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LUPUS AROUND THE WORLD

Clinical and immunological manifestations in 624 SLE patients in Saudi Arabia

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Our objective was to study the demographic, clinical, laboratory features, therapy, and outcome of systemic lupus erythematosus (SLE) patients. In this retrospective study, which covered a 27-year period (1980–2006), 624 SLE patients referring to King Khalid University hospital, Riyadh were included. There were 566 females and 58 males (9.8:1) with a mean age of 34.3 (range 8–71) years and mean age at disease onset of 25.3 years (range 0.08–67). The mean disease duration was 9.3 years (range 0.3–30). The most common disease manifestations were hematological abnormalities (82.7%), arthritis (80.4%), and mucocutaneous symptoms (64.3%). The prevalence of malar rash was 47.9%, discoid rash 17.6%, photosensitivity 30.6%, oral ulcers 39.1%, serositis 27.4%, nephritis 47.9%, and neuropsychiatric manifestations 27.6%. Lymphopenia (40.3%), anti-Ro (53.1%), anti-La (26.6%), anti-Sm (41.6%), anticardiolipin IgG (49.7%), and IgM (33.5%) antibodies were highly prevalent. Antinuclear antibodies were detected in 99.7% and anti-DNA in 80.1% patients. Low C3 and C4 were observed in 45.4% and 42.2%, respectively. Therapy included oral steroids (96.2%), IV cyclophosphamide (34.1%) and azathioprine (32.1%) along with other drugs. Long-term remission was achieved in 82.4%, disease was active in 2.6%, renal failure occurred in 4.3% requiring dialysis, 6.7% lost follow up and 4.0% patients died. Infections (48%) and active SLE (36%) were the common causes of death. The 5- and 10-year patient survival rate was 98% and 97%, respectively. This study suggests that, in our patients, SLE manifests with features similar to SLE patients from other Arab countries and Caucasia. In comparison to Caucasians, higher prevalence of anti-Ro antibodies is observed in our study, in some Middle-Eastern and Asian countries; this may likely be due to inter-ethnic variation owing to genetic differences. Our 5-year patient survival rate was similar to that of western countries, while 10-year survival rate was better than that of most places. *Lupus* (2009) **18,** 465–473.

Key words: clinical manifestations; ethnicity; immunological manifestations; outcome; Saudi Arabia; systemic lupus erythematosus

Introduction

Systemic lupus erythematosus (SLE) is a complex multisystem autoimmune disease that predominantly affects young females.[1] It manifests with a wide spectrum of clinical and immunological abnormalities.[2] The diversity in disease expression of SLE worldwide has been attributed to genetic, environmental, and socio-demographic factors.[3–5] Several studies have reported on differences in prevalence of disease manifestations and outcome of SLE in various ethnic groups, which have shown variations among African Americans, Hispanics, Caucasians, several Asian populations, and Arabs.[6–10] The Hopkins Lupus cohort, a prospective longitudinal study on SLE outcomes has shown that race is a major predictor of clinical manifestations, laboratory and serological tests, and disease-related morbidity.[11]

There are few studies on the characteristics of SLE from different regions of Saudi Arabia.[12–16] They are based on small group of patients[12–14] and some are dealing mainly with infections[15] and morbidity and mortality[16] in SLE. The present study presents a comprehensive account of the clinical, hematological, immunological features, therapy, and disease outcome of SLE in a very large cohort from Saudi Arabia in comparison with other ethnic groups and races.

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Patients and methods

The medical charts of all the patients fulfilling four or more revised American College of Rheumatology (ACR) criteria for the classification of SLE,[17] diagnosed and followed up in Rheumatology clinics at King Khalid University hospital (KKUH), Riyadh, Saudi Arabia during the 27-year period between 1980 and 2006, were retrospectively reviewed. KKUH is a 900-bed, tertiary care referral hospital offering free health care services to Saudis from different regions of Saudi Arabia as well as for its employees of different nationalities and their families. It is a multidisciplinary hospital including fully functional modern renal dialysis units. Candidates for renal transplantation are referred to transplant centres in Riyadh and abroad after work-up.

