

Cognitive impairment in patients with systemic lupus erythematosus

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ABSTRACT

Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease mostly affecting women of child bearing age. It is a multifactorial disease and may affect multiple organs of the body including central nervous system, hematological and immunological system. Various studies have reported variable incidence of cognitive impairment in SLE. The aim of the present study was to assess the frequency and factors affecting cognitive impairment in patients with SLE.

Subjects and Methods: This cross-sectional study was conducted at Department of Rheumatology & Immunology, Sheikh Zayed Hospital, Lahore from January to July 2018. Diagnosed cases of SLE, on basis of American College of Rheumatology Revised Classification Criteria of SLE, visiting outpatient department and Rheumatology ward of the hospital were included in the study. Patients having any organic brain disease or those with known psychiatric illness were excluded from the study. Mini-mental state examination (MMSE) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) were calculated for the patients.

Results: Attention and recall, language and memory were identified as commonly affected domains of cognitive impairment in SLE patients. Positive correlation between duration of the disease and steroid dose was found. Disease activity score was negatively correlated with age, duration of the disease and steroid dose.

Conclusion: Cognitive impairment is present in SLE patients. Age, duration of disease and steroid dose has no significant effect on cognitive impairment in SLE patients.

Keywords:

Cognitive impairment, SLE, MMSE, SLEDAI

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an autoimmune disease affecting multiple organ systems of the body.¹ The etiology of the disease is largely unknown and a number of genetic, epigenetic, hormonal and environmental factors are implicated.² SLE is either classified by using American College of Rheumatology (ACR) Revised Classification Criteria or Systemic Lupus Collaborating Clinics (SLICC) criteria.³ Clinical manifestations may vary greatly from mild to severe depending upon the organ systems involved.⁴ Neurological manifestations in SLE are common which portends worse prognosis.⁵ Neurological involvement has been reported in 21-67% of SLE patients with variable presence of cognitive impairments and cognitive dysfunctions and depression are considered as earliest symptoms of neuropsychiatric

SLE (NPSLE).⁶⁻⁸ Studies have reported 3-80% incidence of cognitive impairment in patients with SLE which is associated with significant functional disability.^{2,9,10} Cognitive dysfunction in SLE are associated with considerable negative impact on quality of life and functional abilities, especially intelligence, reading, listening, learning, self-confidence and complex problem solving ability.^{11,12} Significant correlation between degree of cognitive impairment and duration of disease has been reported. However, no significant relationship exists between disease activity and steroid dose used for the treatment.¹³ Early diagnosis of cognitive impairment is important as this can improve the quality of life in these patients.¹⁴ Mini-mental state examination (MMSE) is used to screen cognitive dysfunction. It contains 11 variables which assess various cognitive domains including memory, language, attention and calculation, orientation in time and visual construction.¹⁵ Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) is a

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Table 1: Analysis of variance across cognitive impairment groups

	No Cognitive Impairment (MMSE= 27-30)	Mild Cognitive Impairment (MMSE=24-26)	Moderate Cognitive Impairment (MMSE=19-23)	p-value
No. of participants	28	29	10	
Age (years)	28.39 ± 10.44	26.55 ± 8.87	28.00 ± 10.39	0.767
Duration of disease (years)	5.15 ± 5.51	3.29 ± 4.94	4.63 ± 5.19	0.400
SLEDAI score	4.14 ± 6.50	5.69 ± 7.31	5.50 ± 7.17	0.685
Steroid dose (mg)	27.44 ± 24.22	17.32 ± 20.20	26.00 ± 24.25	0.221
Education (years)	11.68 ± 2.57	10.41 ± 4.11	10.80 ± 3.65	0.386

tool used to assess the activity of the disease in last 10 days. The index is scored on the presence and absence of various clinical and hematological items.¹⁶ Extreme variability in the incidence of cognitive dysfunction warrants further research to identify factors affecting cognitive impairment in SLE patients. The aim of present study was to assess the frequency and factors affecting cognitive impairment in patients with SLE.

SUBJECTS AND METHODS

This is a descriptive cross-sectional study conducted at Department of Rheumatology and Immunology, Sheikh Zayed Hospital Lahore from January to July 2018. The study was approved by Institutional Review Board. Cases of SLE, diagnosed on basis of American College of Rheumatology Revised Classification Criteria of SLE, visiting outpatient department and Rheumatology ward of the hospital were included in the study. Patients having psychiatric illness, or any other organic brain disease were excluded. Sample size was calculated to be 68 using 95% confidence interval, 90% power with expected frequency of cognitive disorders in SLE as 33.3%. Demographic details including age, sex, education etc. and clinical details comprising disease activity score, duration of disease and steroid dose etc. were entered in a pre-designed proforma. All patients were evaluated employing MMSE score. Based on MMSE score, the patients were divided into four groups: 0-18 (severe cognitive impairment), 19-23

(moderate), 24-26 (mild) and 27-30 (no cognitive impairment).^{17,18} The data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 20. Qualitative data was given in the form of frequencies, while quantitative data was described using mean ± S.D. Parametric and non-parametric tests were used to compare various study parameters between groups. Pearson correlation was applied to observe correlation between parameters.

