RHEUMATOLOGY RESEARCH JOURNAL

Vol. 2, No. 2, April 2017, 51-59
Webpage: http://rheumres.org
Email: editor@rheumres.org
ISSN: 2476-5856
doi: 10.22631/rr.2017.69997.1017

Research Article **Open Access**

Clinical picture of lupus nephritis in patients with systemic lupus erythematosus (SLE): Results of a large survey

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Systemic lupus erythematosus (SLE) is a chronic multisystem disorder. Lupus nephritis (LN) is a common serious complication of SLE. LN needs prolonged care and complex therapeutic modalities. This study assessed the characteristics of Persian SLE patients with LN (LN subgroup) and an SLE subpopulation without LN (non-LN subgroup). Furthermore, the association of LN with extrarenal manifestations of SLE was studied. This study assessed 2355 SLE patients from the electronic database of the Rheumatology Research Center (RRC), Tehran University of Medical Sciences (TUMS). The clinical and laboratory data of enrolled patients was retrieved. The chi-square test was used to compare extrarenal manifestations of the LN and non-LN subgroups. Odds ratios (OR) were used to present the strength of associations. The LN subgroup included 1604 cases (68.1%) with a mean age at SLE onset of 24.6±12.5 years and a female-to-male ratio of 8.7/1. Class IV nephritis was the most common type of LN (53.1%). The comparison of extrarenal manifestations revealed statistically significant differences between LN and non-LN subgroups. Major organ involvement including cardiopulmonary, hematologic, musculoskeletal and neuropsychiatric features was significantly more common in LN patients. On the contrary, discoid rash was significantly more common in the non-LN subgroup. This study revealed that LN is positively associated with musculoskeletal, mucocutaneous, and neuropsychiatric features of SLE.

Keywords: kidney, nephritis, systemic lupus erythematosus.

Introduction

Systemic lupus erythematosus (SLE) is a chronic and recurrent autoimmune disease with diverse clinical manifestations and a highly variable prognosis [1]. The underlying pathogenesis and causative factors of SLE are yet to be elucidated. A combination of genetic and environmental factors have been implicated in disease susceptibility [2, 3].

An overall incidence rate of 1.4 to 21.9 and a prevalence rate of 7.4 to 159.4 per 100,000 have been reported for SLE [4]. Marked disparities in prevalence rates of SLE have been noted across different ethnicities [4]. The reported prevalence of SLE in the Persian population is 40 per 100,000 [5]. There is significant patient-to-patient variability in the clinical manifestations and severity of SLE [6]. Population-specific risk factors play key roles in the development of SLE clinical variants based on ethnicity and geography [2].

Renal involvement is common in SLE. It is estimated that up to 90% of SLE patients have pathologic evidence of renal involvement on biopsy, while only 50% of cases develop clinically-significant nephritis [7]. A study of lupus in a Spanish population reported a 30.5% prevalence rate for LN. The response rate in this study was 68.3%, and 10.35% of LN cases developed end-stage renal disease [8]. A study by Maroz et al. revealed that 10-15% of the progression of LN to ESRD occurred within 15 years of diagnosis [9]. Another survey in a multi-ethnic population reported a prevalence rate of 32.9% for LN among SLE patients [10]. It is noteworthy that this survey emphasized the differential prevalence of LN among various ethnic subpopulations [10].

LN incidence and prevalence rates depend on the selected population and the SLE diagnostic criteria [7, 11]. Furthermore, according to previous large surveys, LN tends to develop at a younger age [12]. The cumulative incidence of LN is relatively higher in Asian, African, and Hispanic populations in comparison with Caucasians [4, 6, 11, 13, 14].

A number of clinical features have been reported by previous studies as risk factors for the development of LN, such as malar rash, pericarditis, arterial

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Received: 10 December 2016; **Accepted:** 05 February 2017

hypertention, anemia, low levels of serum complements, and raised anti-dsDNA [8, 9, 10]. Risk factors for progressive LN are male gender, African lineage, Hispanic ethinicity, age less than 24 years, hypertension, anemia, serum antiphospholipid antibodies, and non-compliant patients [7].

