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Assessment of psychosis and psychiatric disorder prevalence in subjects with systemic lupus erythematosus and their correlation with disease activity and severity: A case-control study

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Abstract
Background: Neuropsychiatric disorders and their manifestations seen in Systemic Lupus Erythematosus [SLE] are attributed to dysfunction of both peripheral and central nervous systems. Neuropsychiatric disorders and their manifestations are seen in SLE are attributed to dysfunction of both peripheral and central nervous systems.
Aims: The present clinical study was carried out to assess psychosis and psychiatric disorder prevalence in SLE subjects, to correlate disease severity with neuropsychiatric disorders in SLE subjects, to compare stress, morbidity, and quality of life in subjects with and without SLE, and to assess the relationship of psychosocial stress and psychiatric disorders in these subjects.
Materials and Methods: The following tools were utilized in the present study: MINI International Neuropsychiatric Interview, Systemic Lupus Activity Measure-Revised (SLAM-R) for measuring disease activity, The World Health Organization Quality of Life (WHOQOL- BREF), Presumptive Stressful Life Events Scale, and Hospital Anxiety and Depression Scale for 20 subjects of both groups. The collected data were subjected to statistical evaluation.
Results: In cases 55% (n=11) subjects had active SLE. Neuropsychiatry disorders were present in 15% (n=3) controls and 60% (n=120 cases. The mean of PSLE scores were significantly lesser in controls and cases respectively were 1.55±0.730 and 3.35±1.098 (p< 0.0001). PSLE scores were significantly higher among cases (*p*< 0.0001). Concerning the quality of life, it was seen that concerning social relationship domain, physical domain, environmental domain, psychological domain, and total quality of life, the mean values were statistically lesser in cases compared to controls with p-values were < 0.0001.
Conclusion: Within its limitations, the present study concludes that subjects with SLE are largely affected by psychiatric disorders. With the increase in SLE severity and stress events, the risk of having psychiatric diseases increases. Also, the quality of life is poor in subjects with SLE and psychiatric disorders.

Keywords: Anxiety disorders, mood disorders, neuropsychiatric disorders, psychosis systemic lupus erythematous [SLE]

Introduction
SLE (Systemic Lupus Erythematosus) is an autoimmune disorder of unknown etiology affecting the connective tissues. Immune system dysfunction and connective tissue damage in SLE are seen secondary to affected immune complexes, T lymphocytes, and antibodies. SLE affects blacks more than whites, females more than males (ratio 15:1) with approximately 3.5 females/lakh white females, and 9.2/lakh black females. SLE is commonly seen in Asians and is commonly reported in the age range of 15-64 years. SLE affects one or more systems of the human body with varying symptoms including malar rash, fever, photosensitivity, arthralgia, fatigue, arthritis, weight loss, pleuritis, oral ulcer, anemia, renal disorders, leucopenia, and/or neuropsychiatric disorders [1].
Neuropsychiatric disorders and their manifestations are seen in SLE are attributed to dysfunction of both peripheral and central nervous systems. These disorders include mood disorders, anxiety disorders, psychosis, myasthenia gravis, headache, Guillain-Barre syndrome, plexopathy, polyneuropathy, etc.

These psychiatric disorders in SLE are attributed to either disease treatment, and/or the disease itself, and are sometimes attributed to various other factors making its Etiopathogenesis a multifactorial etiology [2]. The pathogenesis is owned by vascular injury to the cranial nerves and inflammatory alterations secondary to antineuronal antibodies, cytokine production, phospholipid-associated proteins, and/or anti-ribosomal antibodies. The diagnosis of the disorder is difficult owing to the non-availability of any single diagnostic test, and hence, various investigations are done to diagnose the disease and its severity [3].

The neuropsychiatric disorders and their manifestations in subjects with SLE are classified into 5 categories including mood disorder (bipolar and depression), psychosis, anxiety disorder, cognitive dysfunction, and delirium (acute confusional state). The prevalence of these psychiatric disorders in SLE is different as reported by different authors in literature, which can be attributed to different methods and criteria in different areas. However, the majority of studies report their prevalence of 17-75% approximately [4].

