

Examine the Prevalence and Risk Factors of Cognitive Dysfunction in Systemic Lupus Erythematosus Patients

JAVED IQBAL¹, MUHAMMAD TAHIR², MUZAMUL SHAHZAD³, MUHAMMAD IMRAN ASLAM⁴, MUHAMMAD ASHFAQ ZIA⁵, MUNAZA JAVED⁶

¹Associate Prof. of Medicine, CMH Lahore Medical College, Lahore,

²Associate Prof. of Medicine, Rahbar Medical and Dental College, Lahore,

³Prof. of Medicine, University College of Medicine and Dentistry, University of Lahore,

⁴Assistant Prof. of Medicine, Nawaz Sharif Social Security Teaching Hospital, Lahore/ University of Lahore,

⁵Assistant Prof. of Medicine, CMH Lahore Medical College, Lahore,

⁶Associate Prof. of Medicine, University College of Medicine and Dentistry, University of Lahore.

Correspondence to Dr. Javed Iqbal, Email: brigjavediqbal.ji@gmail.com Cell: 0321-4358587,

ABSTRACT

Aim: To determine the prevalence of cognitive disorders in systemic lupus erythematosus patients and also examine the risk factors associated to cognitive dysfunctions.

Study design: Cross-sectional/Observational Study.

Place & duration: The current study was conducted at CMH Lahore Medical College, Lahore from the period January, 2016 to December, 2016.

Methods: In this study total 110 systemic lupus erythematosus patients were included. Patients were ages above than 20 years. Patient's detailed medical history including age, sex education and disease duration was examined after taking informed consent from patients and attendants. Patients had previous history of psychiatric illness and those had other brain diseases were excluded from the study. Mini mental state examination MMSE was performed to all of patients. Risk factors associated to cognitive impairment was examined.

Results: Out of total 110 SLE patients 23 (20.91%) patients found to have cognitive impairment. In 23 CI patients 19 (82.61%) patients were females while 17.39% were males. 10 (43.48%) patients were ages 20 to 40 years while 13 (56.52%) patients had ages >40 years. 9 (39.13%) patients study duration was < 10 years and 14 (60.87%) patients had education duration was >10 years. Mean disease duration was 9.96±9.74 years. We found chloroquine was a protective factor in cognitive dysfunction P-value 0.002; other risk factors were not significant.

Conclusion: We concluded that cognitive disorders rated high prevalence in systemic lupus erythematosus patients and the use of chloroquine as a protective factor contributes to increase the prevalence ratio.

Keywords: Systemic Lupus Erythematosus, Cognitive Dysfunction, Prevalence, MMSE

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is a chronic, multisystem, relapsing remitting autoimmune disorder having a wide range of clinical spectrum ranging from mild to life threatening manifestations¹. SLE is clinically defined by 1997 American College of Rheumatology (ACR) Revised Classification Criteria of Systemic Lupus Erythematosus and patient needs to fulfill 4 out of 11 criteria to be classified as having SLE². SLE can involve any system of body and nervous system is one of them. Only two central nervous system manifestations are included in the ACR Classification criteria but there are various neuropsychiatric manifestations in SLE^{3,4}. American College of Rheumatology, in 1999, elaborated a total 19 neuropsychiatric manifestations in SLE, which can be present in central or peripheral nervous system such as meningitis, headache, anxiety, fits, psychosis, disorders of mood and cognitive dysfunction⁵. Cognitive dysfunction related symptoms are frequent among SLE patients and neuropsychiatric evaluation techniques have found increased frequency of cognitive impairment in patients of SLE as compared to general population⁶. Cognitive dysfunction can negatively impact interpersonal communication, self image, intelligence and memory and

quality of life⁷. The pathophysiological mechanisms underlying the development and progression of rheumatic disease-associated cognitive impairment are unclear, and it appears that multidimensional factors contribute. A review of the literature revealed that the following risk factors have been associated with cognitive impairment in rheumatic diseases: (1) demographic-related factors (age, gender, and education) (2) health-threatening factors (smoking, alcohol consumption, and obesity) (3) underlying diseases (cardiovascular diseases, hypertension, and diabetes mellitus) (4) steroid treatment and (5) psychosocial factors (anxiety, depression, and stress)⁸⁻¹¹.

PATIENTS AND METHODS

In this study total 110 SLE patients of both genders were included. Patients were ages above than 20 years. Patient's detailed medical history including age, sex education and disease duration was examined after taking informed consent from patients and attendants. Patients had previous history of psychiatric illness and those had other brain diseases were excluded from the study.

Mini mental state examination MMSE was performed to all of patients. Risk factors associated to cognitive impairment was examined and noted as education time duration, obesity, systemic arterial hypertension, steroid treatment i.e., use of benzodiazepine, use of

Received on 27-07-2018

Accepted on 10-12-2018

cyclophosphamide and chloroquine, and psychosocial factors.