The current study assessed the clinical, laboratory, and therapeutic aspects of LN in a large sample of SLE patients and compared these characteristics with those of SLE patients without LN.

Materials and Methods

In this cross-sectional study, the electronic database of the Rheumatology Research Center (RRC) of Tehran University of Medical Sciences (TUMS) was used, which had the registered and updated demographic features, clinical and paraclinical manifestations of 2355 SLE patients between 1976 and 2011. The electronic database, launched in 2007, contains the data of ongoing referrals of SLE patients to this academic center since 1987. Patients diagnosed with SLE based on the American College of Rheumatology (ACR) criteria for classification of SLE [11, 12] were enrolled. Patient follow-up visits were scheduled every 1–3 months depending on the severity of the disease.

Laboratory tests included complete blood count (CBC), urinanalysis, biochemistry, immunologic tests such as antinuclear antibody (ANA) (Antibodies Incorporated, Davis, USA), anti-double stranded DNA (dsDNA) (Biomatik,Wilmington, USA), and complement factors (C3 and C4) (Abcam, Cambridge, USA).

Renal involvement was defined by persistant abnormal proteinuria (>150 mg/24 hour) and/or the presence of cellular cast. Patients with dipstick-positive proteinuria were further evaluated by a 24-hour urine study. A renal biopsy was performed for patients with confirmed proteinuria (>0.5 g in 24-hour urine samples) or active urinary sediment, and specimens were studied by light and immunofluorescence microscopy. All biopsies were examined by one pathologist at the academic hospital. The classification of lupus nephritis was based on the 1982 WHO classification criteria [13, 15]. In the current study, a serum creatinine level between 1.5 and 3 mg/dl was considered as a mild to moderate rise, and >3mg/dl was considered as a severe creatinine rise. Hypertension was defined as a persistently elevated blood pressure above 140/90 mmHg and/or the use of antihypertensive treatment [14].

Clinical manifestations of SLE were compared in LN and non-LN subgroups. Moreover, the LN cases in this study were compared with those in other large surveys. Histologic findings and treatments were compared between patients with creatinine rise and normal creatinine.

Statistical analysis

For LN patients' charactristics, either means with standard deviations (Mean±SD) or percentages were determined. Chi-square and Fisher's exact tests were used to examine statistical differences. Odds ratios (OR) and a 95% confidence interval (95% CI) were calculated to evaluate the effect size of the association. T test was used to compare mean ages. A p-value less than 0.05 was considered as statistically significant. This statistical analysis was performed by SPSS software version 20.0 (Chicago, IL).

Results

Among the 2355 SLE patients, nephritis developed in 1604 (68.1%) cases. The LN subset was comprised of 1439 female (89.7%) and 165 male patients (10.3%). In LN cases, the female-to-male ratio was 8.7/1. The mean age at disease onset was 24.6±12.5 years, and the mean disease duration was 8.4±9.3 years. Renal involvement was the first presenting manifestation in 58 patients (3.6%, CI: 2.7-4.5).

Renal biopsies of 832 patients (51.8% of patients with renal involvement) were available for analysis. Class IV was the most common type of LN (53.1%) and class III was the second most common type of nephritis (25.12%) (Table 1).

A total of 1470 (91.4%) patients had persistent proteinuria after confirmation of LN and while receiving treatment. In 24.3% of the patients, proteinuria was in the nephrotic range. Renal biopsies in this group identified class III nephritis in 134 cases and class IV in 256 cases. Cellular cast and hematuria were seen in 33.5% and 59.4% of patients, respectively. Furthermore, hypertension and edema were detected in 28.9% and 24% of the patients, respectively (Table 1).

Among the patients in this study, 22.8% had a rise of creatinine in the course of their disease. Patients with raised creatinine levels had more common history of oral cytotoxic, methylprednisolone and cyclophosphamide pulse administration. Conversely, patients with a creatinine rise had a lower rate of antimalarial drug consumption and a lower prevalence of class II histological type (Table 2).

