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Clinical and Laboratory Manifestations of Yemeni Patients with Systemic *Lupus Erythematosus*

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الأعراض السريرية و المخبرية للمرضى اليمنيين المصابين بمرض الذئبة الحمراء الجهازية

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abstract: ***Objectives:*** Systemic *lupus erythematosus* (SLE) is a chronic autoimmune disease characterised by multi-systemic involvement. This is the first study undertaken to determine the relationships between serological marker positivity and age, gender, signs and symptoms, risk factors and the treatment of SLE in Yemen. ***Methods***: We investigated the cases of 149 patients with SLE admitted to Al-Thawra Hospital in Sana'a city between November 2009 and November 2010. Of the 149 patients, females represented 75.2% and males, 24.8%. ***Results***: The most frequent presenting signs and symptoms were fatigue (84.6%), fever (81.9%), arthropathy (81.2%), anaemia (64.4%), photosensitivity (54.4%), renal involvement (53%), malar rash (52.3%), and alopecia (49%). Antinuclear antibodies (ANA) were detected in 95.3% of the patients and were associated significantly with most clinical presentations, except weight loss, hypertension and serositis. Anti-ds deoxyribonucleic acid (anti-dsDNA) was detected in 59.7% of the patients, and was associated significantly with fever and fatigue. Anti-Smith (anti-Sm) antibodies were detected in 27.5% of the patients, but were not significantly associated with all clinical presentations. Social stress was the most important risk factor for inducing SLE, with an odds ratio (OR) of 6.0, followed by common exposure to sunlight (OR = 2.2). ***Conclusion***: In this study, SLE was more prevalent among females and young adults. The clinical presentation was characterised by a high incidence of fatigue and fever, and a low incidence of oral ulcers and serositis. ANA was associated with most clinical presentations except weight loss, hypertension, and serositis. Anti-dsDNA antibodies were most frequently associated with fever, fatigue and hypertension. There was no significant association of the anti-Sm antibodies with any clinical presentations.

Keywords: Systemic lupus erythematosus (SLE); Autoantibodies; Antinuclear antibodies (ANA); Anti-ds DNA; Anti-Smith Antibodies (Anti-Sm); Yemen.

الملخص: **الهدف**: مرض الذئبه الحمراء هي عبارة عن مرض مناعي ذاتي مزمن يتميز بإصابة أكثر من جهاز من أجهزة جسم الانسان. تعتبر هذه الدراسة هي الأولى في اليمن لتحديد العلاقات بين العلامات المصلية الإيجابية والسن والجنس وعلامات وأعراض هذا المرض وعوامل الخطر والعلاج لهذا المرض. الطريقة: تمت دراسة 149 مريضا يعانون من مرض الذئبة الحمراء وذلك بمستشفى الثورة في مدينة صنعاء؛ مثلت الإناث 75.2% والذكور 24.8% من كل المرضى في الدراسة. النتائج: كانت العلامات والأعراض الأكثر شيوعا هي التعب (84.6%)، والحمى (81.9%)، الاعتلال المفصلي (81.2%)، الحساسية للضوء (54.4%)، تأثر الكلى (53.0%)، وطفح وجني (52.3%)، فقدان الوزن وفقدان و تساقط الشعر (49.0%). تم الكشف عن الأجسام المضادة للنواة في 95.3% من المرضى و كانت مرتبطة بشكل كبير مع معظم الأعراض السريرية فيما عدا فقدان الوزن وارتفاع ضغط الدم و التهاب المصلية. تم الكشف عن الأجسام المضادة للحمض النووي الريبي في نحو 59.7% من المرضى، وكانت لديهم أعراض حمى وتعب وحمى. وجدت أضداد سميث في 27.5% من المرضى، ولكنها لم تكن مرتبطة بأي مرض. وكان التوتر الاجتماعي عامل الخطر الأكثر أهمية في إحداث مرض الذئبة الحمراء بنسبة ترجيحية تبلغ 6.2% تليها التعرض لأشعة الشمس بنسبة ترجيحية تبلغ 2.2%. الخلاصة: كان مرض الذئبه الحمراء أكثر انتشارا بين الإناث وصغار البالغين. تميزت الأعراض السريرية بنسبة عالية من عرضي التعب والحمى، وحدوث منخفض لقرح الفم والالتهاب المصلي. ارتبطت الأجسام المضادة للنواة مع معظم الأعراض السريرية باستثناء فقدان الوزن، ارتفاع ضغط الدم، و الالتهاب المصلي. وارتبطت الأجسام المضادة للحمض النووي الريبي مع معظم المصابين بالحمى، والتعب، وارتفاع ضغط الدم. ولم يكن هناك ارتباط كبير لأضداد سميث مع أي من الأعراض السريرية.