The data were retrieved on a pre-designed protocol form. Information gathered included patients' present age, age at onset, sex, marital status, nationality, disease duration (calculated from symptoms onset to end of the study or patients death), duration of follow up, different manifestations at presentation and follow up, pulmonary, gastrointestinal, and other symptoms. Laboratory data collected included the hematological, renal and immunological parameters consisting of complete blood counts, leucopenia (WBC $< 4 \times 10^9$/L), anemia (Hb < 12 gm/dL), lymphopenia, thrombocytopenia (platelets $< 100 \times 10^9$/L), erythrocyte sedimentation rate (ESR), serum creatinine, 24-h urinary protein excretion, creatinine clearance, antinuclear antibodies (ANA), double stranded (ds) DNA antibodies, anti-SSA/Ro, anti-SSB/La, anti–Smith (Sm), anti-ribonucleoprotein (RNP) antibodies, rheumatoid factor (RF), anticardiolipin (aCL) antibodies (IgG and IgM), serum complement levels (C3 and C4), and lupus anticoagulant (LAC). Data related to different treatment modalities, hospitalization, and disease outcome were also gathered. The outcome measures were remission (defined as long-term subsidence of manifestations of disease activity including clinical features and laboratory indices either on treatment or off treatment), active disease on treatment, end stage renal disease (ESRD) (defined as the need for initiation of long-term dialysis or renal transplantation), and death.

Statistical analysis

Statistical analysis of the data was performed using SPSS program version 15 and presented as percentages and means. Kaplan–Meier survival analysis was used to compute survival rates and generate the survival plots.

Results

Demographic data

A total of 624 cases of SLE were identified during the 27-year period. The demographic data are presented in Table 1. The study cohort comprised 566 females (90.7%) and 58 males (9.3%). The female:male ratio (F:M) was 9.8:1. There were 551 Saudi nationals (88.3%), 61 (9.8%) non-Saudi Arabs (from Middle East and North Africa) and 12 Asians (1.9%). Among the Asians, four were Indians, three Pakistanis, three Indonesians, one Bangladeshi, and one Filipino. As the proportion of Asians (non-Arabs) in our population was very negligible, they were not excluded or analyzed separately to study the differences in ethnicity among our cohort. Of the 247 unmarried, 31 were men and 216 were women. The mean age (at the time of study or at the time of death for expired patients) was 34.3 ± 11.9 (range 8–71) years. The sex ratio computed for three different age groups ($\leq$16, 17–50, >50 years) showed female preponderance in adult group of child-bearing age of 17–50 years (F:M; 10.7:1) when compared to overall F:M ratio (9.8:1). The F:M ratio in paediatric group was 3.3:1 and in elderly SLE 6.4:1. The mean age at disease onset was 25.3 ± 11.4 (0.08–67) years; 1 patient was SLE from birth (neonatal lupus). Onset of SLE occurred more frequently (78%) in young individuals (age group 17–50 years) when compared to paediatric and elderly. Nineteen percent were early or paediatric-onset SLE (age $\leq$ 16 years) and 2.9% were late-onset SLE (age > 50 years). The mean disease duration (till the end of the study or death for expired patients) was 9.3 ± 5.3 (range 0.3–30) years and the mean duration of follow up was 5.7 ± 4.8 (range 0.08–22.8) years. Mean duration between the onset of symptoms and the diagnosis was 0.4 ± 1.2 (range 0–7.2) years.

Four ACR criteria were prevalent in 178 (29.3%) patients, 5–8 in 398 (65.7%), and 9–11 in 31 (5.0%). The mean prevalent ACR criteria was 5.7 ± 1.5 (range 4–11). One paediatric onset (at 13 years of age) Saudi patient had all 11 criteria positive at presentation.

Clinical manifestations

The clinical manifestations as per ACR criteria are shown in Figure 1. The most frequent were hematological abnormalities occurring in 516 (82.7%), followed by arthritis in 502 (80.4%) and mucocutaneous symptoms in 401 (64.3%) patients. Malar rash occurred in 299 (47.9%), discoid rash in 110 (17.6%),

