CLINICAL PATHOLOGICAL CHARACTERISTICS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS PRESENTING AT A TERTIARY CARE HOSPITAL - A SINGLE CENTRE STUDY

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ABSTRACT

Objective: To determine the frequency of clinopathological characteristics of systemic lupus erythematosus (SLE) patients presenting to Military Hospital (MH) Rawalpindi.
Study Design: Descriptive cross sectional study.
Place and Duration of Study: The study was carried out at MH Rawalpindi, from Jan 2011 to Dec 2013.
Material and Methods: All patients presenting to Rheumatology department, MH Rawalpindi with a diagnosis of SLE were included in this study. Presenting features, clinical profile and laboratory parameters of patients were recorded.
Results: A total of 76 patients were included in this study, 70 (92.1%) were females and 6 (7.9%) male patients with female- male ratio of 11.6:1. Mean age at presentation was 33 ± 8.31 years. Seventy two patients (94.7%) were anti nuclear antibody (ANA) positive, 63 (83%) were positive for anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibody and 6 (7.9%) were anti Smith positive. Seventy (92.1%) patients had musculoskeletal symptoms, 65 patients (85.5%) had fever, 36 (47.4%) patients had cutaneous symptoms, and 20 patients (26.3%) had oral ulcers. About 13 patients (17.1%) had alopecia and 15 patients (19.7%) had serositis. Forty two patients (55.3%) had nephritis, 20 patients (26.3%) had lupus cerebritis, 57 patients (75%) had hematological involvement, 9 patients (11.83%) had pulmonary involvement, 8 patients (10.5%) had rheumatoid arthritis (RA) factor positive and 7 patients (9.2%) had overlap syndrome.
Conclusion: Renal and hematological involvement was more common in this study population while mucocutaneous features and neuropsychiatric features were comparable to many local studies with exception to that of Lahore based study that showed much higher percentage of these features. These results reflect the need to have a high index of suspicion for kidney and hematological involvement in SLE patients.

Keywords: Clinical characteristics, prevalence, systemic lupus erythematosus (SLE), Pakistan.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease presenting with a wide variety of manifestations involving almost every organ of the body. The diagnosis of SLE is based on a combination of clinical and laboratory findings. The presence of 4 of the 11 American College of Rheumatology (ACR) criteria is used for classification purposes with the sensitivity of 85% and specificity of 95%[1]. These 11 criteria include butterfly rash, discoid lupus, photosensitivity, arthralgias, renal involvement, oral ulcers, serositis, hematological involvement, neurological involvement, immunological phenomena with positive anti-dsDNA antibody or anti-smith antibodies and positive ANA. Systemic Lupus International Collaborating Clinics (SLICC) group revised the American college of Rheumatology (ACR) classification criteria for SLE in 2012 and classified a person as having SLE if there is biopsy-proven lupus nephritis with ANA or anti-dsDNA antibodies or if 4 of the diagnostic criteria, including at least 1 clinical and 1 immunologic criterion, have been fullfilled[2].

In United States of America the prevalence of SLE has been estimated to range from

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Received: 03 Nov 2017; revised received: 18 Dec 2017; accepted: 22 Dec 2017

approximately 5.8 to 130 per 100,000 population[3]. There is considerable variation in prevalence in Asia-Pacific countries; however, overall prevalence ranged from 4.3 to 45.3 per 100,000, and the overall incidence is from 0.9 to 3.1 per 100,000 per year[4].

Asia is the largest continent of the world and it houses different ethnic and cultural groups of the population in different countries. There is a diversity of culture and climate within individual countries as well. Many studies have been done in the world including Asia, and some in Pakistan showing differences in the clinical spectrum of disease manifestations that reflect the varying environmental, socioeconomic, and genetic factors involved in the pathogenesis of disease[5-8].

The rationale of this study was to determine the clinico-pathological features in patients presenting to Military Hospital Rawalpindi and to compare it with those of other Pakistani and Asian studies.