RESULTS

A total of 67 (60 female, 7 male) patients were enrolled in the study. Mean age was 27.7 years, mean duration of disease was 4.24 ± 5.19 years. Mean steroid dose was 22.66 g (±22.63) and systemic lupus erythematosus disease activity index was 5.06 (±6.85). Age, duration of the disease, SLEDAI score and Steroid dose were not different between various groups (Table 1).

Most of the patients were positive for ANA (65, 95.59%) and anti-dsDNA antibodies (60, 88.23%). Oral ulcer, arthritis, proteinuria, malar or discoid rash were present in descending orders. Only a few patients presented with alopecia, serositis, photosensitivity and other symptoms of SLE (Figure 1). Significant positive correlation were found between age and duration of disease (.498, <0.001), age and steroid dose (.355, 0.003) and duration of disease and steroid dose (0.911, <0.001) while negative correlations were observed between SLEDAI score and duration of the disease, age and steroid dose (Table 2).

Table 2: Correlation Between Various Variables

	Age	Duration (years)	SLEDAI Score	Steroid dose (g)
Age	Correlation	1		
	p-value			
Duration (yrs)	Correlation	.498		
	p-value	<.001*		
SLEDAI Score	Correlation	-0.298	-0.344	1
	p-value	0.014*	0.004*	
Steroid dose (g)	Correlation	.355	0.911	-0.270
	p-value	0.003*	<0.001*	0.026*

*p-value of ≤0.05 is considered statistically significant

No significant difference was observed between level of education and cognitive impairment in SLE patients (Table 3).