Table 1. Renal manifestations of systemic lupus erythematosus (SLE)

Presentation	Frequency	
	Number	%
Proteinuria (150-500mg/day)	434	27.0
Proteinuria (500-3000mg/day)	645	40.2
Proteinuria (>3000mg/day)	391	24.3
Cellular Cast	538	33.5
Hematuria (>5 RBC/hpf) [§]	954	59.5
Raised Creatinine (Mild to moderate)[¶]	319	19.9
Raised Creatinine (Severe)[ǂ]	47	2.9
Hypertension	464	28.9
Edema	386	24.0
Biopsy	832	51.8
Class I	3	0.4 [¥]
Class II	92	11.1[¥]
Class III	209	25.1 [¥]
Class IV	442	53.1 [¥]
Class V	86	10.3 [¥]

[¥]: Percent from patients with biopsy, [§]: RBC: Red Blood Cell, hpf: high-power field, [¶]: Creatinine <3mg/dL, [ǂ]: Creatinine >3mg/dL

No difference in mean age at disease onset was observed in patients with or without LN (p-value=0.363).

A comparison of the initial SLE manifestations in LN and non-LN subgroups revealed that constitutional (p-value<0.001, OR=1.72) and musculoskeletal (p-value=0.031, OR=1.21) manifestations were significantly more common in the LN subgroup. Conversely, cutaneous manifestations (p-value=0.005, OR=0.76) were significantly less common in the LN subgroup.

Throughout the course of the disease, LN patients had significantly higher rates of mucocutaneous (82.1% vs. 78.1%, p-value=0.022), musculoskeletal (86.9% vs. 75.8%, p-value<0.001), and neuropsychiatric (27.3% vs. 25.6%, p-value<0.001) features. The detailed comparison of extrarenal manifestations during the course of SLE in LN and non-LN is tabulated in Table 3. Discoid rash was significantly less common in LN patients. Photosensitivity and pulmonary hypertension were less common in LN patients; however, the difference was not statistically significant. Other mucocutaneous, constitutional, musculoskeletal, neuropsychiatric, pulmonary, cardiac, and hematologic manifestations were more common in LN patients, and the differences among all these items were statistically-significant.

The prevalence of positive FANA, raised anti-dsDNA, and low complement levels were higher in the LN subset than the non-LN subgroup with statistically significant differences.

The administration of a moderate to high dose of steroids, oral cytotoxic, methylprednisolone, and cyclophosphamide pulse was more common among the LN subgroup, whereas antimalarial drugs were less frequently used in comparison with non-LN patients (Table 4).

The comparison of LN subsets in the current study and in different surveys revealed a discernible clinical picture of SLE among the studied population (Table 5).

Table 2. Comparison of raised creatinie between various subgroups of lupus nephritis, therapeutic regimens and in Anti ds-DNA positive cases

Manifestations	Raised Cr		Normal Cr		P-value	OR (95%CI)
	N	%	N	%		
Class 1	0	0	3	0.23	0.910	0.88 (0.10-7.91)
Class 2	10	2.82	82	6.54	0.008	0.41 (0.21-0.81)
Class 3	40	11.29	169	13.48	0.280	0.82 (0.57-1.18)
Class 4	145	40.96	297	23.70	0.000	2.23 (1.74-2.86)
Class 5	14	3.95	72	5.74	0.186	0.67 (0.38-1.21)
Antimalarial Drugs	247	69.77	1028	82.04	0.000	0.55 (0.42-0.72)
Pulse methylprednisolone	121	34.18	190	15.16	0.000	3.02 (2.31-3.95)
Oral Cytotoxics	222	62.71	525	41.89	0.000	2.50 (1.95-3.20)
Pulse Cyclophosphamide	164	46.32	432	34.47	0.000	1.72 (1.35-2.19)
Anti-dsDNA positive	250	70.62	905	72.22	0.931	1.01 (0.77-1.32)