MATERIAL AND METHODS

This study was conducted at MH Rawalpindi, Rheumatology department. Permission was obtained from hospital ethical committee prior to conducting the study. Informed Verbal consent was taken from all the patients. The descriptive cross sectional study comprised documentation of all indoor and outdoor SLE cases meeting the 4 out of 11 Revised American College of Rheumatology (ACR) criteria for lupus presenting to rheumatology department Military Hospital, Rawalpindi from Jan 2011 till Dec 2013. Consecutive sampling technique was applied for data collection. Clinical and laboratory data of all the patients was recorded. Statistical analysis was done using SPSS 11.5. Descriptive statistics were given as figures and percentages and *p*-value was calculated using chi square test to determine any statistical significant difference among findings in different studies. The difference was considered statistically significant if *p*-value was equal to or less than 0.05.

RESULTS

A total of 76 patients were included in this study out of which 70 (92.1%) were females and 6 (7.9%) male patients with the female-male ratio of 11.6:1. Mean age at presentation was 33 ± 8.31 years. Seventy patients (92.1%) had musculo-skeletal symptoms comprising arthralgias with joint pain and swelling but joint deformity was not seen in any patient with SLE alone though it was found in 2 out of 7 patients having overlap syndrome. Sixty five patients (85.5%) had fever which was low grade without any rigors. Cutaneous symptoms that included butterfly rash, discoid lupus along with photosensitivity

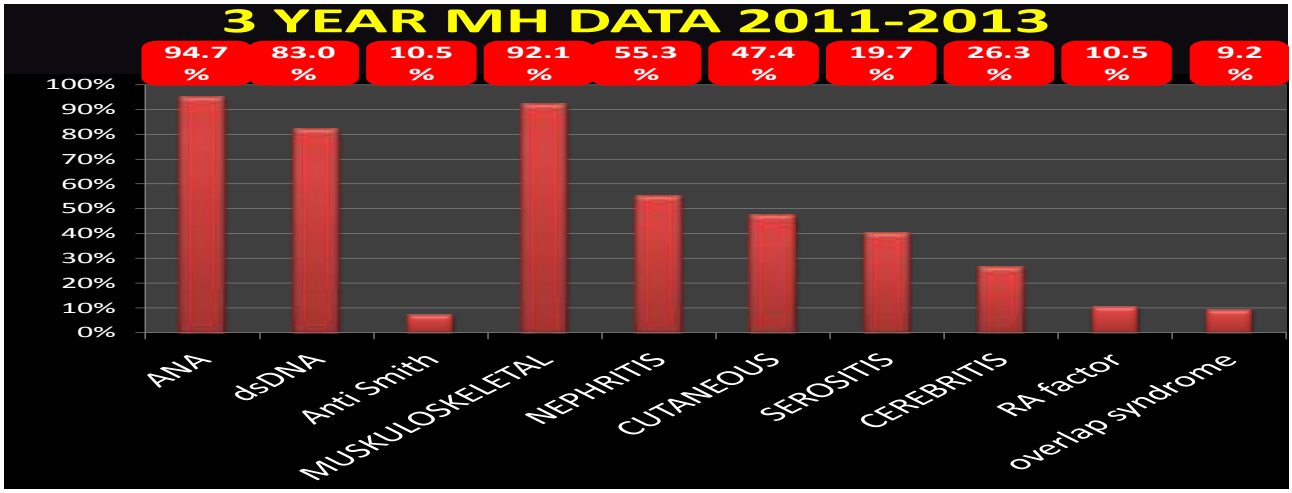

Figure: Clinical-Immunological features of SLE.

were seen in 36 patients (47.4%). Twenty patients (26.3%) had oral ulcers. Thirteen patients (17.1%) had alopecia that was non-scarring, 15 (19.7%) patients had serositis mostly pleural effusion and ascites while none had pericardial effusion. Lupus nephritis documented by either increasing creatinine, proteinuria (>0.5g) or casts was seen in 42 patients (55.3%). Twenty patients (26.3%) had neurological symptoms including headache, seizures and neuropsychiatric symptoms comprising hallucination and psychosis, 57 patients (75%) had hematological involvement comprising either leucopenia or thrombocytopenia or anemia. Nine patients (11.83%) had pulmonary involvement mainly pleurisy (9.2%), pulmonary fibrosis (1.31%) and pulmonary hemorrhage (1.31%). Seven patients (9.2%) had pattern consistent with overlap syndrome (figure).