The development of psychiatric manifestations and disorders in SLE is not solely attributed to disease treatment and disease, but also psychosocial stress in affected subjects. The disease pattern of SLE in India is comparable to what is seen in other countries. However, the prevalence of psychiatric disorders and psychosis in subjects with SLE is studied little in the Indian population [5]. Hence, the present clinical study was carried out to assess psychosis and psychiatric disorder prevalence in SLE subjects, to correlate disease severity with neuropsychiatric disorders in SLE subjects, to compare stress, morbidity, and quality of life in subjects with and without SLE, and to assess the relationship of psychosocial stress and psychiatric disorders in these subjects.

Materials and Methods

The present study was carried out after obtaining clearance from the concerned Ethical committee. The study had two groups, controls (n=20) and cases (n=20) groups with different inclusion and exclusion criteria. Study subjects were recruited from the subjects visiting the Outpatient Department of Rheumatology as cases, and controls were matched and included from the Outpatient department of Medicine, visited for minor diseases treatment.

The inclusion criteria for controls were subjects matched with the cases concerning demographic parameters, mentally fit subjects with no systemic disease, and subjects not ready to give consent for study participation. The excluded subjects were the ones not willing to participate and subjects on substance dependence (except nicotine).

The inclusion criteria for the study cases were subjects with an age of 18 years or more, confirmed diagnosis of Systemic Lupus Erythematosus and were following the criteria by ACR (American College of Rheumatology), subjects in the medical state of giving the consent, and subjects with the diagnosed disease for at least 6 months. The exclusion criteria for the study were subjects with other medical disorders of chronic duration, subjects not willing to give medical consent, subjects with any neuropsychiatric disorder, subjects on any dependence (except for nicotine), end-stage disease subjects, and subjects with dementia or mental retardation history.

After the inclusion of the subjects, both cases, and controls were assessed in the department of psychiatry to rule out neuropsychiatric disorders. After explaining the study design, the informed consent was taken from each included subject. After recording the demographic characteristics, neurological and physical examination of each subject was done. Depression, quality of life, and disease activity of SLE were also evaluated. The following tools were utilized in the present study: MINI International Neuropsychiatric Interview, Systemic Lupus Activity Measure-Revised (SLAM-R) for measuring disease activity, The World Health Organization Quality of Life (WHOQOL- BREF), Presumptive Stressful Life Events Scale (PSLE), and Hospital Anxiety and Depression Scale (HADS).

The collected data were subjected to the statistical evaluation using SPSS software version 21.0, 2012, Armonk, NY, ANOVA, and t-test. The results were formulated keeping the level of significance at $p< 0.05$.

Results

On assessing both cases and controls, demographic and disease-related characteristics are summarized in Table 1. The results showed that all the study subjects were females in both cases and controls. Among less than 20 years, 21-30, 31-40, and more than 40 years, were 20% (n=4), 35% (n=7), 25% (n=5), and 20% (n=4) subjects in both cases and controls. Maximum subjects were in the middle-class group with 60% (n=12) subjects among both controls and cases and 13 (65%) subjects were unmarried. In cases 55% (n=11) subjects had active SLE. Neuropsychiatry disorders were present in 15% (n=3) controls and 60% (n=120 cases. Among disorders encountered, it was seen that psychosis, depression, social and anxiety disorders, dysthymia, and generalized anxiety disorder was seen in 5% (n=1), 30% (n=6), 5% (n=1), 10% (n=2), and 10% (n=2) subjects, whereas, in controls dysthymia, depression, and GAD was found in 5% (n=1) subject each.

The present study also assessed various tools related to neuropsychiatric disorders and the results are described in Table 2. HADS-A scores had mean values of 3.45±2.571 and 7.25±4.943 in controls and cases respectively, whereas the HADS-D score had these respective values as 3.91±3.142 and 8.71±5.868. HADS-A had normal, borderline, and abnormal scores in 90% (n=18), 5% (n=1), and 5% (n=1) subjects respectively. However, in cases these values were 55% (n=11), 30% (n=6), and 15% (n=3) study subjects. For HADS-D in cases normal, borderline, and abnormal were seen in 45% (n=9), 20% (n=4), and 35% (n=7) females, these values in controls were 85% (n=17), 5% (n=1), and 10% (n=2) subjects. The mean of PSLE scores were significantly lesser in controls and cases respectively were 1.55±0.730 and 3.35±1.098 ($p< 0.0001$). PSLE scores were significantly higher among cases ($p< 0.0001$).