RESULTS

Out of total 110 SLE patients 23 (20.91%) patients found to have cognitive impairment. In 23 CI patients 19 (82.61%) patients were females while 17.39% were males. 10 (43.48%) patients were ages 20 to 40 years while 13 (56.52%) patients had ages >40 years. 9 (39.13%) patients had study duration <10 years and 14 (60.87%) patients had education duration was >10 years. Mean disease duration was 9.96±9.74 years.

By using Mini mental state examination MMSE we found 17 (73.91%) had mild CD while 6 (26.09%) had dementia. Risk factors associated to CD were recorded as education duration >10 years 2 (8.70%) patients, Duration of disease >10 years in 2 (8.70%), Obesity in 3 (13.04%), systemic arterial hypertension in 3 (13.04%), use of benzodiazepine in 4 (17.39%), use of cyclophosphamide and chloroquine in 6 (26.09%) and depression and stress in 3 (13.04%). We found chloroquine was a protective factor in cognitive dysfunction and use of this steroid had high prevalence of Cognitive dysfunction p-value 0.002; other risk factors were not significant 0.26 p-values.

Table 1. Baseline characteristics of all the participants.

Characteristics	No.	%age
Cognitive Dysfunction (n=110)	23	20.91%
Gender		
Male	4	17.39%
Female	19	82.61%
Age		
20 to 40 years	10	43.48%
>40 years	13	56.52%
Education		
< 10 years	9	39.13%
>10 years	14	60.87%

Table 2. By using MMSE examination

Characteristics	No.	%age
Mild	17	73.91
Dementia	6	26.09

Table 3. Risk factors followed by cognitive dysfunction

Factors	No.	%age	P value
Education >10 years	2	8.70%	0.26
Disease duration >10 yrs	2	8.70%	
Obesity	3	13.04%	
SAH	3	13.04%	
Psychosocial			
Depression & Stress	3	13.04%	-
Steroids			
Benzodiazepine	4	17.39%	
Chloroquine	6	26.09%	

DISCUSSION

Most of the SLE population is neglected for screening of cognitive disorders due to a limited focus to seizures psychosis. However, the rate of neuro-psychological disorder in this population is not very low. Therefore, routine evaluation may be helpful for SLE cases and health resources.¹² In this study we aimed to determine the frequency and risk factors of cognitive dysfunction in SLE

patients of Pakistani origin using Mini Mental State Examination which is easy to administer and do not require specialized training and can be used in routine clinical practice.

In our study we found high prevalence Cognitive dysfunction in Systemic Lupus Erythematosus patients and reported 20.91%. These results shows similarity to some other studies in which prevalence of cognitive dysfunction was high in SLE patients and rated 17 to 60%¹³⁻¹⁴ and some of studies reported 11 to 66% of cognitive disorder in systemic lupus erythematosus patients¹⁵⁻¹⁶.

In this study we examine 110 patients with SLE. Out of 110 patients 23 found to have cognitive dysfunction. From 23 CD patients we found female patients population was high 82.61% as compared to males 17.39%. A study conducted by O.Vera L et al¹⁷ regarding prevalence and risk factors for cognitive disorder in which they reported female patients population was high and reported 92.59%. Some other studies shows similarity to our study in which women patients was high in numbers compared to men 70 to 90%.¹⁸⁻¹⁹ In this study we use mini mental state examination technique for examine CD in SLE patients. We found 73.91% had mild CD while 26.09% had dementia.

In this current research we found risk factors associated to cognitive impairment such as demographical factors (education >10 years) in 8.70% patients, Disease duration in 8.70%, obesity in 3 (13.04%), systemic arterial hypertension in 3(13.04%), use of benzodiazepine in 4 (17.39%), use of cyclophosphamide and chloroquine in 6 (26.09%) and depression and stress in 3 (13.04%). These results shows difference to other studies in which few of studies reported cardiovascular disease such as hypertension and diabetes mellitus was a major risk factor and few of studies shows duration of education and disease duration was a major risk factor.²⁰⁻²¹ Some of studies shows similarity to our study in which use of steroids had a high prevalence of being cognitive dysfunction and reported 25 to 40%²²⁻²³.

This study was aimed to examine the prevalence and risk factors of cognitive impaired in systemic lupus erythematosus patients and we found a high prevalence of cognitive dysfunction.

CONCLUSION

We concluded that cognitive disorders rated high prevalence in systemic lupus erythematosus patients and the use of chloroquine as a protective factor contributes to increase the prevalence ratio. Moreover, other factors such as depression, disease duration and systemic arterial hypertension contributes a main role of increasing the cognitive dysfunction rate. It is also concluded that early and accurate diagnosis and better treatment modalities can reduce the incidence rate.