مفتاح الكلمات: مرض الذئبه الحمراء؛ الأجسام المضادة للنواة؛ الأجسام المضادة للحمض النووي الريبي؛ أضداد سميث؛ اليمن.

Advances in Knowledge

- *This study provides new information about systemic lupus erythematosus (SLE) in Yemen, including the ratio of males to females affected, as well as the antibody-marker association ratio with clinical manifestations, symptoms and signs. This study also highlights the potential risk factors that contribute to increasing a person's likelihood of developing SLE.*
- *Such information is important in recommending a policy for the treatment and management of SLE in Yemen, especially as there are*

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currently no other studies of this disease in Yemen.

- *Moreover, SLE is likely to be a growing problem in Yemen that could go unrecognised if new information about the disease is not promoted within the national medical community.*

Application to Patient Care

- *The findings of this research could contribute to the formulation of a treatment and management policy for SLE, including, ultimately, the management of its complications and sequelae. However, further studies are required to form a more comprehensive understanding of the risk factors and characteristics of SLE in Yemen.*

Systemic *lupus erythematosus* (SLE) is an autoimmune disorder characterised by multisystem microvascular inflammation with the generation of numerous auto-antibodies, particularly antinuclear antibodies (ANA). SLE can affect persons of both sexes, all ages, and all ethnic groups. However, more than 90% of new patients presenting with SLE are women in their childbearing years.[1] SLE is a disease that affects multiple systems and its symptoms vary widely. The multiple organ damage in SLE is due to the production of auto-antibodies, which include auto-antibodies to antigens of the brain, renal and vascular tissues, ribosomes, nuclear antigens and phospholipids. Intracranial vascular lesions (vasculitis and thrombosis) and inflammation have been related to the local release of cytokines.[1] In addition, recent data have suggested that both renal and neuropsychiatric involvement negatively affects the overall five-year survival rate. However, the neuropsychiatric involvement did not change for the 10-year survival rate, in spite of the fact that the involvement of the nervous system in SLE remains poorly understood.[2]

SLE affects the immune system, thus reducing the body's ability to prevent and fight infection. In addition, many of the drugs used to treat SLE also impair the functioning of the immune system, thereby further reducing the patient's ability to fight infection. The most common infections involve the respiratory tract, urinary tract and skin; these infections do not require hospitalisation if they are treated promptly. Other opportunistic infections—particularly salmonella, herpes zoster and *Candida* infections—are more common in patients with SLE because of altered immune status.[3–5] Fatigue in SLE is probably multifactorial and has been related not only to disease activity, but also to complications such as anaemia or hypothyroidism.

SLE is known to differ among people with different racial, geographical and socioeconomic backgrounds. Asia encompasses people of many sociocultural backgrounds with diverse ethnic groups—broadly Orientals in East and Southeast Asia, Indians in South Asia and Arabs in the Middle East. It has been shown that race is a major predictor of the clinical manifestations of SLE, laboratory and serological tests, and disease-related morbidity. Comparative studies have shown that SLE has a higher prevalence, and higher morbidity and mortality rates, in the Oriental population than among Caucasians.[3–5]

Due to a lack of national epidemiological research, the incidence and prevalence of SLE in Middle Eastern and Arab countries, have only recently been studied. There have been no previous studies on SLE in Yemen; therefore, this study aims to determine the relationships between serological marker positivity and age, gender, signs and symptoms, risk factors and the treatment of SLE in Yemen.