On assessing the quality of life in study subjects, it was seen that concerning social relationship domain, physical domain, environmental domain, psychological domain, and total quality of life, the mean values were statistically lesser in cases compared to controls with p-values were < 0.0001 for all parameters. Concerning SLE activity, the mean values of these 5 parameters to assess the quality of life were significantly higher in subjects where disease activity was absent compared to those with active SLE with the value of $p< 0.0001$ as shown in Table 3. Also, the mean of these parameters assessing the quality of life was higher in

subjects with absent psychiatric morbidity compared to subjects having psychiatric morbidity ($p< 0.0001$).

Discussion

The present clinical study was carried out to assess psychosis and psychiatric disorder prevalence in SLE subjects, to correlate disease severity with neuropsychiatric disorders in SLE subjects, to compare stress, morbidity, and quality of life in subjects with and without SLE, and to assess the relationship of psychosocial stress and psychiatric disorders in these subjects. The study included 20 controls and 20 cases of females.

The study results showed that all the study subjects were females in both cases and controls. Among less than 20 years, 21-30, 31-40, and more than 40 years, were 20% (n=4), 35% (n=7), 25% (n=5), and 20% (n=4) subjects in both cases and controls. Maximum subjects were in the middle-class group with 60% (n=12) subjects among both controls and cases and 13 (65%) subjects were unmarried. In cases 55% (n=11) subjects had active SLE. Neuropsychiatry disorders were present in 15% (n=3) controls and 60% (n=120 cases. Among disorders encountered, it was seen that psychosis, depression, social and anxiety disorders, dysthymia, and generalized anxiety disorder was seen in 5% (n=1), 30% (n=6), 5% (n=1), 10% (n=2), and 10% (n=2) subjects, whereas, in controls dysthymia, depression, and GAD was found in 5% (n=1) subject each. These characteristics were in agreement with the findings by Brey RL *et al*. [6] in 2002 and Kozora E *et al*. [7] in 2007 where authors reported comparable neuropsychiatry characteristics to the present study.

HADS-A scores had mean values of 3.45±2.571 and 7.25±4.943 in controls and cases respectively, whereas the HADS-D score had these respective values as 3.91±3.142 and 8.71±5.868. HADS-A had normal, borderline, and abnormal scores in 90% (n=18), 5% (n=1), and 5% (n=1) subjects respectively. However, in cases these values were 55% (n=11), 30% (n=6), and 15% (n=3) study subjects. For HADS-D in cases normal, borderline, and abnormal were seen in 45% (n=9), 20% (n=4), and 35% (n=7) females, these values in controls were 85% (n=17), 5% (n=1), and 10% (n=2) subjects. The mean of PSLE scores were significantly lesser in controls and cases respectively were 1.55±0.730 and 3.35±1.098 ($p< 0.0001$). PSLE scores were significantly higher among cases ($p< 0.0001$). These findings were similar to the studies by Appenzeller S *et al*. [8] in 2007 and Slattery MJ *et al*. [9] in 2004 where similar findings concerning psychiatry tools were reported by the authors.

On assessing the quality of life in study subjects, it was seen that concerning social relationship domain, physical domain, environmental domain, psychological domain, and total quality of life, the mean values were statistically lesser in cases compared to controls with p-values were < 0.0001 for all parameters. Concerning SLE activity, the mean values of these 5 parameters to assess the quality of life were significantly higher in subjects where disease activity was absent compared to those with active SLE with the value of $p< 0.0001$. Also, the mean of these parameters assessing the quality of life was higher in subjects with absent psychiatric morbidity compared to subjects having psychiatric morbidity ($p< 0.0001$). These results were consistent with the results of Huang HC *et al*. [10] in 2007 and FG Nery *et al* [11] in 2007 where similar results concerning disease activity and neuropsychiatry disorders were seen.