Table 1 Demographic characteristics of 624 SLE patients

Characteristic	*No. (%)*			
Sex: female	566 (90.7)			
Male	58 (9.3)			
Female:male	9.8:1			
Nationality:				
Saudis	551 (88.3)			
Non-Saudi Arabs	61 (9.8)			
Asians (non-Arabs)	12 (1.9)			
Marital status:				
Paediatric	13 (2.1)			
Single	247 (39.6)			
Married	364 (58.3)			
		F	M	F:M
Age (years)				
≤16	13 (2.1)	10	3	3.3:1
17–50	552 (88.5)	505	47	10.7:1
>50	59 (9.5)	51	8	6.4:1
Age at onset (years)		F	M	F:M
≤16	119 (19.1)	107	12	8.9:1
17–50	487 (78)	443	44	10.1:1
>50	18 (2.9)	16	2	8:1
Age (years)				
Mean ± SD (range)	34.3 ± 11.9 (8–71)			
Age of SLE onset (years)				
Mean ± SD (range)	25.3 ± 11.4 (0.08–67)			
Mean duration of disease (years)	9.3 ± 5.3 (0.3–30)			
Mean positive ACR criteria	5.7 ± 1.5 (4–11)			

photosensitivity in 191 (30.6%), and oral ulcers in 244 (39.1%) patients. Serositis was manifested by 171 (27.4%), pleuritis by 99 (15.9%), and pericarditis by 130 (20.8%) patients. Lupus nephritis diagnosed as per the ACR criteria occurred in 299 (47.9%) and neurological abnormality in 172 (27.6%) patients.

SLE was observed in relatives of 28 ($n = 617$) patients giving a rate of familial SLE of 4.5%. The other non-specific symptoms that occurred in our patients are presented in Table 2. Cushingoid facial appearance was a presenting feature in 49 (9.2%), chest pain in 150 (28.2%), cough in 133 (25.0%), shortness of breath in 165 (31.1%), ankle swelling in 148 (27.9%), and raised Jugular venous pressure in 30 (5.6%) patients (all $n = 531$). Lymphadenopathy was a presenting symptom in 125 (20.0%) patients, of whom 33 had cervical, 20 had axillary, and 36 had both cervical and axillary lymphadenopathies. Hyperlipidemia was observed in 93 (14.9%) patients. Pulmonary system was affected in 175 (28%) and gastrointestinal in 241 (38.6%) patients.

Hematological, renal and immunological abnormalities

Anemia (63.1%) was the most frequently occurring hematological abnormality in our patients (Table 3), followed by lymphopenia (40.3%), and leucopenia (30.1%). Regarding the prevalence of different antibodies, we found that ANA was positive in 622 (99.7%) patients. The two patients with ANA negative titres were positive for >4 ACR criteria of SLE diagnosis. High ANA titres of ≥1:640 were seen in 451 (72.3%) patients. The mean ANA titre was 2236.4 ± 2643.89 (1:40–1:10240). Of the 560 patients for whom data on ANA pattern were available, it was coarse speckled in 335 (59.8%), homogenous in 174 (31.1%), nucleolar in 15 (2.7%), antimitochondrial in 20 (3.6%), cytoskeletal in 9 (1.6%), centromeric in 3 (0.5%), and rim in 4

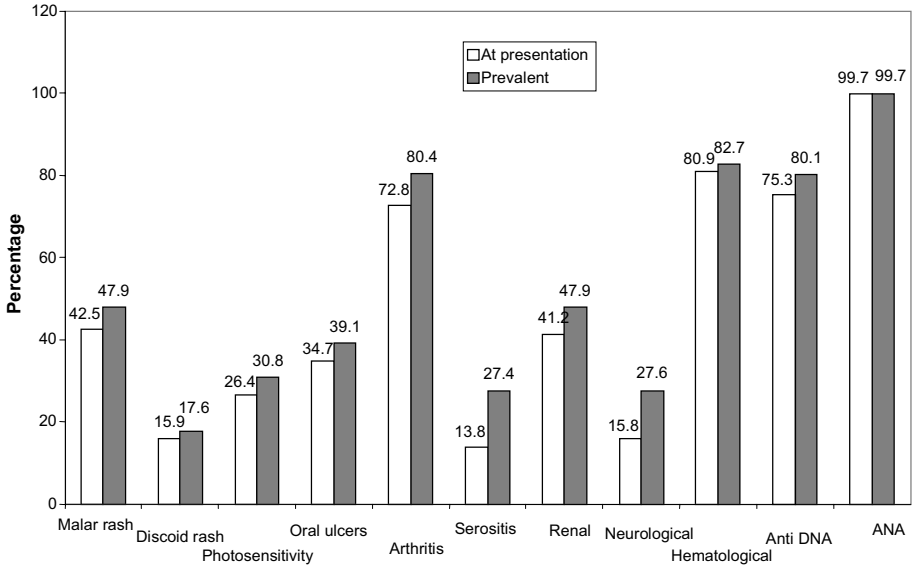

Figure 1 ACR criteria positive at presentation and prevalent.