Cr: Creatinine, N: Number

Table 3. Comparison of demographic features and clinical manifestations between lupus nephritis (LN) and non-LN subgroups

Characteristics/Symptoms	LN		Non-LN		Comparison		
	N	%	N	%	Chi	p Value	OR (95% CI)
Female	1439	89.5	677	89.9	0.072	N.S	-
Male	165	10.3	74	9.8	0.109	N.S	-
Constitutional Manifestations	1072	66.7	367	48.7	69.581	<0.001	2.12 (1.78-2.52)
Musculoskeletal Manifestations	1396	86.9	571	75.8	45.026	<0.001	2.14 (1.71-2.67)
-Arthritis	886	55.1	352	46.7	14.463	<0.001	1.41 (1.18-1.67)
-Aseptic Necrosis	96	6.0	16	2.1	16.804	<0.001	2.93 (1.71-5.01)
-Myositis	58	3.6	11	1.5	8.338	0.003	2.53 (1.32-4.85)
Mucocutaneous Manifestations	1319	82.1	588	78.1	5.265	0.022	1.28 (1.03-1.59)
-Malar Rash	1003	62.4	418	55.5	10.199	0.001	1.34 (1.12-1.60)
-Photosensitivity	904	56.3	447	59.4	2.025	N.S	-
-Oral ulcer	674	41.9	237	31.5	23.704	<0.001	1.58 (1.31-1.89)
-Discoid Lesions	189	11.8	149	19.8	26.920	<0.001	0.54 (0.43-.068)
Neuropsychiatric Symptoms	439	27.3	193	25.6	32.124	<0.001	1.74 (1.44-2.11)
-Convulsions	240	14.9	69	9.2	15.009	<0.001	1.74 (1.31-2.31)
-Psychosis	90	5.6	23	3.1	7.291	0.007	1.89 (1.18-3.01)
-Peripheral Neuropathy	109	6.8	30	4.0	7.246	0.007	1.76 (1.16-2.66)
Pulmonary Manifestations	403	25.1	102	13.5	40.541	<0.001	2.14 (1.69-2.71)
-Pleuritis/ Pleurisy	296	18.4	82	10.9	21.611	<0.001	1.85 (1.42-2.40)
-Lupus Pneumonitis	41	2.6	6	0.8	7.213	0.007	3.27 (1.38-7.73)
-Pulmonary hypertension	3	0.2	2	0.3	0.755	N.S	-
Cardiac Manifestations	324	20.2	74	9.8	39.058	<0.001	2.32 (1.77-3.04)
-Pericarditis	182	11.3	32	4.2	31.134	<0.001	2.88 (1.96-4.24)
-Valvular lesions	73	4.5	14	1.9	10.399	0.001	2.51 (1.41-4.49)
-Cardiomyopathy	31	1.9	4	0.5	5.934	0.015	3.69 (1.30-10.50)
Leucopenia	630	39.2	199	26.4	36.726	<0.001	1.80 (1.49-2.18)
Hemolytic Anemia	77	4.8	22	2.9	4.461	0.035	1.68 (1.03-2.71)
Thrombocytopenia	314	19.5	108	14.3	9.431	0.002	1.45 (1.15-1.84)
Positive FANA	1296	80.6	560	74.4	12.032	<0.001	1.45 (1.18-1.78)
Raised Anti-dsDNA	1212	75.4	464	61.6	48.475	<0.001	1.93 (1.60-2.31)
Low C3	910	56.6	228	30.3	142.566	<0.001	3.02 (2.51-3.63)
Low C4	907	56.4	258	34.3	100.893	<0.001	2.50 (2.08-2.99)

LN: Lupus nephritis, CI: Confidence intervals, N.S.: Non-significant

Table 4. Comparison of therapeutic agents between lupus nephritis (LN) subgroup and non-LN subgroup