Autoimmune profile revealed that ANA was the most prevalent antibody followed by anti-dsDNA antibody whereas anti-smith antibody was seen in only minority of patients. Eight patients (10.5%) had RA factor positive out of which only 3 patients (4%) had features of rheumatoid arthritis. Two (2.63%) out of those 3 patients with rheumatoid arthritis had hand joint deformities and 1 (1.31%) patient had not developed any deformity yet.

DISCUSSION

This is a unique study as it shows comparison of not only the Pakistani data but also the comparison with different studies of regional countries at the same time. SLE is a multi-system autoimmune disease the exact mechanism of which is unclear however various factors implicated in the disease pathogenesis include hormonal, immunological and environmental factors on the background of genetic predisposition[9,10]. It is predominantly seen in female patients. This increased female preponderance depicts the hormonal factors especially increased estrogen role in altering the immune responses in women of childbearing age[11,12]. In this study female-male ratio was 11.6:1 which shows some similarity to other Pakistani and regional studies except for the study conducted by Batool S et al[13] that showed a lowest ratio of 4:1 (table-I) and study carried out in Dubai that revealed a highest ratio of 20.5:1 (table-II). This difference in Lahore based study could be a random finding considering small sample size[13]. Mean age of presentation in this study was 33 years that is comparable to some regional studies (table-II). In this study musculoskeletal symptoms comprising joint pains remained the most common symptom (92.1%) quite comparable to Lahore based study but less than

Table-I: Comparison of this study with other Pakistani studies.

	This study	Tahir et al[14] (Rawalpindi)	*p*-value	Ishaq et al[15] (Karachi)	*p*-value	Rabbani et al[16] (Agha Khan)	*p*-value	Batool et al[13] (Lahore)	*p*-value
No of patients	76	49		105		198		61	
Female-Male ratio	11.6:1			16:1		7:1		4:1	
Mean age at presentation	33					31			
Musculoskeletal	92.1	98	0.1646	77	0.0195	38	0.0001	90.2	0.6895
Renal	55.3	38	0.0718	22.8	0.0001	33	0.0007	75.4	0.0145
Neuropsychiatric	26.3	14	0.1106	14	0.0431	29	0.6836	65.5	0.0001
Hematological	75	22	0.0001			26	0.0001	98.4	0.0001
Serositis	19.7			8.6	0.0288	29	0.1275	39.3	0.0115
Pulmonary	11.83	12	0.9461	2.8	0.0165			23	0.0838
Cardiac	0	12	0.0001					13.1	0.0011
Cutaneous	47.4	64	0.0819	37	0.1681	29	0.0036	40	0.3468
Oral ulcers	26.3	58	0.0005	22.8	0.4994	20	0.2733		
Alopecia	17.1	34	0.0246			22	0.3967	86.9	0.0001
ANA	94.7	100	0.1026			86	0.0001	90.0	0.3065
Anti-dsDNA	83	64	0.0131	74	0.1683	74	0.1106	85.2	0.7095
Anti smith	7.9					50	0.0001	26.0	0.0037

that studied by Tahir et al[14] in which it is noted to be highest (98%).These symptoms were much higher than other Pakistani studies by Ishaq et al[15] and Agha khan based study by Rabbani et al[16] (*p*-value <0.05). This striking difference from Karachi based study could be due to under raised creatinine in this study was quite high as compared to many other studies done in Pakistan with exception of Lahore based study which showed the highest percentage of kidney involvement among all studies (table-I). Regionally this data is comparable to the studies

Table-II: Comparison of this study with other Asian studies.