Methods

This study was carried out over a period of one year from November 2009 to November 2010. The study was approved by the Department of Medical Microbiology & Clinical Immunology of the Faculty of Medicine & Health Sciences at Sana'a University, Yemen. A consent form was completed by each participant.

A total of 149 Yemeni patients, admitted to medical wards and/or attending medical clinics at Al-Thawra Hospital in Sana'a city, were enrolled in this study. All patients fulfilled four or more of the revised American College of Rheumatology (ACR) criteria for the diagnosis of SLE.[6] The specifically-designed questionnaires were analysed retrospectively for relevant data such as patients' age, sex, their clinical manifestation at presentation and during follow-up, and their exposure to possible risk factors of SLE. The treatments, either initially or during their follow-up appointments,

Table 1: Gender and age distribution among systemic *lupus erythematosus* patients attending Al-Thawra hospital in Sana'a city, Yemen

Age in years	Male	Female	Total
	n (%)	n (%)	n (%)
<15	2 (5.4)	15 (13.4)	17 (11.4)
16–25	9 (24.3)	38 (33.9)	47 (1.5)
26–35	16 (43.2)	32 (28.6)	48 (32.2)
36–45	8 (21.6)	21 (18.8)	29 (19.5)
>45	2 (5.4)	6 (5.3)	8 (5.4)
Total	**37 (24.8)**	**112 (75.2)**	**149 (100)**
Mean age years	30.2	28.3	28.8
Variance years	69.9	127.8	113.5
Standard deviation years	8.3	11.3	10.7
Min years	12	11	11
Max years	49	57	57
Median years	30	26	29
Mode years	30	45	25

were also recorded, as well as any complications. Laboratory data include leukopaenia (white blood cells <4000/mm^9), anaemia (haemoglobin <11 gm\dL) and thrombocytopaenia (platelets <100,000/mm^9). Laboratory data also included Raised erythrocyte sedimentation rate, positive ANA, positive rheumatoid factor, high anti-DNA and anti-Sm antibody. ANA was measured by two different methods: indirect immunofluorescence (IIF) and enzyme-linked immunosorbent assay (ELISA), anti-ds deoxyribonucleic acid (anti-dsDNA) and anti-Smith (anti-Sm) antibodies were measured by the ELISA method (INOVA Diagnostics Kits, San Diego, California, USA). Lupus nephritis was confirmed by renal biopsy, which was graded according to the World Health Organization classification of II, III, IV or V.[6] Photosensitivity was recognised by specific skin lesions induced by sunlight. The odds ratio (OR) for the association of auto-antibody markers with clinical presentations of SLE, and their Cornfield 95% confidence limits, were calculated by the analysis of a single table (the simplest contingency table being the 2 x 2 table). Furthermore, the Chi-square (X^2) value for statistical significance was calculated using Yates' continuity correction. However Fisher's exact test was employed for small cell sizes with a two-tailed probability value (*P*), using the Epi-Info Version 6 software (Centers for Disease Control and Prevention, Atlanta, Georgia, USA). The various medications used in patient treatment ranged from non-steroidal anti-inflammatory drugs (NSAIDs), hydroxychloroquine and steroids, to intermittent cyclophosphamide with intravenous methylprednisolone in *lupus* nephritis. Warfarin was the anticoagulant used in the cases of venous thrombosis.

