2, 3]. Among the various systems affected by SLE, nervous system involvement is critically challenging in terms of diagnosis and treatment.

Neuropsychiatric manifestations of SLE (NPSLE) comprise of a broad heterogeneous spectrum of neurologic and psychiatric features involving both central and peripheral nervous systems. Ranging from stroke, seizure, psychosis to headache, anxiety, and cognitive dysfunction, 19 NP syndromes have been well defined by a standardized nomenclature system of American College of

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Rheumatology (ACR) (Table 1) [4]. Despite such recognition, it is probably the least understood but one of the most frequently occurring manifestations of SLE. Globally, statistics indicate that neuropsychiatric lupus affects from 11 to 81% of adult SLE patients and up to 95% of pediatric cases at any time during the course of the disease [5, 6]. The great variation in prevalence in different studies is attributable to differences in ethnicity, geographical distribution, selection bias, screening methods, the nomenclature used for defining the event, lack of specificity of NP symptoms, and whether or not the event is attributed to SLE [5, 7, 8]. Neuropsychiatric lupus may present as the first indication of SLE in cases who exhibit no signs of disease activity in other organ systems and is also considered a poor prognostic factor and a leading cause of death in SLE patients [9, 10]. Moreover, the condition often goes underdiagnosed due to lack of a single diagnostic tool (a radiologic or biological marker) and thereby reduces the quality of life [11, 12].

In developing countries like Bangladesh, very few studies on SLE have been conducted focusing on other systemic involvements [13–15]. Thereby, data on prevalence and characteristics of neuropsychiatric lupus in the Bangladeshi population are almost non-existent in the literature which make misdiagnosis and maltreatment of such cases even more inevitable. Furthermore, if left untreated, NPSLE invariably poses life-threatening impacts on the sufferers by disrupting all vital aspects of life and even causes death. Hence, early recognition and treatment of these symptoms are not just of great significance but mandatory in clinical practice, especially in resource-limited settings. Therefore, this study aimed to determine the pattern and prevalence of specific neuropsychiatric manifestations and their possible associations with clinical and sociodemographic characteristics among SLE patients in Bangladesh.

Table 1 Neuropsychiatric syndromes in SLE patients according to the American College of Rheumatology nomenclature and case definitions [4]

Central nervous system	*Peripheral nervous system*
Aseptic meningitis	Acute inflammatory demyelinating polyradiculoneuropathy
Cerebrovascular disease	Autonomic disease
Demyelinating syndrome	Mononeuropathy (single/multiplex)
Headache	Myasthenia gravis
Movement disorder (chorea)	Neuropathy, cranial
Myelopathy	Plexopathy
Seizure disorder	Polyneuropathy
Acute confusional state	
Anxiety disorder	
Cognitive dysfunction	
Mood disorder	
Psychosis	

SLE systemic lupus erythematosus

Methods

This retrospective study included 100 previously diagnosed female SLE patients visiting the SLE clinic and Inpatient Medicine Department of the tertiary care hospital, Bangladesh, between January and December 2018. Due to the female predominant nature of lupus, all cases were purposively selected from the same gender for this study. All participants were Bangladeshi in origin (aged between 16 and 46 years) and fulfilled at least four of the ACR criteria for SLE classification [16]. Adolescent cases were included as neurological involvement pose greater damage and higher prevalence among pediatric group of SLE patients [6]. Exclusion criteria involved pregnancy, severe illness, infections, thyroid disorders, previously diagnosed epilepsy, other known neurological and psychiatric conditions, and coexistent connective tissue disorders. The study protocol was approved by the Ethical Review Committee of DMCH (memo no. MEU-DMC/ECC/2018/16). After ensuring complete anonymity and no disclosure of the patients' personal information, all respondents participated voluntarily and provided written informed consent before the study commencement.