Table 2 Non-specific manifestations in SLE patients

Clinical manifestation	*No*	*%*
General		
Fever at presentation	191	30.6
Fatigue	265	42.5
Weight loss	144	23.1
Lymphadenopathy	125	20.0
Skin–alopecia	297	47.6
Joints		
Early morning stiffness (n = 531)	126	23.7
Knee effusion (n = 531)	184	34.7
Synovitis of joints (n = 531)	169	31.8
Jaccoud's arthropathy (n = 531)	22	4.1
Avascular necrosis of hip (n = 531)	15	2.8
Vascular		
Raynaud's phenomenon	54	8.7
Livedo reticularis	4	0.6
Budd–Chiari syndrome	3	0.5
Deep-vein thrombosis	46	7.4
Hypertension	177	28.4
Pulmonary		
Pulmonary embolism	16	2.6
Interstitial lung disease	28	4.5
Lupus pneumonitis	10	1.6
Gastrointestinal		
Ascites	56	8.9
Hepatosplenomegaly	38	6.1

n = 624 where not indicated in brackets.

(0.7%). Ds DNA antibodies were positive in 80.1%, with a mean titre of 776.1 ± 830.9 (31–5120 IU/mL). Anti-SSA/Ro were found positive in 53.1% and anti-SSB/La in 26.6% (n = 207) patients. Anti-Sm antibodies were prevalent in 41.6% (n = 216), anti-RNP antibodies in 38.1% (n = 105), aCL antibodies (IgG and IgM) in 49.7% and 33.5% patients, respectively (n = 233). LAC was found positive in 27% (n = 248) patients.

Table 3 Laboratory findings in SLE patients

Parameter leucopenia	*No*	*%*
Leucopenia	188	30.0
Anemia	393	63.0
Thrombocytopenia	68	10.9
Lymphopenia (n = 350)	141	40.3
Prolonged ESR (>50)	341	54.6
Elevated serum creatinine	82	13.1
24-h urinary protein excretion		
>0.5 g/day	209	33.5
≥3.5 g/day	62	9.9
Abnormal creatinine clearance	197	31.6
Rheumatoid factor (n = 326)	75	23.0
Hypocomplementemia		
C3	283	45.4
C4	263	42.2
Anti-SSA/Ro antibodies (n = 207)	110	53.1
Anti-SSB/La antibodies (n = 207)	55	26.6
Anti-Sm antibodies (n = 216)	90	41.6
Anti-RNP antibodies (n = 105)	40	38.1
aCL antibodies		
Ig G (n = 233)	116	49.7
Ig M (n = 233)	78	33.5
Lupus anticoagulant (n = 248)	67	27.0
Anti-dsDNA antibodies	500	80.1
ANA	622	99.7

n = 624 where not indicated in brackets.

Therapy

Oral prednisolone was received by 600 (96.2%), intravenous cyclophosphamide by 213 (34.1%), and azathioprine by 200 (32.1%) patients in different combinations with other drugs. The other drugs prescribed were chloroquine given to 91 (14.6%), hydroxychloroquine to 422 (67.6%), mycophenolate mofetil to 51 (8.2%), methylprednisolone to 105 (16.8%) patients. Treatment also included plasmapheresis, methotrexate, rituximab, immunoglobulin, and cyclosporine. NSAIDS were received by 294 (47.1%) and calcium carbonate, 1 alpha, and Vitamin D were given to 272 of 434 (62.7%) patients.

Hospitalization

Patients were hospitalized for one or more reasons including SLE evaluation, disease flare up, intravenous cyclophosphamide administration, rituximab doses, renal flares, renal biopsy, dialysis, infections, and other complications. The mean number of admissions (n = 471) was 8.0 ± 8.3 (range 1–57) with a mean duration of hospital stay of 33.8 ± 33.1 (1–230) days (n = 344).