Symptoms	LN			Non-LN			Comparison		
	N	%	CI	N	%	CI	Chi	p Value	OR (95% CI)
Oral Cytotoxics	596	37.1	34.7-39.5	163	21.6	18.7-24.5	56.033	<0.001	2.14 (1.75-2.62)
Antimalarial Drugs	1275	79.3	77.3-81.3	663	88.0	85.7-90.3	26.475	<0.001	0.53 (0.41-0.68)
Moderate Dose Steroids ¥	710	44.2	41.8-46.6	196	26.0	22.9-29.1	71.434	<0.001	2.26 (1.87-2.73)
High Dose Steroids ǂ	677	42.1	39.7-44.5	142	18.9	16.1-21.7	122.529	<0.001	3.14 (2.55-3.87)
Pulse Methylprednisolone	311	19.4	17.5-21.3	29	3.9	2.5-5.3	99.918	<0.001	6.00 (4.06-8.88)
Pulse Cyclophosphamide	747	46.5	44.1-48.9	50	6.6	4.8-8.4	363.942	<0.001	12.25 (9.05-16.60)
Azathioprine	142	8.8	7.4-10.2	38	5.0	3.4-6.6	10.453	0.001	1.83 (1.26-2.64)
Methotrexate	57	3.5	2.6-4.4	33	4.4	2.9-5.9	0.976	N.S.	-
IVIG	2	0.1	-0.1-0.3	2	0.3	-0.1-0.7	1.726	N.S.	-
Plasmapheresis	15	0.9	0.4-1.4	2	0.3	-0.1-0.7	2.332	N.S.	-
Aspirin	81	5.0	3.9-6.1	26	3.5	2.2-4.8	2.986	N.S.	-
Warfarin	16	1.0	0.5-1.5	14	1.9	0.9-2.9	3.047	N.S.	-
ACEI	89	5.5	4.4-6.6	14	1.9	0.9-2.9	16.627	<0.001	3.10 (1.75-5.48)

N: Number, N.S: Non-significant, ¥ Moderate Dose Steroids: 16-30 mg, ǂ High Dose Steroids: 31-60 mg, IVIG: Intravenous immunoglobulin, ACEI: Angiotensin Converting Enzyme Inhibitor

Table 5. Comparison of demographic and clinical features of lupus nephritis in our study and some of the previous surveys

Country	Iran	Saudi Arabia	Lebanon	Spain	France	USA
Article reference	Current article	18	19	21	20	14
Author	Faezi	Al Arfaj	Uthman	Cortés	Huong	Bastian
Number of patients	1604	299	50	78	180	88
Prevalence (%)	68.1	47.9 *P*= 0.004 OR= 2.30 (1.30-4.09)	-	-	41 *P*= 0.000 OR= 3.06 (1.71-5.46)	54.3 *P*= 0.042 OR= 1.81 (1.02-3.22)
Female to male ratio	8.7/1	8.3/1	6.2/1	3.87/1	4.45/1	-
Age at disease onset	24.6± 12.5	23.4+10.2 *P*= NS	24 *P*= NS	29±12 *P*= 0.002	25±10 *P*= NS	-
Duration of disease	8.4±9.3	9.3+5.1		11±6		1.6±1.3
Photosensitivity	904 (56.3)	76 (25.4) *P*= 0.000 OR=3.77 (2.85-4.98)	-	-	51 (28.3) *P*= 0.000 OR= 3.25 (2.32-4.56)	-
Oral Ulcers	646 (40.2)	116 (38.8) *P*= NS	-	-	-	-
Malar Rash	959 (62.5)	148 (49.5) *P*=0.001 OR= 1.51 (1.17-1.93)	-	22 (28) *P*=0.000 OR= 3.77 (2.28-6.23)	111 (61.6) *P*= NS	-
Discoid Rash	189 (11.8)	51 (17.1) *P*= 0.011 OR= 0.64 (0.46-0.91)	-	-	-	-

