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Patterns of Organ Involvement and Outcomes of SLE: A Real-Life Experience in Lupus Clinic

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Abstract:

SLE is one of the most common autoimmune disorders of women of childbearing age.It often manifests with various constitutional symptoms as well as combination of major organ involvement and outcome varies in different studies with current treatment. The present study is to see the patterns of organ involvement and outcomes at least after 6 months with standard treatment.

This retrospective study was conducted in lupus clinic of two largest tertiary care hospitals in Dhaka city of Bangladesh over 2010 to 2019. It included 277 patients of SLE, diagnosed on the basis of ACR lupus diagnostic criteria and ACR lupus nephritis guideline and had received standard treatment. Outcomes were assessed by SLEDAI.

The most common clinical manifestations were fever (71.8%), joint pain (71.4%), oral ulceration (54.8%), alopecia (36.4%), butterfly rash (28.5%), photosensitivity (32.1%) and Raynaud's phenomenon (16.6%). Commonly involved major organ-systems were renal (41.5%), CNS (16.6%), pulmonary (7.2%), cardiac (3.2%) and hematological (12.2%). Renal biopsy was done in 91cases and the histology showed majority (37.3%) in class-IV. With standard treatment, a significant reduction of mean serum creatinine, proteinuria and SLEDAI was observed at least after 6 months. A total 35(12.63%) flares and 6 (2.17%) deaths occurred during the course of treatment.

Renal and CNS are the most commonly involved major organ systems next to skin and joints. The overall outcome is favorable with standard treatment.

Key words: *Systemic lupus erythematosus (SLE), Lupus nephritis (LN), CNS lupus, SLEDAI.*

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Introduction:

Systemic lupus erythematosus (SLE) is a multi system autoimmune disease that affects more than 300,000 people in the US and millions of people world wide[1]. The etiology of SLE is thought to be multifactorial. The disease is characterized by the production of autoantibodies which leads to immune complex deposition, inflammation, and eventually permanent organ damage. SLE is considered to be one of the most common autoimmune disorders of women of childbearing age, having an estimated prevalence of 14.6 to 50.8 per 100,000 persons in this category in the United States. There is a female: male ratio of approximately 6-10:1, with a peak incidence between the ages of 15 to 40.[2-4] However, SLE can affect all age groups. SLE most often manifests as a mixture of constitutional symptoms, with skin, musculoskeletal, renal, central nervous system, pulmonary and hematological involvement and others. Diagnosis and management are broadly based on ACR recommendations. Proper assessment of SLE is desirable as it has a variable disease course, and cumulative morbidity over time, as new organ system involvement may be seen over time in many patients even 5 to 10 years after diagnosis.[5] Recent studies showed 5-year survival rates exceeding 90% during the last few decades.[6]This study was done to see the different clinical presentations of SLE including major organ involvement and their outcome with standard treatment at least after6 months of follow up.

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Materials and methods:

This retrospective study was done in lupus clinic of two tertiary care hospitals in Dhaka city(Shaheed Suhrawardy Medical College Hospital from January 2010 to June 2016 and Dhaka Medical College Hospital from July 2016 to December 2019). It included 277 patients of SLE, diagnosed on the basis of ACR lupus diagnostic criteria[7,8] and ACR lupus nephritis guideline[9] and had received guideline based treatment (Patients with major organ involvement especially renal lupus treated with I/V methylprednisolone for initial 3 days followed by oral prednisolone and pulse I/V cyclophosphamide or MMF followed by maintenance with azathioprine or MMF).Treatment response was assessed by SLEDAI.[10]The study was a part of standard patient care who attended the outpatient lupus clinic or inpatient department of these two tertiary care hospitals and the study involved the retrospective analysis of the hospital data from the lupus clinic. So, formal informed written consent and ethical clearance was waived for this study.