REFERENCES

1. Merola JF, Bermas B, Lu B, Karlson EW, Massarotti E, Schur PH. Clinical manifestations and survival among adults with SLE according to age at diagnosis. *Lupus*. 2014;23(8): 778-784.
2. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum*. 1997;40(9):1725.

3. Kivity S, Agmon-Levin N, Zandman-Goddard G, Chapman J, Shoenfeld Y. Neuropsychiatric lupus: a mosaic of clinical presentations. *BMC Med.* 2015;13:43.
4. Monov S, Monova D, Rashkov R, Shumanlieva R. Systemic lupus erythematosus: neuropsychiatric manifestations. *Ann Rheum Dis.* 2016;75(2):1078
5. ACR Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. *Arthritis Rheum.* 1999; 42(4):599–608.
6. Hanly JG, Omisade A, Su L, Farewell V, Fisk JD. Assessment of cognitive function in systemic lupus erythematosus, rheumatoid arthritis, and multiple sclerosis by computerized neuropsychological tests. *Arthritis Rheum.* 2010;62:1478–86.
7. Muhammad H, Goyal M, Lal V, Singh S. Neuropsychiatric manifestations are not uncommon in Indian lupus patients and negatively affect quality of life. *Lupus* 2018; 27(4):688-693.
8. Abdul-Sattar AB, Goda T, Negm MG. Neuropsychiatric manifestations in a consecutive cohort of systemic lupus erythematosus: A single center study. *International Journal of Rheumatic Diseases*, 2013;16, 715-723.
9. Can SS, Gencay-Can A. Assessment of cognitive function in patients with fibromyalgia using the clock drawing test. *J Musculoskeletal Pain*, 2012;20, 177-182.
10. Fava A, Plastino M, Cristiano D, Span A, Cristofaro S, Opirari C, Bosco D. Insulin resistance possible risk factor for cognitive impairment in fibromyalgic patients. *Metabolic Brain Disease*, 2013;28:619-627.
11. Katz P, Julian L, Tonner MC, Yazdany J, Trupin L, Yelin E, Criswell L. A. Physical activity, obesity and cognitive impairment among women with systemic lupus erythematosus. *Arthritis Care Res (Hoboken)*, 2012;64, 502-510.
12. Mahdavi AA, Haghghi A, Malakouti SK. Prevalence of cognitive disorders in patients with systemic lupus erythematosus. *Arch Iran Med.* 2016; 19(4): 257-261.
13. Carbotte RM, Denburg SD, Denburg JA. Prevalence of cognitive impairment in systemic lupus erythematosus. *J NervMent Dis.* 1986;174:357–64.
14. Hanly JG, Liang MH. Cognitive Disorders in Systemic Lupus Erythematosus Epidemiologic and Clinical Issues. *Ann NY Acad Sci.* 1997; 823: 60-68.
15. Appenzeller S, Cendes F, Costallat LT. Cognitive impairment and employment status in systemic lupus erythematosus: a prospective longitudinal study. *Arthritis Rheum.* 2009;61(5):680–687.
16. Sanna G, Bertolaccini ML, Cuadrado MJ. Neuropsychiatric manifestations in systemic lupus erythematosus: Prevalence and association with antiphospholipid antibodies. *J Rheumatol* 2003; 30: 985–992.
17. O Vera-Lestra, M Castrejon. Prevalence and risk factors of cognitive dysfunction in SLE patients. *Br Med J.* 2017;75:2.
18. Meara A, Davidson N, Steigelman H, Zaho S, Brock G, Jarjour WN et al. Screening for cognitive impairment SLE using These administered gerocognitive exam. *Lupus* 2018; 27(8): 1363-1367.
19. Vera-Lastra O, Castrejon M, Sepulveda-Delgado J, Cuz-Dominguez MDP, Medina G, Jara LJ. Prevalence and risk factors for cognitive impairment in systemic lupus erythematosus. *Ann Rheum Dis*, 2016; 75(2)
20. Benedict RHB, Shucard JL, Zivadinov R, Shucard DW. Neuropsychological impairment in systemic lupus erythematosus: a comparison with multiple sclerosis. *Neuropsychol Rev.* 2008;18(2): 149–166.
21. Petri M, Naqibuddin M, Carson KA, Sampredo M, Wallace DJ, Weisman MH, et al. Cognitive function in a systemic lupus erythematosus inception cohort. *J Rheumatol.* 2008;35(9):1776–1781.
22. Nantes SG, Su J, Dhaliwal A, Colosimo K, Touma Z. Performance of screening tests for cognitive impairment in systemic lupus erythematosus. *J Rheumatol.* 2017;44(11):1583-9
23. Cordell C, Borson B, Boustani M. Alzheimer's Association recommendations for operationalizing the detection of cognitive impairment during the Medicare Annual Wellness Visit in a primary care setting. *Alzheimers Dement*, 2013;9:141–50