Outcome

Of the 624 patients, 464 (74.4%) achieved long-term remission on maintenance therapy; Out of these 464, some had 3–5 years of treatment-free remission periods in between. Cessation of therapy was possible in 11 (1.8%) who achieved long-term remission off treatment and had no disease flares (Table 4). Six percent could be maintained on hydroxychloroquine alone without having any relapses. In the case of 2.6%,

Table 4 Disease outcome in SLE patients

Outcome	*No*	*%*
Remission on treatment	464	74.4
Remission, therapy discontinued	11	1.8
Remission on HCC alone	39	6.3
Active disease	16	2.6
On dialysis (ESRD)	27	4.3
Lost follow up	42	6.7
Expired	25	4.0

Abbreviations: HCC: hydroxychloroquine; ESRD: End stage renal disease.

Table 5 Causes of death in 25 expired SLE patients

Causes of death	*Patients with renal failure no.*	*Patients without renal failure no.*
Active SLE, pulmonary hemorrhage	4	
Active SLE, DIC, pulmonary hemorrhage, MODS	2	
DIC, intra-cranial bleeding	1	
Sepsis, DIC, MODS	1	1
Sepsis, ARDS, MODS	1	2
Pulmonary infection, ARDS		2
Sepsis/septic shock, MODS		3
Sepsis, endocarditis/myocarditis		2
Active SLE, lupus pneumonitis		2
Active SLE, CNS complication		1
Subarachnoid hemorrhage		1
Gastrointestinal tract bleeding		1
Budd–Chiari syndrome, other complications		1

Abbreviations: ARDS: adult respiratory distress syndrome; MODS: multi-organ dysfunction syndrome; DIC: disseminated intravascular coagulopathy; CNS: central nervous system.

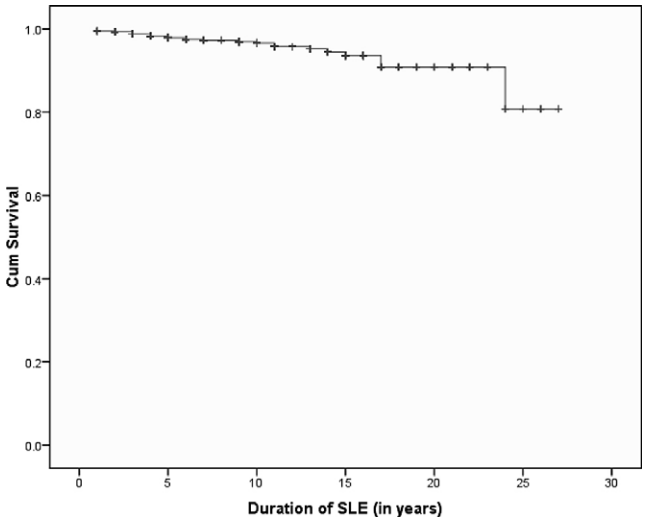

Figure 2 Kaplan–Meier survival curve of 624 SLE patients.

symptoms remained active in spite of aggressive therapy with different treatment modalities requiring repeated hospital admissions. Thirty-six (5.8%) lupus nephritis patients progressed to ESRD requiring dialysis of whom 27 (4.3%) were alive. Forty-two patients lost follow up and 25 (4.0%) patients died. The causes of death, which are listed in Table 5, show that 12 patients (48%) died due to infections. Renal failure occurred in nine (36%) patients as a contributing factor as the majority had multiple factors for death. Nine (36%) patients died due to active SLE and the remaining due to other causes. Twelve (48%) were early deaths (<5 years disease duration) and 13 (52%) were late deaths (>5 years disease duration). Early deaths were more often caused by active SLE (28%) than infections (20%), while late deaths more by infections (24%) than active SLE (12%). Gastrointestinal tract bleeding (4%) and vascular events (12%) occurred in late deaths. Almost two-thirds ($n = 15$) were aged <35 years and 20 (80%) were aged <45 years at the time of death. Mean age of expired patients was 36.5 ± 13.8 years (range 17–64), 21 were females and 4 were males. Among the youngest patients, a 17-year-old male who had LAC-positive antiphospholipid syndrome, livedo reticularis, Libman–Sacks endocarditis, died of Budd–Chiari syndrome, axillary vein thrombosis, and complications and a 17-year-old female who had lupus nephritis died of pneumonia, septic shock, disseminated intravascular coagulopathy, and renal failure. Survival analysis by Kaplan–Meier yielded a 5-year survival rate of 98% and a 10-year survival rate of 97% (Figure 2). The 5- and 10-year renal survival rates in nephritis patients were 96% and 95%, respectively.