	Pakistan	Iran [19]	*p*-value	India[20]	*p*-value	Saudia[21]	*p*-value	Dubai[17]	*p*-value
Number of patients	76	2280		1366		624		151	
Female-Male ratio	11.6:1	9:1		11:1		9.8:1		20.5:1	
Mean age at presentation	33	24.4						35.5	
Musculoskeletal	92.1	83.2	0.0397	85	0.0877	80.4	0.0121	88	0.3519
Renal	55.3	65.4	0.0684	73	0.0008	47.9	0.2740	50	0.4827
Neuropsychiatric	26.3	23.4	0.5521	51	0.0001	27.6	0.8179	15.9	0.0609
Hematological	75	66.4	0.1178					61.6	0.0440
Serositis	19.7		0.0428	22	0.6477	27.4	0.1531		
Pulmonary	11.83	21.5	0.042			20.4	0.0766	30.5	0.0020
Cardiac	0	17.2	0.0001			20.8	0.0001	30.5	0.0001
Cutaneous	47.4	81.1	0.0001	58.5	0.0559	47.9	0.9280	60.3	0.0647
Oral ulcers	26.3			55	0.0001	64.3	0.0001	27.2	0.8933
Alopecia	17.1							50	
Overlap syndrome	9.2	7.6	0.6003						
ANA	94.7			98	0.0001	98	0.0001	98	0.0001
Anti dSDNA	83	83.2	0.9439	67	0.0039	93	0.0025	88.7	0.2196
Anti Smith	7.9			31	0.0001	40	0.0025		

Table-II: Comparison of this study with other Asian studies.

	Pakistan	Kuwait[22]	*p*-value	Malaysia[23]	*p*-value	Hongkong[18]	*p*-value	Korea[24]	*p*-value
Number of patients	76	108		539		709		466	
Female-Male ratio	11.6:1								
Mean age at presentation	33								
Musculoskeletal	92.1	87	0.2768	36	0.0001	77.8	0.0036	70.4	0.0001
Renal	55.3	37	0.0254	50	0.8900	33	0.0001	36.7	0.0021
Neuropsychiatric	26.3	23	0.7275	23	0.5235	5.6	0.0001	5.8	0.0001
Hematological	75								
Serositis	19.7			6	0.0001	50	0.0001	27.5	0.1562
Pulmonary	11.83								
Cardiac	0								
Cutaneous	47.4	43	0.0588	61	0.0231	56	0.1507	25.5	0.0001
Oral ulcers	26.3	33	0.2348	24	0.6499	16.6	0.0353	31.8	0.3413
Alopecia	17.1	44	0.0001			84	0.0001		
Overlap syndrome	9.2								
ANA	94.7	94	0.0001						
Anti-dSDNA	83	58	0.0013			65	0.0017		
Anti Smith	7.9	13	0.2405			12	0.2894		

reporting by patients in those studies apart from environmental factors. Arthralgias were also higher than all other studies done in regional countries (table-II). In this study there was no joint deformity in those patients having solely SLE. However, joint deformities were present in patients having concomitant RA. Renal involvement in the form of proteinuria, casts or carried out in Dubai by Saleh et al[17] and Hong Kong based study[18] but less than that of Iranian study by Akbarian et al[19] and Indian study by Malaviya et al[20]. This signifies that renal involvement is quite common in our country in contrast to some other Pakistani studies done previously and as shown in Lahore based study. It might be because the patient population

presenting late with complications to this tertiary care hospital after having been managed at local facilities for some time.