Results:

Among 277 patients, 252 (91%) were female with a female to male ratio of 10:1. Age ranged from 14 to 57 years with a mean of 26.5±10.68 (SD) year and more than 80% patients were between the ages of 15-40 years. Median follow up was 3.7 years.The most common clinical manifestations were fever (71.8%), joint pain (71.4%), oral ulceration (54.8%), alopecia (36.4%), butterfly rash (28.5%), photosensitivity (32.1%) and Raynaud's phenomenon (16.6%). Commonly involved major organ-systems were renal (41.5%), neuropsychiatric (16.6%), pulmonary (7.2%), cardiac (3.2%) and hematological (12.2%) (table-1). In case of lupus nephritis, apart from proteinuria (>0.5 gm/day), 41.7% had pus cells >5/HPF, 26% had RBC >5/HPF and 20% had either RBC or cellular cast in urinalysis (table-2). Serum creatinine was raised above the normal reference range in 23 (8.3%) patients with a mean of 1.68±0.96 mg/dl. Renal biopsy was done in 91 cases and the histology showed majority (37.3%) in class-IV (Table-II). Inadequate biopsy materials was found in 6% patients. With standard treatment, a significant reduction of mean serum creatinine, SLEDAI was observed at least after 6 month and mean proteinuria reduced from 1.94±1.13 gm/24hours to 0.27±0.11 gm/24hours(P<0.001) (table-3). Total flare occurred in 35 (12.63%) cases, among them renal flare was in 12 (4.33%), CNS flare in 8 (2.89%) and other flare in 15 (5.42%). Six (2.17%) deaths (3 renal lupus, 2 CNS lupus and 1 lupus carditis) occurred during the course of treatment.One lupus nephritis patient died before starting the treatment. The rest of lupus nephritis patients including one CNS lupus and lupus carditis patient died due to severe flare of the disease as they discontinued the treatment and another CNS lupus patient died as the treatment was non responsive from the very beginning. The probable cause of death was severe organ damage as the post mortem was not done in any of the cases. No death was associated with infection or malignancy.

Table I: *Common clinical manifestations and organ involvement in SLE*

Clinical features	No of patients (%)
Fever	199 (71.8)
Joint pain	198(71.4)
Oral Ulceration	152(54.8)
Photosensitivity	89 (32.1)
Alopecia	101 (36.4)
Malar rash	79 (28.5)
Discoid rash	19 (6.8)
Raynaud's phenomenon	46 (16.6)
Vasculitis	31 (11.1)
Serositis	14 (5.0)
Fetal loss	33 (11.9)
Major organ involvement	14 (5.0)
Renal	115 (41.5)
Neuropsychiatric	46 (16.6)
Pulmonary	20 (7.2)
Hematological	34 (12.2)
Cardiac	9 (3.2)

Table II : *Urinary and renal biopsy findings of Lupus Nephritis*

Urinary findings	No of patients (%)
24 hr. UTP > 0.5 gm	115 (100%)
Pus cells >5/HPF	48 (41.7%)
RBC >5/HPF	30 (26.0%)
Cast (either RBC or Cellular)	23 (20.0%)
Renal biopsy findings	
Class-II	8 (6.9%)
Class-III	23 (20%)
Class-IV	43 (37.3%)
Class-V	17 (14.7%)
Inadequate biopsy material	07 (6.0%)

Table III: *Outcome of lupus*

Involved major organ	Mean SLEDAI ±SD		
	At presentation	At least after 6 months	P value
CNS lupus	32.38±14.99	3.0±2.63	<0.001
Lupus pneumonitis	22.8±9.38	2.67±4.62	<0.001
Lupus carditis	22.67±9.9	2.67±3.06	<0.001
Hematological involvement	22.67±4.16	4.0±2.0	<0.001
Without organ involvement	10.21±4.38	0.89±1.55	<0.001
Renal lupus	34.5±2.9	2.3±2.2	<0.001
		Mean proteinuria (gm/24 hr±SD)	
	1.94±1.13	0.27±0.11	<0.001
		Mean serum creatinine (mg/dl)	
	1.68±0.96	1.08±0.14	<0.001

Discussion:

The diagnosis of SLE is based on clinical and laboratory criteria. The classification criteria developed by the American College of Rheumatology (ACR) is most widely used.We used same criteria to diagnose our cases. In our study, the findings are almost similar with other studies with a female to male ratio of 10:1 and age of more than 80% patients in between 15-40 years. SLE most often manifests as a mixture of constitutional symptoms, with skin and musculoskeletal involvement. However, some patients present with predominantly hematologic, renal, or neuropsychiatric manifestations.[11] The most frequent manifestations include: arthritis (64-91%), skin lesions (55-86%), renal involvement (28-73%), Raynaud's phenomenon (24-61%), central nervous system involvement (11-49%), gastrointestinal symptoms (39%), pleurisy (27-36%), pericarditis (12-20 %), lymphadenopathy (10-30%), nephritic syndrome (13-14%), lung involvement (7-14%), thrombophlebitis (5-14%), myositis (4-9%) and myocarditis (2-3%).[12] In our study the most commonclinical manifestations were fever (71.8%), joint pain (71.4%), oral ulceration (54.8%), alopecia (36.4%), malar rash (28.5%), photosensitivity (32.1%) and Raynaud's phenomenon (16.6%). Commonly involved major organ-systems were Renal, CNS, Hematological, Cardiac and Pulmonary which are also more or less similar with the findings of other studies. But we didn't find any case of significant gastrointestinal involvement and thrombophlebitis.

Lupus nephritis is defined as clinical and laboratory manifestations that meet ACR criteria (persistent proteinuria >0.5 gm per day or greater than 3+ by dipstick, and/or cellular casts including red blood cells [RBCs], granular, tubular, or mixed).[13] Biopsy is highly recommended in patients with the characteristics indications. A cohort study of 1827 patients of SLE conducted by HanlyJG,et al[14] found that lupus nephritis occurred in 700 (38.3%) patients and biopsy revealed most of them were in class IV (43.2%). Other studies in Bangladesh by Faroque MO et al[15]andAkhter S et al[16] showed, class IV lupus nephritis was most common histological type that occurred in 35% and 90% of patients respectively. In our study we found 115 (41.5%) patients of lupus nephritis and among them most were in class-IV (37.3%) histological type who were biopsied. CNS manifestation is one of the most common presentation in SLE. It is reported in 25 to 75% of patients and can involve all parts of the nervous system.[17]A small prospective study in Bangladesh by Miah T, et al[18]showed, 36% patients had some degree of renal and 6% patients had severe neuropsychiatric features. Neuropsychiatric manifestation (16.6%) was the second most common major organ involvement in our study. Other major organ involvement like pulmonary, cardiac, hematological etc. are also found in significant numbers in different studies.[19]We observed 7.2% pulmonary, 3.2% cardiac and 12.2% hematological involvement in our study.

The mainstay of treatment in SLE is Hydroxychloroquin (HCQ), NSAIDs and Corticosteroid and other immunosuppressive agent like Cyclophosphamide (CYC), Azathioprine (AZA), Mycophenolate mofetil (MMF) and biologics are used especially in major organ involvement.[9,20,21]Our patients received guideline recommended treatment as needed based on severity of the disease, availability of the drugs and affordability of the patients. Treatment was found to be effective in most of the

cases in our study as there was significant reduction in SLEDAI at least after 6 month though35 (12.63%) flare and 6 (2.17%)death occurred during the course of treatment. Miah T, et al[18] in their small study found that with appropriate treatment 52% patients were leading a normal life, 30% patients had a fluctuating course and 9% patients died. A large cohort study by Hanly JG, et al[14] concluded that Lupus nephritis is associated with a substantial risk of end-stage renal disease and death. Another cohort study by Moss KE, et al[22] found 14% death associated with SLE and major cause of death was malignancy and infections.But in our patient group death was not that much high. Among the 6 deaths no one died of malignancy or infection which was also a different findings comparing those cohorts.

Limitations: Long term follow up in our settings is very tough as there are many patients not complying with the instructions properly and not regularly coming to the follow up clinic. So the reported outcomes may be under reported in the study.

Conclusion:

Renal and CNS are the most commonly involved major organ other than skin and musculoskeletal systems. Despite few case fatalities the overall outcome of SLE is favorable with standard treatment protocol.

Conflict of Interest: No authors declared any conflict of interest.

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