The diagnoses of NP manifestations were based on overall clinical impression following history, physical examination, review of medical records, and neuropsychological measures. Data were collected on sociodemographic characteristics and disease-related factors using face-to-face interview with a structured questionnaire. The diagnosis of NPSLE was confirmed with the aid of a rheumatologist. All past and current NP events experienced by the participants were included and classified according to the standardized nomenclature case definitions of ACR [4]. In this sample, only seven of the 19 ACR NP manifestations were studied, namely headache, cerebrovascular disease, seizure, psychosis, anxiety, depression, and cognitive impairment. Headache, cerebrovascular disease, and seizure were determined using the SLE disease activity index (SLEDAI) score. It is a validated model for evaluating the disease activity of lupus prepared by experienced clinicians' global assessments [17]. Assessment of the psychiatric symptoms (anxiety, psychosis, and depression) was based on clinical impression and Adult Psychiatric Morbidity Questionnaire (APMQ) score. The APMQ was utilized as a screening instrument to characterize symptoms of psychosis and common mental disorders (depression, anxiety, and somatoform conditions) [18]. Cognitive impairment was evaluated using the Mini-Mental State Examination (MMSE) score which is often used to indicate the presence of cognitive dysfunction by testing the patient's

orientation, attention, memory, language, and visual-spatial skills [19]. The individual test results were compared to standard scores to determine the presence of NP manifestations among the cases.

Data were analyzed using SPSS version 23.0. Multiple responses were recorded in case of NPSLE symptoms. Between the NPSLE and non-NPSLE patients, categorical data outcomes (sociodemographic and disease-related factors) were compared using the chi-square test and Fisher's exact test, as appropriate. A p value < 0.05 was considered statistically significant.

Results

In this study, the prevalence of NPSLE was 55%, which means at least one NP manifestation was identified in 55 SLE patients of this sample. Table 2 represents the prevalence of the individual observed NP manifestations in our study. A total of 244 NP events were recorded with headache (55%) being the most frequent symptom, followed by cognitive dysfunction (50%), anxiety (49%), psychosis (43%), seizure (23%), depression (17%), and cerebrovascular disease (ischemic type, 7%). Four symptoms of any combination were most evident (n = 25, 45.5%) with headache, anxiety, and cognitive dysfunction being in majority symptom combinations. The presence of a single symptom and all seven symptoms together were least observed (1.8% each) in this study sample.

The majority of the study participants' current ages were in between 21 and 29 years (n = 42), but there was no significant association with NPSLE symptoms. However, age at diagnosis was statistically significant (p = 0.038) indicating that patients with early onset of disease have greater chances of developing the NP symptoms. On the contrary, level of education, occupation, and residence were not significantly associated with NPSLE (Table 3).

Table 4 shows the relation between disease-related factors and NPSLE development. Here, we can see that 64 SLE patients had Raynaud's phenomenon with almost two third of which (n = 41) suffered from NPSLE, and the association was statistically significant (p = 0.015). Substantial associations were also observed between the development of NP symptoms and other organ involvement (p < 0.001), SLEDAI score at diagnosis (p < 0.001), and time of NPSLE development (p < 0.001). Conversely, though majority of the respondents with disease duration of about 2 to 5 years (43.6%) and no other co-morbid conditions (76.3%) suffered from the NP manifestations, none of these factors had significant associations with NPSLE development.

Table 2 Prevalence of observed NP manifestations among study population

NPSLE	Frequency (n)	Percentage (%)
Headache	55	55.0
Cognitive dysfunction	50	50.0
Anxiety	49	49.0
Psychosis	43	43.0
Seizure	23	23.0
Depression	17	17.0
Cerebrovascular disease	7	7.0

Multiple responses
NP neuropsychiatric, *NPSLE* neuropsychiatric systemic lupus erythematosus

Table 3 Sociodemographic factors of respondents and their association with NPSLE

Factor	Total n = 100	NPSLE n (%)	Non-NPSLE n (%)	p value
Current age (years)				
≤ 20	32	20 (36.4%)	12 (26.7%)	0.461
21–29	42	23 (41.8%)	19 (42.2%)	
30 and above	26	12 (21.8%)	14 (31.1%)	
Age at SLE diagnosis (years)				
≤ 20	52	34 (61.8%)	18 (40%)	**0.038**
21–29	34	17 (30.9%)	17 (37.8%)	
30 and above	14	4 (7.3%)	10 (22.2%)	
Level of education				
Illiterate	7	2 (3.6%)	5 (11.1%)	0.490
Primary	32	17 (30.9%)	15 (33.3%)	
Secondary	29	17 (30.9%)	12 (26.7%)	
Graduation	32	19 (34.5%)	13 (28.9%)	
Occupation				
Student	29	20 (36.4%)	9 (20%)	0.070
Unemployed	6	5 (9.1%)	1 (2.2%)	
Homemaker	32	13 (23.6%)	19 (42.2%)	
Working woman	33	17 (30.9%)	16 (35.6%)	
Residence				
Urban	52	32 (58.2%)	20 (44.4%)	0.171
Rural	48	23 (41.8%)	25 (55.6%)	

p value less than 0.05 is considered statistically significant; NPSLE, neuropsychiatric systemic lupus erythematosus; *Non- NPSLE* patients without neuropsychiatric manifestations of systemic lupus erythematosus, *SLE* systemic lupus erythematosus