Discussion

The diversity in the prevalence of various manifestations of SLE suggests that ethnic factors play a crucial role in the expression and severity of the disease.[18] The prevalence of clinical and immunological features of SLE have been described in various ethnic groups including African Americans,[6] Hispanics,[6] Caucasians,[6] Africans,[19] Asians,[7,8,20] and Arabs.[9,10,12–16,21–27] Table 6 shows the comparison of demographic, clinical and laboratory features in different ethnicities. The female:male ratio found in our study is closer to Europeans[1] (9.9:1), Indians[28] (11.1:1), Tunisians[24](11.5:1), but higher than in African Americans (8.1:1) and Caucasians (4.6:1) in LUMINA cohort[6], Pakistanis[8] (7.2:1), Lebanese[10] (6.4:1), and Iranians[26] (6.6:1). The rate of familial SLE observed in our study (4.5%) is similar to previous reports from Iran[26] (6.8%) and Tunisia[24] (8%), but much lower than reported from Israel [22] (24%) and Oman[23] (48%). Mean age at onset has been shown to be in the range of 25–30 years worldwide, which is similar to our finding. A study from UK has reported mean age at onset of 35.1 years.[29] The frequency of paediatric-onset SLE in our study (19.1%) was similar to Indians[28] (21%), but more than that reported in Europeans[1] and Chinese[20] (8% and 5.6%, respectively). A higher proportion of Hispanics and African Americans in LUMINA cohort,[6] Texans[30] remained unmarried when compared to patients in our study, while it was the reverse in Caucasians in LUMINA cohort[6] and Puerto Ricans.[30] The mean number of ACR criteria obtained in our study (5.7) is similar to other studies that have reported a mean of 6[6,24,30] with a range of

Table 6 Comparison of demographic, clinical, and laboratory features of SLE patients from different ethnicities worldwide

	Saudi Arabia										*6 USA - LUMINA cohort 1999*				
Ethnicity features	*Riyadh our study 2008*	*15 Riyadh 2007*	*16 Jeddah 2007*	*12 Riyadh 1995*	*26 Iran 2008*	*25 UAE 2008*	*24,27 Tunisia 2004*	*23 Oman 2003*	*22 Israel 2002*	*1 Europe 1993*	*Hispanics*	*African Americans*	*Caucasians*	*8 Pakistan 2004*	*28 India (Mean of 4 regions) 1997*
No. of patients	624	199	93	87	410	110	100	73	34	58	70	88	71	196	1366
Age onset Mean ± SD	25.3 ± 11.4	–	24	25.3 ± 10.5	–	–	32	19.0 ± 18.2	–	29.0 ± 13.0	–	–	–	31.0	24.5
Range	0.08–67									4–78				14–76	4–75
F:M	9. 8:1	4.4:1	10:1	8.7:1	6.6:1	–	11.5:1	23:1	–	9.9:1	15.7:1	8.1:1	4.6:1	7.2:1	11:1
Malar rash	47.9	27.6	37	56	60.5	62	63	–	26	58	–	–	–	29	58.5
Discoid lupus	17.6	–	7	18	49	12.8	18	–	3	10	–	–	–	14	7
Photo- sensitivity	30.6	21.6	22	26	54.5	45	53	–	24	45	–	–	–	6	48
Oral ulcers	39.1	19.1	–	16	28	23.9	–	11.9	15	24	–	–	–	19.7	55
Arthritis	80.4	–	68	90.8	65.5	86.2	78	47.8	94	84	–	–	–	38	85
Serositis	27.4	–	27	56.3	38	16.5	45	–	15	36	–	–	–	22	22
Pleuritis	15.8	–	19	–	26	–	29	23.9	–	–	–	–	–	–	36
Pericarditis	20.7	–	13	–	12	–	16	7.5	–	–	–	–	–	–	15
Nephritis	47.9	53.7	61	63.2	47.8	46.8	43	50.7	18	39	62	59	32	33	73
Neuropsychi atric	27.6	36.2	–	25.3	31.5	15.6	25	33.8	24	27	68	67	59	26	38
Hematological	82.7	–	–	78	78	60.5	–	–	–	–	90	86	77	–	21
Leukopenia	30.1	22.6	25.8	33	64.5	51.0	–	23.5	48	–	–	–	–	22	16
Thrombocytopenia	10.9	16	16	20.7	44.5	17.4	12	10.4	12	22	–	–	–	26	11
Lymphopenia	40.3	15.1	62	70	43	–	50	49	–	–	–	–	–	–	14
Anti-DNA	80.1	–	90	93	83	85.3	59.9	92	85	78	44.3	40.9	21.1	74	55
Anti-Sm	41.6	–	–	40	–	18.3	61.2	50	18	10	4.5	9.5	4.4	50	29
Anti-Ro	53.1	–	–	–	–	55	64	44	39	25	31.3	38.1	36.8	–	34
Anti-La	26.6	–	–	–	–	22	33.6	41	15	19	0.0	1.2	4.4	–	14
aCL	–	–	62	–	26	–	66	47	45	–	7	10.9	4.8	35	34.5
aCL IgG	49.7	–	–	–	–	16.5	63.5	–	–	24	–	–	–	–	–
aCL IgM	33.5	–	–	–	–	22	40.6	–	–	13	–	–	–	–	–
Lupus anti coagulant	27.0	–	–	–	–	16.5	–	–	–	15	–	–	–	–	11
ANA	99.7	–	95	98	93	98.2	100	97	100	96	98.6	97.7	91.4	86	98