Table 2: The relationship between clinical manifestations and presence of antinuclear antibodies (ANA) auto-antibodies among systemic *lupus erythematosus* patients

Signs and symptoms	Positive ANA (n = 130)	OR	CI	χ^2	*P*
	n (%)				
Fever (n = 122)	114 (93.4)	9.8	3.1–32	20.2	<0.0001
Fatigue (n = 126)	117 (92.8)	10	3.1–33.4	19.9	<0.0001
Weight loss (n = 73)	67 (91.7)	2.3	0.75–7.3	1.9	0.16
Arthropathy (n = 121)	112 (92.5)	6.9	2.2–21.9	13.9	0.0001
Renal involvement (n = 79)	75 (94.9)	5.11	1.5–19.4	7.5	0.006
Malar rash (n = 78)	75 (96.2)	7.3	1.86–33.2	10.1	0.001
Alopecia (n = 73)	71 (97.2)	10.2	2.1–66.9	11.2	0.0008
Photo-sensitivity (n = 81)	78 (96.2)	8	2.1–36.5	11.34	0.0007
Serositis (n = 14)	8 (57.1)	0.14	0.04–0.55	9.8	0.003*
Oral ulcers (n = 16)	7 (43.7)	0.06	0.02–0.24	26.3	<0.0001*
Hyper-tension (n = 55)	46 (83.6)	0.6	0.2–1.8	1.02	0.03*

*ANA = antinuclear antibodies; OR = odds ratio; CI = 95% confidence interval; *Fisher's exact test P value; Significant result $\chi^2 \geq 3.84$, $P < 0.05$.*

Results

The mean age of patients was 28.8 years (range 11–57 years). Females had a higher SLE prevalence

Table 3: The relationship between clinical manifestations and presence of ds deoxyribonucleic acid (dsDNA) auto-antibodies among systemic *lupus erythematosus* patients

Signs and symptoms	Positive anti-dsDNA (n = 89)	OR	CI	χ^2	*P*
	n (%)				
Fever (n = 122)	79 (64.8)	3.1	1.2–8.12	5.96	0.01
Fatigue (n = 126)	80 (63.5)	2.7	1–7.4	3.84	0.05
Weight loss (n = 73)	49 (63.4)	1.8	0.9–3.7	2.68	0.1
Arthropathy (n = 121)	77 (63.6)	2.3	0.94–5.85	3.3	0.07
Renal involvement (n = 79)	51 (64.5)	1.5	0.75–3.13	1.23	0.26
Malar rash (n = 78)	49 (62.8)	1.3	0.6–2.6	0.41	0.52
Alopecia (n = 73)	46 (67.1)	1.3	0.64–2.7	0.4	0.52
Photo-sensitivity (n = 81)	47 (58)	0.86	0.4–1.74	0.09	0.76
Serositis (n = 14)	5 (35.7)	0.34	0.09–1.2	2.76	0.1*
Oral ulcers (n = 16)	5 (31.3)	0.34	0.09–1.18	2.69	0.1*
Hypertension (n = 55)	39 (71)	2.15	1–4.6	3.84	0.05

OR = odds ratio; CI = 95% confidence interval;
**Fisher's exact test P value; Significant result $\chi^2 \geq 3.84$, P <0.05.*

Table 4: The relationship between clinical manifestations and presence of anti-Smith antibodies (anti-Sm) auto-antibodies among systemic *lupus erythematosus* patients

Signs and symptoms	Positive anti-Sm (n = 41)	OR	CI	χ^2	*P*
	n (%)				
Fever (n = 122)	37 (30.3)	2.5	0.75–9.23	1.9	0.16
Fatigue (n = 126)	38 (30.2)	2.9	0.75–12.9	2.06	0.15
Weigh loss (n = 73)	22 (30.1)	1.3	0.6–2.8	0.27	0.6
Arthropathy (n = 121)	35 (28.9)	1.5	0.5–4.5	0.32	0.57
Renal involvement (n = 79)	20 (25.3)	0.8	0.36–1.7	0.21	0.64
Malar rash (n = 78)	25 (32.1)	1.6	0.73–3.6	1.24	0.26
Alopecia (n = 73)	24 (32.9)	1.7	0.77–3.7	1.57	0.2
Photo-sensitivity (n = 81)	22 (27.2)	0.96	0.44–2.1	0.01	0.93
Serositis (n = 14)	2 (14.3)	0.4	0.06–2.1	0.72	0.35*
Oral ulcers (n = 16)	4 (25)	0.86	0.2–3.1	0.00	1.0
Hypertension (n = 55)	15 (27.3)	0.98	0.43–2.2	0.02	0.889