Discussion

Neuropsychiatric lupus (NPSLE) is well recognized for its diverse clinical presentations and varied prevalence in different populations [5, 9]. Our study aimed to determine the pattern and prevalence of these manifestations along with their sociodemographic and clinical characteristics among 100 Bangladeshi female SLE patients. Like Audemard-Verger et al. [20], the selection of cases from only one gender in our study is well justified due to the female predominant nature of lupus. With a total

Table 4 Disease-related factors of SLE patients and their association with NPSLE

Factor	Total n = 100	NPSLE n (%)	Non-NPSLE n (%)	*p* value
Disease duration				
Up to 2 years	43	19 (34.5%)	24 (53.3%)	0.158
2–5 years	39	24 (43.6%)	15 (33.3%)	
More than 5 years	18	12 (21.8%)	6 (13.3%)	
Raynaud's phenomenon				
Present	64	41 (74.5%)	23 (51.1%)	**0.015**
Absent	36	14 (25.5%)	22 (48.9%)	
Comorbid conditions				
DM	1	0	1 (2.2%)	0.088
HTN	17	13 (23.6%)	4 (8.9%)	
Absent	82	42 (76.3%)	40 (88.9%)	
Kidney involvement				
Present	29	24 (43.6%)	5 (11.1%)	**< 0.001**
Absent	71	31 (56.4%)	40 (88.9%)	
SLEDAI score at diagnosis				
Low activity (< 10)	81	36 (65.4%)	45 (100%)	**< 0.001**
High activity (> 10)	19	19 (34.6%)	0	
Time of NPSLE development				
Before starting treatment	39	39 (70.9%)	0	**< 0.001**
After starting treatment	16	16 (29.1%)	0	

p value less than 0.05 is considered statistically significant; *NPSLE* neuropsychiatric systemic lupus erythematosus, *Non- NPSLE* patients without neuropsychiatric manifestations of systemic lupus erythematosus, *SLE* systemic lupus erythematosus, *DM* diabetes mellitus, *HTN* hypertension, *SLEDAI* the SLE disease activity index score

of 244 neuropsychiatric events, the prevalence of NPSLE in our study was found to be 55% (55/100 SLE patients) which was similar to the finding of Giovanni et al. [21] and was within the overall range reported previously (11–81%) [5, 6]. Prevalence of NPSLE varies between different studies due to numerous factors such as differences in ethnicity, geographical distribution, study design, patient selection criteria, etc. Headache was the most frequent NP symptom among our respondents (55%) as observed in most previous studies [7, 10, 11, 21–23], and its prevalence was also in line to that of Ainiala et al. [24] and Brey et al. [23]. However, lupus headache is often considered multifactorial and lack of a standard protocol further enhances the perplexity of establishing it entirely to the disease itself or some additional factors (stress, medication, etc.). Lupus patients also have a high prevalence of cognitive dysfunction (17–66%) [23–25] as seen in our cases (50%). Since the evaluation of cognitive impairment among SLE patients is quite challenging and time-consuming with no simple screening tests available for routine use [26], most studies prefer the ACR nomenclature for demonstrating dysfunction in one or more of the eight cognitive domains [4, 24] and attribute the findings to SLE activity in the brain, corticosteroid use, emotional distress, or metabolic disturbances.

Seizures have been invariably evident among SLE patients worldwide and our finding (23%) depicted the same as those of Hajighaemi et al. (26.4%) [11] and Mok et al. (28%) [27]. All kinds of seizures (generalized, tonic-clonic, etc.) can take place any time during SLE either in isolation or association with other neurological conditions [28, 29]. Most of our patients experienced seizures of focal onset in nature. Psychiatric disorders—anxiety, psychosis, and depression—are common among NPSLE patients and vary between 17 and 75% supposedly due to various neuropsychological testing [11]. Although several past studies reported a low prevalence of psychosis [5, 7, 22], our study finding (43%) correlated with the ones from Western India (75%) [30], Thailand (22.3%) [26], and Iran (26.4%) [11] where psychosis was among the most frequently reported symptoms. Cerebrovascular disease was the least common manifestation among our participants (7%) which was consistent with previous reports (2–15%) and the possible pathomechanisms include bleeding, atherosclerosis, hypertension, and coagulopathy [11, 31].