Values are percentages; F:M = female:male, aCL = anticardiolipin antibodies.

4–10, but we had a patient with all 11 criteria positive at presentation.

Incidence of malar rash in our patients was similar to Kuwaitis,[9] Lebanese,[10] and Texans,[30] but a higher prevalence has been reported from Tunisians,[24] Dubai Arabs,[25] Iranians,[26] Puerto Ricans,[30] and Vietnamese.[31] A low incidence of photosensitivity has been observed in our patients when compared to majority of the studies,[1,9,24–26,28–31] which may be partly explained by lower exposure of our patients to sunlight as per traditional covering of face practiced in Saudi society. However, photosensitivity rate in our patients is similar to that in Black Caribean SLE patients[32] and Chinese, Malayan and Indian SLE patients reported by Thumboo *et al.*[7]

In comparison to other studies, we had a higher prevalence of hematological abnormalities.[9,10,23,25,31] However, our results in this regard are comparable to LUMINA cohort[6] and Iran.[26] Lymphopenia was similar to other studies in Arab patients,[23,24,26] but much lower than in UK English[29] and Texans.[30] We found ANA prevalence of 99.7%, which is similar to majority of the studies[1,6,9,12,24–26,28,30] and higher than in Pakistanis[8] (86%), Lebanese[10] (87%), and in Indians (71.4%) reported by Thumboo *et al.*[7] Ds DNA antibodies were also comparable to other reports but higher than those reported in Kuwaitis,[9] Lebanese,[10] Tunisians,[24] and Vietnamese.[31] Anti-Ro, anti-La, anti-Sm, aCL IgG and IgM were all highly prevalent in our patients when compared to Europeans,[1] African Americans,[6] Hispanics,[6] Caucasians,[6] Puerto Ricans,[30] and Indians[7,28] but similar to Arabs from Oman,[23] Dubai,[25] and Tunisia.[27] Anti-Ro antibodies are found to have a higher prevalence among these Arab patients (44.0–64%),[23,25,27] Hong Kong Chinese (59%)[20] and our patients (53.1%) when compared to Hispanics and Caucasians (25–37%) and African Americans (38%).[1,6] The high prevalence of anti-Ro antibodies in these Arab SLE patients[23,25,27] has been linked to the higher occurrence of malar rash in their patients, as an association between the anti-Ro antibodies and the cutaneous manifestations has been observed earlier.[27,33] However, we did not find high prevalence of malar rash and photosensitivity when compared to western countries, despite finding high prevalence of anti-Ro antibodies. The higher prevalence of anti-Ro antibodies observed in Arab and other Asian SLE patients when compared to Caucasian SLE patients may likely be due to inter-ethnic variation owing to genetic differences, as there is genetic influence on SLE. The immunogenetics of anti-Ro antibodies have been most extensively studied in Japanese patients, which revealed different association from those in Caucasians[34] and it is likely that similar differences may also apply to Middle-Eastern population.