OR = odds ratio; CI = 95% confidence interval;
**Fisher's exact test P value; Significant result $\chi^2 \geq 3.84$, P <0.05.*

than males, with a female to male ratio of 3:1. The prevalence of SLE was greater in the 16–35 years age group [Table 1]. The clinical presentation of SLE was characterised by a high incidence of fatigue and fever, while there was a low incidence of oral ulcers and serositis [Table 5]. The blood picture of the patients showed a low prevalence of leukopaenia and lymphopaenia, and a high prevalence of thrombocytopaenia [Table 5]. Tables 2, 3 and 4 show the relationship between the auto-antibody positivity and the clinical symptoms. ANA was statistically significant (χ^2 >3.9 and *P* <0.05) and associated with most clinical presentations (OR 5.1–10.2) except weight loss, hypertension and serositis [Table 2]. Anti-dsDNA antibodies, which are a specific marker for SLE, showed a statistically significant association with fever (OR = 3.12; CI: 1.2–8.12; X^2 = 5.9; *P* = 0.01); fatigue (OR = 2.7; CI: 1–7.4; X^2 = 3.84; *P* = 0.05), and hypertension (OR = 2.15; CI: 1.0–4.6; χ^2 = 3.84; *P* = 0.05) [Table 3]. Anti-Sm antibodies, which are a highly specific marker for SLE, were not significantly associated with any clinical presentations [Table 4]. *Lupus* nephritis was significantly associated with red blood cell (RBC) casts, proteinuria, hyaline casts, elevated creatinine levels and hypertension. The two main risk factors in Yemeni SLE patients were found to be frequent exposure to sunlight (OR = 6.0; CI: 2.6–13.9; *P* <0.0001) and to social and mental stress (OR = 2.8; CI: 0.4–9.6; *P* = 0.04), while the use of contraceptives by females was not a risk factor (OR = 0.5; CI: 0.1–1.5; *P* = 0.17). Similarly, chewing *qat* (plant containing an amphetamine-like stimulant native to the horn of Africa and the Arabian Peninsula) was not found to be a risk factor for SLE in this study (OR = 0.5; CI: 0.2–0.9; *P* = 0.01) [Table 6]. Table 5 shows the frequencies of clinical and laboratory features of SLE among different ethnicities compared with the present study. The

Table 5: Frequencies of clinical and laboratory features of systemic *lupus erythematosus* among studies of different ethnicities compared with the current study

	Yemen	Saudi Arabia[7]	UAE[9]	Kuwait[18]	Lebanon[17]	Tunis[15]	Iran[14]	Spain[10]	Pakistan[3]
Year	2010	2009	2008	1998	1999	2004	2008	2004	2004
Number of patients	149	624	151	108	100	100	410	600	196
Mean age	28.8	25.3	28.9	31.5	25	32	30.3	29	31
Male:female ratio	1:3	1:9.8	1:20.5	1:9.8	1:6.1	1:11.5	1:6.6	1:8	1:7.1
Signs and symptoms in %									
Fatigue	84.6	42.5	-	-	-	-	30.2	-	-
Fever	81.9	30.6	51.0	-	-	-	63.4	42	-
Arthropathy	81.2	80.4	81.1	87	95	78	65.5	83	38
Photosensitivity	54.4	30.6	43	48	16	53	54.5	41	6
Renal involvement	53.0	47.9	51	37	50	43	47.8	34	33
Malar rash	52.3	47.9	60.3	43	52	63	60.5	54	29
Alopecia	49	-	-	44	-	-	23.0	81	22
Oral ulcers	10.7	39.1	30.5	33	40	4	27.8	30	19.7
Serositis	9.4	27.4	27.2	-	40	45	38	-	22
Hemolytic anaemia	-	-	9.9	-	10	6	12.5	8	-
Anaemia	64.4	63.1	44.3	-	-	-	74.6	19	-
Leucopaenia	28.2	30	53.6	83	17	-	64.5	66	22
Lymphopaenia	36.2	40.3	-	-	-	50	43.4	82	-
Thrombocytopaenia	44.3	10.9	18.5	26	33	12	44.6	30	26
ANA	95.3	99.7	88	94	87	100	93	99	86
Anti-dsDNA	59.7	80.1	88.7	58	50	56	83	90	74
Anti-Sm	27.5	-	19.7	13	-	61.2	-	12	50