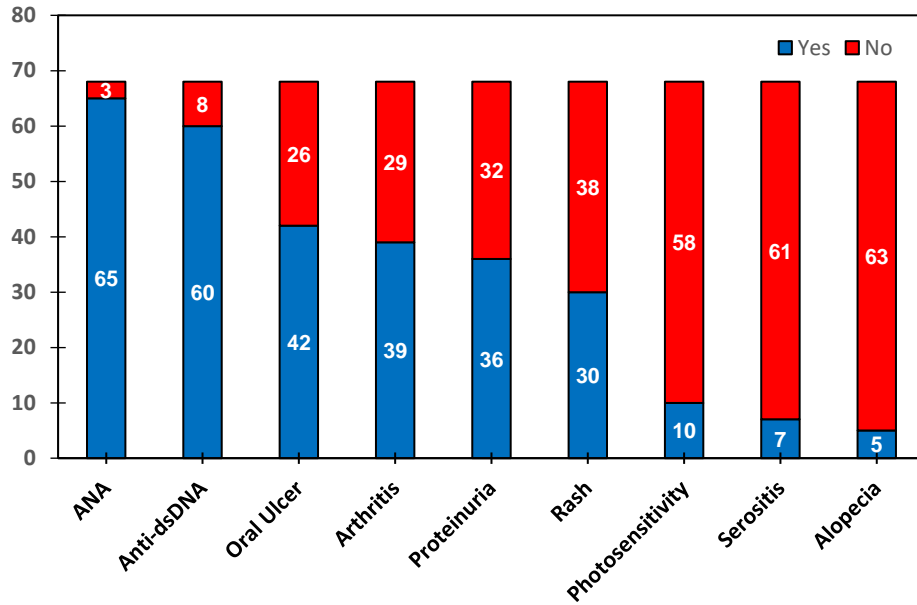


Figure 1: Frequency of various presenting complaints of SLE patients

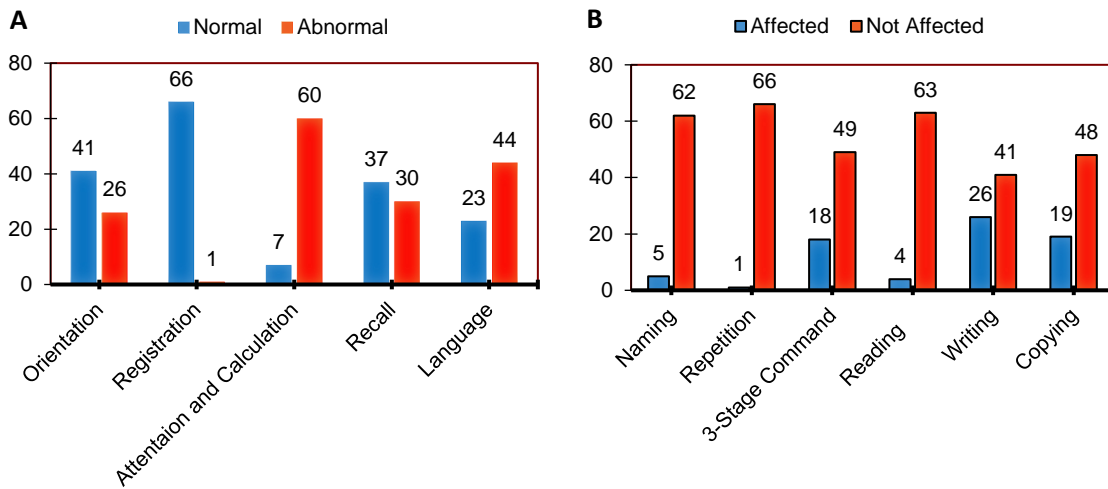


Figure 2: (a) Components of Cognitive impairment affected in SLE patients (b) Language sub-components affected in SLE patients

Most of the SLE patients were unable to give proper attention and make calculations. Language was second most commonly affected component in cognitive impairment followed by recall (memory) and spatial orientation. Among the language component, the most commonly affected sub-component was writing, followed by copying and following commands (Figure 2).

DISCUSSION

Cognitive impairment (CI) is common in SLE patients. Neuropsychiatric SLE patients (NPSLE) are more prone to develop CI abnormalities compared to non-NPSLE patients.¹⁹ Cognitive impairment can profoundly impair workplace performance, self-confidence and memory of the patient. Some studies have reported that low level of education has direct

Table 3: Chi-square analysis between cognitive impairment and education level

		No Cognitive Impairment	Mild Cognitive Impairment	Moderate Cognitive Impairment	p-value
Primary	Count	1	4	2	0.348
	Expected	1	3	2.9	
High School	Count	16	19	5	
	Expected	6	17.3	16.7	
Graduate	Count	11	6	3	
	Expected	3	8.7	8.4	
Total		28	29	10	

4 cells (44.4%) have expected count less than 5
The minimum expected count is 1.04

impact on cognitive impairment, while others have found no significant relation between these two.^{2,13,20-22} Results of the present study shows that 58.21% of SLE patients in local population have some degree of cognitive impairment. Mean age of the patients was 27.75(9.75) years, while mean education was 11.04 (± 3.46) years. The results of this study are comparable to another local study where authors reported that 65.1% of the patient have cognitive impairment with mean age of 28.72 years and 10.98 mean duration of education.²³ Prevalence of Cognitive impairment in local population with SLE is high. A number of national and international studies have also reported variable preference. This variability in results may be due to different selection criteria used by studies, population dynamics, socio-economic factors and burden of diseases.

Dementias like symptoms have been observed in patients using long-term glucocorticoid therapy. This study did not find any association between cognitive impairment with steroid dose, disease activity and duration of SLE. Ceccarelli and colleagues found no correlation between cognitive decline and various demographic factors, gender and treatment.² Benedict and coauthors concluded that cognitive impairment is not associated with glucocorticoid use or duration of disease.²⁴ Various other studies also reported no correlation between disease activity and CI.^{13,22,25} However, contrary to this, some authors have reported significant association between disease activity and cognitive impairment.²⁶⁻²⁸ Similarly, studies have reported variable correlation between steroid dose and cognitive impairment. El-Shafeyet and associates and Kivity and coworkers found no significant correlation between steroid dose and cognitive impairment, while other studies have reported cognitive decline with use of corticosteroids.^{13,29-31} Studies have also reported that poor cognitive function is associated with duration of the disease.^{32,33} These observational differences may be since some studies included only symptomatic patients

while other studies have considered all the patients. Difference in data due to retrospective studies may be another possible reason. Long term use of glucocorticoids has been marked with reversible and irreversible changes in hippocampus structure, another possible factor for cognitive impairment in these patients.

Mean disease activity score was 5.06 (6.85) in the patients. Manteen and co-workers reported significant correlation between disease activity and rate of cognitive decline, while others have reported opposing results.³⁴⁻³⁷ Studies have reported memory loss, learning disabilities, slow processing of information and poor working memory in SLE patients.²⁴ Measuring disease activity is crucial to the outcome of disease in SLE. Disease activity index has been modified from time to time to observe differences in patients based on treatment offered and other variables. Results of this study indicated that attention and recall were the most affected domain of cognitive impairment followed by language and short-term memory (registration and recall) respectively. Result of a large cross-sectional study from Iran, reported orientation as the most commonly effected domain followed by memory and language components.³⁷ Another study reported impairment of memory process and audio-visual memory components in SLE patients.³⁸ This difference from other studies may be due to the tool used to assess cognitive impairment, selection criteria of the patients and severity of the disease. Whether age and duration of disease causes cognitive impairment, or it is the use of corticosteroids which accelerates cognitive impairment in SLE patients remains debatable. Large scale longitudinal studies or clinical trials are needed to determine time-related changes and cause effect relationship.

CONCLUSION

Age, duration of disease and SLEDAI score have no effect on cognitive impairment in SLE patients.

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