Country	Iran	Saudi Arabia	Lebanon	Spain	France	USA
Arthritis	886 (55.1)	208 (69.6) *P*= 0.000 OR= 0.53 (0.41-0.70)	50 (100) *P*= 0.000 OR= 0.2 (0.00-0.17)	24 (31) *P*= 0.000 OR= 2.76 (1.69-4.51)	153 (85) *P*= 0.000 OR= 0.22 (0.14-0.33)	-
Pleuritis	285 (18.6)	-	-	-	46 (25.5) *P*= 0.000 OR= 0.04 (0.02-0.06)	-
CNS Involvement	439 (27.31)	-	9 (18) *P*= NS	7(9) *P*= 0.000 OR= 3.81 (1.74- 8.35)	39 (21.6) *P*= NS	7 (8) *P*= 0.000 OR= 4.35 (1.99- 9.49)
Hemolytic Anemia	74 (4.8)	229 (76) *P*= 0.000 OR= 0.01 (0.01-0.02)	-	1(1) *P*= NS	111 (61.6) *P*= 0.000 OR= 0.03 (0.02-0.04)	-
Leucopenia	630 (39.2)	79 (26.4) *P*= 0.000 OR= 1.79 (1.36-2.37)	-	26 (33) *P*= NS	90 (50) *P*= 0.005 OR= 0.64 (0.47-0.88)	33 (37) *P*= NS
Thrombocytopenia	302 (19.7)	35 (11.7) *P*= 0.003 OR= 1.20 (1.20-2.54)	-	10 (13) *P*= NS	55 (30.5) *P*= 0.000 OR= 0.53 (0.37- 0.74)	15 (17.1) *P*= NS
Hypertension	464 (28.9)	137 (45.8) *P*= 0.000 OR= 0.47 (0.37-0.61)	-	-	6 (3.3) *P*= 0.000 OR= 11.59 (5.10-26.35)	11 (12) *P*= 0.001 OR= 2.79 (1.47-5.31)
ANA	1239 (80.7)	297 (99.3) *P*= 0.000 OR= 0.02 (0.01-0.09)	45 (90) *P*= 0.033 OR= 0.37 (0.15- 0.94)	78 (100%) *P*= 0.000 OR= 0.04 (0.01- 0.31)	169 (93.8) *P*= 0.000 OR= 0.22 (0.12- 0.41)	84 (95.2) *P*= 0.000 OR= 0.16 (0.06- 0.44)
Anti-dsDNA	1104 (71.9)	244 (81.6) *P*= 0.000 OR= 0.49 (0.36-0.68)	40 (80) *P*= 0.092 OR= 0.55 (0.27-1.11)	550±746	142 (78.8) *P*= 0.005 OR= 0.59 (0.41-0.86)	45 (51.2) *P*= 0.001 OR= 2.11 (1.37-3.25)

NS: non-significant

Discussion

Nephritis is a major cause of morbidity and mortality in SLE patients, specifically in developing countries [16]. The characteristics of LN patients have been described in several studies, but data relating to Middle Eastern countries has been scarcely reported. Iran is a country in the Middle East with a Caucasian majority population [3]. Therefore, it is a good candidate for the evaluation of the impact of genetic and environmental factors on different features of the disease.

This study identified a lupus nephritis prevalence rate significantly higher than that reported in a previous study (48%) conducted in Fars province of Iran between 2001 and 2006 [17]. This comparison may be indicative of an alarming incremental pattern of nephritis in the Persian SLE population or of a more elaborate examination of patients in the current study.

Previous studies have emphasized malar rash, pericarditis, arterial hypertension, anemia, hypocomplementemia, and elevated anti-dsDNA values as the risk factors for the development of LN [8, 9, 10]. In the current study, manifestations of 1604 SLE patients with lupus nephritis were reported. The large sample size of this study allowed for a more accurate investigation of the associations of LN in comparison with past reports.

The characteristics of the current study population were compared with those of other major surveys from

other regions in the Middle East, Europe, and North America [14, 18-21]. The overall prevalence rate of lupus nephritis was higher in the current study compared to notable surveys [22, 23]. It is noteworthy that previous studies have suggested that the highest rate of renal involvement in the world (73%) was found in Indo-Asians [16, 24].