UAE = United Arab Emirates; ANA = antinuclear antibodies; Anti-dsDNA = anti-ds deoxyribonucleic acid; Anti-Sm = anti-Smith antibodies.

mortality rate in our study was 4.7%; the causes of death were pulmonary embolism (2%), septicaemia (2%) and disseminated intravascular coagulopathy with refractory heart failure (0.7%).

Discussion

The ratio of male patients to female patients in the current study was 1:3. This result is in disagreement with the results of other studies which have reported an even higher prevalence of SLE among females; these include male to female ratios of 1:7.2, 1:9 and 1:9.9.[3,7,8]

The mean patient age in the present study of 28.8 years was similar to that reported from Dubai, United Arab Emirates (28.9 years)[9] and Spain (29 years).[10] The majority of patients (88.6%) were adults, while 11.4% were children under 15 years. This is similar to the study by Alballa whose patients were predominately above 15 years.[11] The high rate among adults may be related to adult sex hormones which play an important role in triggering the disease.[12]

Fatigue, the most common constitutional symptom associated with SLE, could be caused by active SLE, medications, lifestyle habits or concomitant fibromyalgia—or affective disorders. Fatigue due to active SLE generally occurs in concert with other clinical and laboratory markers.[3] The most frequent clinical symptom among the SLE patients in this study was fatigue (84.6%). This finding is in contrast to other studies performed in Saudi Arabia and Iran, where the frequency of fatigue was reported as 9.2%[13] and 30.2%,[14]

Table 6: The potential risk factors of systemic *lupus erythematosus* among the patients of the current study

Risk factors	Frequency	OR	CI	χ^2	*P*
	n (%)				
Type of stress**					
Social	60 (40.2)	6.0	2.6–139	24.0	<0.0001*
Mental	19 (12.8)	2.8	0.4–9.6	3.9	0.04
Financial	7 (4.7)	0.5	0.1–1.5	1.8	0.17
Exposure to sun light (at least 2 hours/ day)	42 (28.2)	2.2	1.1–4.7	5.0	0.02*
Qat chewing†	30 (20.1)	0.5	0.2–0.9	5.6	0.01*
Oral contraceptive use	14 (12.5)	0.8	0.4–2.0	0.17	0.68

OR = odds ratio; CI = 95% confidence interval.

**Fisher's exact test P value; Significant result $\chi^2 \geq 3.84$, $P < 0.05$.*

***The stress assessment was done by the psychiatrists at Al-Thawra Hospital, Sana'a city.*

†*Qat = plant containing amphetamine-like stimulant native to the horn of Africa and the Arabian Peninsula.*

respectively. This could be explained by the fact that our questionnaire included fatigue as a potentially important symptom of SLE, while questionnaires used in previous studies did not consider fatigue to be important.