Raynaud's phenomenon occurred with a low prevalence (8.7%) in our patients when compared to European[1] (34%) and UK (65%)[29] studies. It was also less than that reported from other Arab nations (19–28%).[9,24,26] Fever was a presenting symptom in 30.6% of our patients when compared to 52% in Europeans[1] and less than those reported in studies on Arabs[9,23,25,26] (31–63%). The prevalence of lymphadenopathy in our patients (20%) was more than in Iranians[26] (14%) and Europeans[1] (12%) and less than in Indians[28] (47%). Jaccoud's arthropathy occurred in our patients (4.1%) with prevalence similar to the report from Kuwait[9] (5%) and avascular necrosis (2.8%) was similar to the report from Kuwait[9] (4%) and Tunisia[24] (2%). The prevalence of gastrointestinal symptoms (38.6%) was similar to LUMINA cohort[6] in Hispanics (35%) and Caucasians (42%) but lesser than in African Americans (53%). Lupus anticoagulant (27%) was found in higher prevalence than in Europeans[1] (15%) and in UK[29] (13%).

Mortality rate of 4.0% found in our study is less than that reported from Tunisia[24] (15%), Blacks from Curacao (27%),[32] by LUMINA cohort (11.8%),[35] UK (14%),[36] and by Cervera *et al.* (6.8%).[37] Infection was the cause of deaths in 48% of our patients, similar to reports from Saudi Arabia (50%)[15] and Tunisia (40%).[24] The causes of death are similar to previous studies reporting infections and active SLE as major causes.[15,24,32,35–37] Death due to cardiovascular events (atherosclerosis and myocardial infarction) was absent in our patients; however, three (12%) deaths were of vascular etiology (intracranial bleeding, subarachnoid hemorrhage, Budd–Chiari syndrome). The low frequency of vascular complications in our deceased patients when compared to previous studies (17–26%)[35–37] could be due to high early mortality rate in our patients (48% at <5 years disease duration) compared to 24% early deaths in a previous report.[36] Further, the mean age of deceased patients in our study (36.5 years) was much lower than that reported (52.6; range 16–87 years).[36] Majority (80%) of our deceased patients were younger than 45 years.

The 5-year survival rate of 98% obtained in our patients is comparable to reported prevalence of 94.5% in Dubai Arabs,[25] 93% in Chinese,[20] and 95% in Caucasians in Euro Lupus cohort.[38] During recent decade, the mortality in SLE patients has declined substantially in most parts of the world where a 5-year survival rate of >90% is seen frequently in western countries.[39] Our 5-year survival rate is higher than that reported in Tunisians (86%),[24] Black Caribeans

(90.5%),[32] and Indians (65%).[28] The 10-year survival rate of 97% in our patients is higher than that reported by Cervera *et al.* (92%),[37] in Caucasians in Euro Lupus cohort (85%),[38] Black Caribeans (70%),[32] and Indians (50%).[28]

In comparison to previous studies on SLE from Saudi Arabia,[12–16] our study is much larger in reporting large number of patients and manifestations. The two reports published recently are dealing mainly with infections[15] and morbidity and mortality[16] in SLE. Two studies from this region have reported a very low sex ratio of 5.5:1[13] and 4.4:1[15], while other report [14] shows that SLE is very rare in males from that region (53:1). Thirty percent of our patients presented with fever, which is less than that reported by recent Saudi studies[15,16] (53–58%). In comparison to above two studies[15,16], we found a higher frequency of malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, pericarditis, and a low frequency of nephritis, neuropyschiatric manifestations, thrombocytopenia, and dsDNA antibodies in our patients. We have also reported on the prevalence of anti-Ro, anti-La, anti-Sm, aCL antibodies (IgG and IgM). Our mortality rate (4.0%) is comparable to two previous reports from Saudi Arabia (3%, 4%),[13,15], but is lower than that in other two studies, which reported a rate of 8% in 1995[12] and 9% in 2007.[16] Our 5-year and 10-year survival rates (98% and 97%)) are higher than those reported (92% and 69%) from Saudi Arabia.[16]

In conclusion, our patients had clinical disease spectra similar to those described in SLE patients from neighbouring Arab countries and from Caucasian population. The 5-year survival rate in our patients was similar to that in western countries. However, the 10-year survival rate was better than most of the other places.

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