Neuropsychiatric manifestations including a headache, seizures, and psychosis were almost equal to study carried out in Agha Khan and slightly more than study in Rawalpindi but there was marked difference from the Lahore based study (table-I). Regional comparison of neurological features showed CNS features comparable to studies by Al Afraj et al in Saudi Arabia[21], Al-Jarallah et al[22] in Kuwait and Wang et al[23] in Malaysia along with Iran based study (table-II). On the other hand Korean study by Chun et al[24] and Hong Kong based study had much lower frequency while Indian study showed much higher frequency of CNS involvement (table-II). It underscores the role of various stressors including chemical, dietary and environmental factors at play on the background of genetic differences in various population[9]. Hematological involvement was much higher in this study amounting to 75% that included anemia (35%), leucopenia (75%) thrombocytopenia (40%). These figures are higher than most other local and regional studies except the study in Kuwait[22] that showed 83% leucopenia and Lahore based study[13] showing >90% of anemia. Iranian data echoed a similar outcome of hematological involvement in about 66% of patients (table-II). These differences could be because the patients undergoing treatment in different centers had better hematological profile than those without management or delay in treatment before reaching tertiary care hospital.

Cutaneous features also had significant differences from some local and regional studies. Although a declining trend in the malar rash was noted in Karachi based study by Ishaq et al[15] (37%), a significant decrease was present in Agha khan based study by Rabbani et al[16] showing it to be much less at 29% (p-value<0.05) but these features were more often seen in the study by Tahir et al[14] at 64%. The results of this study were consistent with many regional countries except those of Akbarian et al[19] in Iran where cutaneous features were noted to be highest at 81.1%, while in Korean study[24] these features were significantly less constituting only 25.5% of the sample population (p-value of 0.0001). Alopecia, though comparable to some previous Pakistani studies had a striking difference from that of Batool et al[13] that had the highest percentage of alopecia (88.6%) among Pakistani studies (table-I). This data regarding alopecia was also lower than most other regional studies (table-II). These differences also highlight the hormonal and environmental factors especially ultraviolet (UV) light affecting varyingly in disease pathogenesis[9,12]. Oral ulcers were also comparatively lower than previous Pakistani study by Tahir et al[14] but similar to Karachi based studies (table-I) and it was also lower than that of Indian, Saudi Arabian, and Singapore based studies (table-II). This variation might reflect the painless nature of lesions leading to under-reporting by patients at initial presentation.

The pulmonary manifestations were noted in 11.83% comprising pleural effusion, pulmonary fibrosis and alveolar hemorrhage. These results were consistent with other Pakistani studies including those of Tahir et al[14] and Lahore based study[13]. The Agha khan based study[16] depicted[17] lung involvement while Ishaq et al[15] showed 2.8% pulmonary involvement and 8.6% serositis. But these figures were lower than that of Saudi Arabian study[21] (20.4 %) with 15.9% pleurisy and 4.5% pulmonary fibrosis and Iran based study[19] (21.5%). There was no cardiac involvement in these patients as was also noted by Ishaq et al[15] in contrast to other local and regional studies that showed cardiac features of ranging from 12-30%. (table-I & II). Overall serositis including pleural effusion and ascites was seen in 19.7% of this patient population. Overlap syndrome with other connective tissue diseases including rheumatoid arthritis and scleroderma was noted in 9.2% similar to that of Iranian study[19] where it was 7.6%. There was no mention of it in other local studies.

Among autoimmune profile ANA was present in more than 90% of these patients that

matched with many local and regional studies (table-I, II) but anti-dsDNA antibody was also seen in majority of patients (83%) in this study which is consistent with other local studies but significantly higher than study by Tahir et al[14] where it was 64%. Regionally dsDNA was comparable to Iran and Dubai based study but higher than Kuwait, Hong Kong and Indian studies and less than Saudi Arabia based study (p-value<0.05) (table-II).

The limitations of this study include a small sample size of 76 patients as compared to many studies done in Asia. Findings of this study cannot be generalized as the study was conducted in a single tertiary care hospital. Increased incidence of renal and neurological features might represent the late presentation to the tertiary care hospital and delay in diagnosis and treatment.

CONCLUSION

Renal and hematological involvement was more common in this study population while mucocutaneous features and neuropsychiatric features were comparable to many local studies with exception to that of Lahore based study that showed much higher percentage of these features. These results reflect the need to have a high index of suspicion for kidney and hematological involvement in SLE patients.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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