Table 1: Demographic and psychotic characteristics of the study subjects

Characteristics	Controls (n=20)	Percentage (%)	Cases (n=20)	Percentage (%)
Sex				
Males	0	100	0	100
Females	20	100	20	100
Age (in years)				
Less than 20	4	20	4	20
21-30 years	7	35	7	35
31-40 years	5	25	5	25
More than 40 years	4	20	4	20
Socioeconomic status				
Upper	2	10	2	10
Middle	12	60	12	60
Lower	6	30	6	30
Marital Status				
Unmarried	7	35	7	35
Married	13	65	13	65
Disease activity (SLE)				
Inactive	-	-	11	55
Active	-	-	9	45
Neuropsychiatry Disorders				
Present	3	15	12	60
Not-present	17	85	8	40
Type of Disorders				
Psychosis			1	5
Depression	1	5	6	30
Social and Anxiety			1	5
Dysthymia	1	5	2	10
GAD (Generalised Anxiety Disorder)	1	5	2	10

Table 2: Assessment of Psychiatry tools in study subjects

Study Groups	Parameter		Percentage (%)	Number (n)	p-value
Controls (n=20)	HADS-A	Normal	90	18	-
		Borderline	5	1	
		Abnormal	5	1	
Mean±S.D			3.45±2.571		-
Cases (n=20)	HADS-A	Normal	55	11	-
		Borderline	30	6	
		Abnormal	15	3	
Mean±S.D			7.25±4.943		-
Controls (n=20)	HADS-D	Normal	85	17	-
		Borderline	5	1	
		Abnormal	10	2	
Mean±S.D			3.91±3.142		-
Cases (n=20)	HADS-D	Normal	45	9	-
		Borderline	20	4	
		Abnormal	35	7	
Mean±S.D			8.71±5.868		-
Presumptive Stressful Life Events	Controls		1.55±0.730		< 0.0001
	Cases		3.35±1.098		
PSLE Score	Controls		81.18±37.610		< 0.0001
	Cases		184.68±69.307		

Table 3: Assessment of quality of life-based on disease activity and psychiatric disorders in study subjects

Parameter	Study Group	Mean±S.D	p-value
Social Relationship Domain	Controls	82.08±15.653	< 0.0001
	Cases	38.38±17.361	
Physical Domain	Controls	64.38±6.643	< 0.0001
	Cases	46.88±10.929	
Environmental Domain	Controls	82.51±13.631	< 0.0001
	Cases	41.38±14.404	
Psychological Domain	Controls	72.18±10.783	< 0.0001
	Cases	45.51±9.939	
Total Quality of Life	Controls	75.29±10.605	< 0.0001
	Cases	43.04±11.968	
Parameter	Psychiatric Morbidity	Mean±S.D	p-value
Social Relationship Domain	Present	28.75±12.742	< 0.0001
	Absent	50.98±14.435	
Physical Domain	Present	39.27±5.667	< 0.0001
	Absent	56.83±7.528	
Environmental Domain	Present	31.39±7.161	< 0.0001
	Absent	54.44±10.334	
Psychological Domain	Present	40.57±6.757	< 0.0001
	Absent	51.98±9.893	
Total Quality of Life	Present	34.99±6.976	< 0.0001
	Absent	53.56±8.348	
Parameter	SLE disease activity	Mean±S.D	p-value
Social Relationship Domain	Present	29.55±9.984	< 0.0001
	Absent	46.10±18.971	
Physical Domain	Present	39.12±6.127	< 0.0001
	Absent	53.67±9.647	
Environmental Domain	Present	30.48±6.597	< 0.0001
	Absent	50.92±12.468	
Psychological Domain	Present	40.34±6.430	< 0.0001
	Absent	50.04±10.403	
Total Quality of Life	Present	34.87±6.374	< 0.0001
	Absent	50.18±11.179	

Conclusion

Within its limitations, the present study concludes that subjects with SLE are largely affected by psychiatric disorders. With the increase in SLE severity and stress events, the risk of having psychiatric diseases increases. Also, the quality of life is poor in subjects with SLE and poorer in subjects with SLE, stress, and psychiatric disorders than in SLE subjects without psychiatric disorders. Morbidity is more in subjects with SLE and psychiatric illness. Early identification and treatment involving both Rheumatologists and psychiatrists can help the affected subject.

However, the study had few limitations including case-control nature, smaller sample size, shorter monitoring period, and single-institutional study. Hence, more longitudinal studies with a larger sample size and

monitoring period are needed to reach a definitive conclusion.

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