Fever was also common in the patients int this study (81.9%), and their temperature usually showed diurnal variation—being high in the afternoon and evening. The frequency of fever was higher than that reported in other studies—in Spain 42% of patients studied experienced fever, while in Saudi Arabia it was 30%.[10,7]

Arthropathy was a common sign (81.2%) in this study, and this result is similar to findings reported from Dubai (81.1%)[9] and Saudi Arabia (80.4%).[7] However, the rates of arthropathy in Yemen were far higher than those experienced in Pakistan (38%).[3] Photosensitivity occurred in 54.5% of the current study's patients, which was similar to that reported in Tunisia (53%)[15] and Iran (54.5%).[14] However, lower prevalence rates have been reported from Pakistan (6%),[3] Saudi Arabia (22%)[16] and Europe (22.9%).[8] This difference can be explained by the patients' high exposure to sunlight in this study.

In this study group, renal involvement of SLE was variable in clinical presentation and prognosis, ranging from mild asymptomatic proteinuria to rapidly progressive glomerulonephritis (GN) leading to end-stage renal disease. Renal involvement affected 53.3% of the patients. Similar findings were reported by studies in Lebanon (50%)[17] and Dubai (51%),[8] but these are in contrast to the low frequencies reported in Pakistan (33%)[2] and European countries (27.9%).[9] Yemen's findings of similar renal involvement to that of other Arabic countries (Lebanon and Dubai) may be due to the shared factors (genetic, environmental and dietary) that could trigger or control the presentation of the disease.

Malar rash was present in 52.3% of the current study's patients which is similar to findings in Lebanon (52%)[16] and Spain (54%)[9] but is in disagreement with the lower prevalence found in Pakistan (29%).[3] Alopecia occurred in 49% of our patients, which is similar to the study in Kuwait (44.0%) by Al-Jarallah *et al*,[18] but lower than that of Spain (81%), reported by Font *et al*.[10] Oral ulcers were less frequent in our study (10.7%) and were of similar occurrence to findings from Latin America (10.5%)[19] but lower than those from Lebanon (40%)[17] and Saudi Arabia (39.1%).[7] The present study had the lowest incidence of serositis (9.4%) compared to studies in Lebanon (45%)[17] and in Iran (38%).[14] This finding could be related to a failure of physicians to record the symptoms.

The presence of ANA is a hallmark of SLE disease and one of the diagnostic criteria established by the ACR. In the present study, the prevalence of ANA was 95.3% [Table 5]. Similar findings have been reported from Saudi Arabia (95%)[16] and European countries (96%),[8] but an even higher prevalence was noted in Tunisia (100%).[15] However, our figure was slightly higher than those of India (71.4%),[20] Lebanon (87%)[17] and Pakistan (86%).[3] In spite of its apparent importance, some researchers have not agreed that ANA is a hallmark of SLE disease. Anti-dsDNA antibodies are quite specific and diagnostically important for SLE.[21] The prevalence of circulating anti-dsDNA antibodies in Yemeni patients was 59.7% [Table 5]. Very similar results have been obtained from Tunisia (56%)[15] and Kuwait (58%),[18] but are in contrast to the higher frequency found in Saudi Arabia (93%),[11] Spain (90%)[10] and Dubai (88%).[9] These differences may reflect a variable prevalence of anti-dsDNA in the world. In the current study, the prevalence of anti-Sm antibodies was 27.5% [Table 5] which indicates that anti-Sm antibodies are highly specific and of considerable diagnostic value for SLE as they appear

almost exclusively in SLE, as reported by Tan *et al.*[22] Our prevalence is higher than that in Spain (12%)[10] but lower than that in Tunisia (61.2%).[15]

The great diversity of clinical manifestations in SLE, ranging, for example, from arthritis and serositis to life-threatening neuropsychiatric manifestations, is accompanied by a high titre of auto-antibodies.[23] The current study found a strong statistical correlation between ANA and most clinical manifestations except weight loss, serositis and hypertension [Table 2]. There was also a significant correlation between anti-dsDNA and clinical manifestations such as fever, fatigue and hypertension, but no significant correlation with weight loss, arthropathy, renal involvement, alopecia, malar rash, serositis, oral ulcer and photosensitivity [Table 3]. The absence of a statistically significant correlation between anti-dsDNA and renal involvement in our study, even though dsDNA is known to be one of the main markers of *lupus* nephritis as described by Raz *et al.*,[24] may be related to unknown factors in Yemen that need to be clarified. There was no significant association between anti-Sm antibodies and most of the clinical manifestations in Table 4, except fever, as has been confirmed by Hitchon and Peschken.[25]