Although associations between sociodemographic factors and NPSLE development are rare in the literature [10, 32], our study findings denoted a difference. The age at which SLE is diagnosed serves as a crucial factor for NPSLE development and worldwide these manifestations are often observed among the pediatric age group of patients [6, 30]. Our study also illustrated a significant association (p = 0.038) between age group at SLE diagnosis and NPSLE development with notably younger SLE patients (below 20 years, 61.8%) manifesting the symptoms more. Since our study aimed to evaluate the association of the age with NPSLE development, it was more convenient to stratify this variable into groups to determine which age range of SLE patients are more prone to suffer from these manifestations. Also, some disease-related or clinical factors have exhibited some degree of association with NPSLE. For instance, Raynaud's phenomenon remained a frequent finding among NPSLE patients, the cause of which remains unknown [33], and like our study (p value = 0.015), Mathieu et al. demonstrated a significant association between the phenomenon and active neuropsychiatric manifestations (p value = 0.02) [34]. Similarly, SLE being a multisystem disorder concomitantly involves renal and nervous systems of its patients and about 40–80% of NPSLE patients suffer from renal disorders [35] as also seen in our study (43.6%). The finding of higher SLEDAI score at diagnosis among our NPSLE patients is not uncommon and rather consistent with previous reports [5, 8] as this disease activity score has often been considered a lone predictor of neuropsychiatric damage. Time of NPSLE development has been considered a significant factor for the condition [36] as about 28–40% of NP symptoms manifest before or around the time of SLE diagnosis in adults [7, 12]. Our study finding also denoted a noteworthy association (p < 0.001); however, our parameter of time frame (before or after starting SLE treatment) varied from the other studies.

Besides showcasing several strong and novel features, the present study had certain limitations. The first being its hospital based nature failed to detect the cases not requiring hospitalization. Similarly, the retrospective design, case selection from a single center, and exclusion of severely ill patients for their inability to participate might not have portrayed the exact prevalence of NPSLE in the population and thereby limited the generalizability of the study. In addition, due to the retrospective nature, some recall bias effect had been present. Also, a small sample size weakened the statistical power of analysis. All in all, to overcome these shortcomings, further studies are warranted with larger sample size, inclusion of multiple centers, and conduction of case-control or cohort study designs, to provide a better association with the factors in question and to comprehend the true picture of the burden of neuropsychiatric lupus among SLE patients in Bangladesh.

Conclusion

In conclusion, NP symptoms are common among the SLE cases of Bangladesh with headache and cognitive dysfunction being the most common features. Young age and more active disease at the time of SLE diagnosis are some of the crucial predictors for NP damage. Clinicians must remain aware of these manifestations during their clinical practice and should routinely screen for neuropsychiatric symptoms among suspected SLE cases presenting with these features, as this will not only ensure early and timely management of the cases but also improve their overall quality of life.

Abbreviations

ACR: American College of Rheumatology; APMQ: Adult Psychiatric Morbidity Questionnaire; BDT: Bangladesh Taka; CVD: Cerebrovascular disease; DM: Diabetes mellitus; DMCH: Dhaka Medical and College Hospital; HTN: Hypertension; MMSE: Mini Mental State Examination; NP: Neuropsychiatric; NPSLE: Neuropsychiatric systemic lupus erythematosus; SD: Standard deviation; SLE: Systemic lupus erythematosus; SLEDAI: Systemic lupus erythematosus disease activity index; SPSS: Statistical Package for Social Sciences; USD: United States dollar

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Authors' contributions

FH conceptualized and collected data for analysis. MDHH, DKM, and MHN contributed greatly to the data interpretation. FH wrote the first draft of the paper, MDHH, DKM, and MHN contributed in the data analysis, and the entire paper was thoroughly revised by MDHH, DKM, MHN, and MMR. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author and are ready to be shared upon reasonable request.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethical Review Committee of DMCH (memo no. MEU-DMC/ECC/2018/16). After ensuring complete anonymity and no disclosure of the patients' personal information, all respondents participated voluntarily and provided written informed consent prior to the study commencement.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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