Moreover, the female-to-male (f/m) ratio in LN cases was higher in comparison with numerous previous studies. However, no significant difference in LN prevalence between the two genders was noted. According to a review article by Al Attia et al., nephritis is more prevalent in male SLE patients [25], while Flowers et al. [26] reported no difference between genders. The f/m ratio in the current study may suggest an under-diagnosis of SLE among the male population.

Clinical and laboratory findings regarding photosensitivity, malar rash, CNS involvement, and ANA positivity were more prevalent among the current study population. Conversely, arthritis and hemolytic anemia were less frequently observed in LN cases of this study. This discordance may be due in part to the sample size and inclusion criteria of various studies. However, this notion may stress the role of geographic and ethnical variations on genetic and environmental factors. It can show the combinative role of environmental factors and genetic factors on LN presentation in patients of the current study.

The mean age at SLE onset in this study was comparable to numerous other reports [14, 18-20]. Class IV was the most common type of LN in this study, similar to reports from North America, Europe, and other countries in the Middle East [18-20, 27]. In contrast a number of surveys have reported class III type of nephritis as most prevalent in SLE patients [28, 29]. This controversial result can be due to the low number of biopsies conducted in these studies.

The comparison of LN and non-LN subgroups in the current study revealed that the involvement of major organs, including the central nervous system, hematologic, cardiopulmonary, and musculoskeletal involvements were more common in LN patients.

The comparison of the clinical picture of LN and non-LN subsets of SLE patients was performed in some previous surveys. Ayana et al. reported that pleuritis, hemolytic anemia, and hypertension were more prevalent in LN patients [30]. In a study by Huong et al., malar rash, psychosis, myocarditis, pericarditis, lymphadenopathy, and hypertension were more prevalent in patients with renal involvement [20]. In Asian SLE cases, hypertension, thrombocytopenia, and leucopenia were found to be predictors of nephritis [31]. The association between hypertension and end-stage renal disease was reported in some other studies [32, 33]. In accordance with the current results, Pristiner et al. described LN patients as having an increased frequency of central nervous system involvement, anemia, thrombocytopenia, and low complement levels [34]. Other studies have reported psychosis, pericarditis, alopecia, and articular complications were more common in the LN subset [35, 36].

According to the current results, discoid rash was significantly more common in the non-LN subset of this study. This result is in agreement with a number of previous studies [30, 37]. Nonetheless, some opposing results have been seen in a study of an Arab population which reported a positive association between discoid rash and LN development [25, 38]. These contradictory results may be due to the small sample size in some of the surveys, the variable duration of follow-up in different series, and the roles of genetics and environment on manifestations of disease as the current study was conducted in Iran and all studied cases investigated patients of Persian ethnicity.

The prevalence rates of positive FANA, raised anti-dsDNA, and hypocomplementemia were significantly higher in LN patients in the current study. These laboratory findings were in accordance with a number of previous studies [1, 20, 39-43]. Moreover, neuropsychiatric manifestations were more common in the LN subset, psychosis, peripheral neuropathy, and convulsions were significantly more common in the LN subset.

Although the number of subjects in the current study was substantial, its unicenter nature may be a limiting factor for this study. Furthermore, the authors did not have access to all renal biopsies. It is noteworthy that the center is the major referral center for SLE diagnosis and management in the country. Moreover, the current survey covered different ethnicities in Iran; however, the dataset did not discriminate among ethnicities. The diversion can be addressed in future studies.

Conclusion

This study showed that LN is associated with more extrarenal manifestations other than discoid rash that had a negative association with LN. Moreover, the results revealed that type IV nephritis was the most common type of lupus nephritis. The results suggest a

more elaborate renal work-up, specifically in the male SLE population, in order to prevent long-term sequels.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgments

The authors would like to thank the patients who confided in them.

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