Patients with SLE have a complex array of abnormalities involving their immune system. A history of multiple cytopaenias such as leukopaenia, lymphopaenia, anaemia or thrombocytopaenia may suggest SLE, among other aetiologies.[1,2] In our series, anaemia was the most frequently occurring haematological abnormality in our patients [Table 5]. It occurred in about 64.4% of our patients, similar to the rate reported in Saudi Arabia (63.1%),[7] but higher than that reported in Spain (19%).[10] Lymphopaenia was present in 36.2% of our patients, the same as (30%) in Saudi Arabia,[6] but lower than the 50% rate in Tunisia[15] and 82% rate in Spain.[10] The low incidence can probably be explained by the fact that the immunological response of our patients was not typical of the disease, in which the auto-antibodies in SLE are directed against a wide variety of self-antigens. Leukopaenia occurred in 28.2% of our patients. This is quite similar to other studies reported by Agrawal *et al.*[26] and Al-Arfaj and Khalil,[7] but much lower than the 83% reported by Al-Jarallah *et al.*[18] and the 64.6% recorded by Nazarinia *et al.*[14] Our study found a high prevalence of thrombocytopaenia (44.3%); a similar result was reported in Iran by Nazarinia *et al.*,[14] while lower prevalence was reported from Tunisia (12%),[15] Kuwait (26%)[18] and Saudi Arabia (10.9%).[9]

Erythrocyte sedimentation rate (ESR) is one of the major monitoring tests for acute phase inflammation because it correlates with increased levels of acute phase reactants, in particular fibrinogen. In the present study, the frequency of ESR was 89.9%. A similar finding was reported in a study on Indian children (98.5%) by Agrawal *et al.*,[26] which is in contrast to studies with low frequency in Iran(64.6%)[14] and Saudi Arabia (54%).[7] This difference may be due to many factors that affected the ESR result, including the patient's age, sex, red blood count morphology, haemoglobin concentration and serum levels of immunoglobulin.[27]

The mortality rate in our patients was low (4.7%) and was somewhat similar to the rates in three different studies from Saudi Arabia; 3%,[13] 4%,[11] and 5.4%.[7] This could be attributed to early diagnosis and effective treatment in controlling the disease.

The second aim of this study was to examine the risk factors that could have influenced the occurrence of SLE among our study group, this being the first study designed to determine the risk factors of contracting SLE in Yemen. Frequent exposure to sunlight and stress (social and mental) were found to be risk factors in Yemeni SLE patients. This might be explained by the fact that psychological stress can activate an acute phase response, which is part of the innate immune inflammatory response; it is also evidence that the inflammatory response is contained within the stress response, and that stress can induce an inflammatory response.[28] This study also indicates that sunlight, especially ultraviolet B light (290–320 nm), plays an important role in inducing this systemic disease.[29] Oral contraceptive pills, especially those with high oestrogen doses, may provoke flares of SLE.[30] In the present study, however, no association was discovered between oral contraceptives and SLE.

Conclusion

SLE was more prevalent among females and young adults. The clinical presentation was characterised by a high incidence of fatigue and fever, and a low incidence of oral ulcers and serositis. ANA

was significantly associated with most clinical presentations except weight loss, hypertension and serositis. Anti-dsDNA antibodies were a specific marker and significantly associated with fever, serositis, oral ulcer, fatigue, hypertension and arthropathy. Anti-Sm antibodies were highly specific markers for SLE and significantly associated with oral ulcers.

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