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Assessing the relation between systemic lupus erythematosus and metabolic syndrome in Syria: a cross-sectional study

Noura Mallouhi[1], Ahmad Nabil Alhouri[2*], Naram Khalayli[3], Hasan Nabil Alhouri[4], Mayssoun Kudsi[1] and Younes Kabalan[5]

Abstract

Background Systemic Lupus Erythematosus (SLE) affects all organ systems. As a result, fat intake and sedentary life are evident in the modern world. The prevalence of metabolic syndrome, with its components, increased, leading to increased mortality. We aimed to investigate the prevalence of metabolic syndrome in SLE and its relationship with disease activity.

Methods A cross-sectional study was conducted on 70 SLE patients at Al Mouwasat University Hospitals in Damascus, Syria, between November 2021 and November 2022. The patients were divided into two groups based on the presence or absence of metabolic syndrome. The SLE Disease Activity Index (SLEDAI) was assessed in each group and compared with different disease parameters.

Results Out of the 70 patients, 65 were females. The mean age was 32.19 ± 7.15 years, and the mean disease duration was 4.4 ± 2.96 years. Metabolic syndrome was found in 32 patients (45.7%). Metabolic syndrome in SLE patients was associated with a higher disease activity index, older age, delayed age at first diagnosis, longer disease duration, higher frequency of renal involvement, and use of cyclophosphamide.

Conclusion Our study highlights the importance of evaluating and treating metabolic syndrome and its components in patients with SLE, as it may play a role in controlling disease activity. We recommend conducting larger studies in the future to overcome the limitations of this research, such as including a larger number of patients, conducting multicenter studies to generalize the results, and including a healthy control group.

Keywords Systemic lupus erythematosus, Metabolic syndrome, Prevalence, Syria

*Correspondence:
Ahmad Nabil Alhouri
alhouri.ahmad@gmail.com
[1]Rheumatology Department, Damascus University, Damascus, Syria
[2]Diagnostic Radiology Department, Damascus University, Damascus, Syria
[3]Psychiatry Department, Damascus University, Damascus, Syria
[4]Internal Medicine Department, Damascus University, Damascus, Syria
[5]Endocrinology Department, Damascus University, Damascus, Syria

Background

Systemic Lupus erythematosus (SLE) is a systemic immune disease that affects almost all organs and tissues. Although (SLE) can affect both genders, it primarily affects women who are in their reproductive age [1]. The course of the disease is characterized by periods of remission and activity. Its pathogenesis is not fully understood; many factors, such as genetic, environmental, and immune, may play a role [2]. As a result of the increase in fat intake and the sedentary life in the modern world, The prevalence of metabolic syndrome, with its components like obesity, hypercholesterolemia, dyslipidemia, and insulin resistance, has increased [3]. The most used definitions of metabolic syndrome were the definition of the World Health Organization (WHO) and the National Cholesterol Education Program Adult Treats of the Met Panel III [4]. The WHO first defined the component of the metabolism disorder [5]. Then, the National Cholesterol Education Program Adult Treats of the met Panel III proposed the following criteria: systolic blood pressure, glucose fasting, triglycerides (TG), high-density lipoprotein (HDL), and waist circumference to define the metabolic syndrome as a presence of the three conditions mentioned above, which, in turn, represented a risk of cardiovascular disease and type 2 diabetes mellitus [4]. The metabolic syndrome causes chronic inflammation due to the release of adipokines from adipocytes) such as tumor necrosis factor (TNF), C-reactive protein (CRP), Interleukin-1 (IL-1), and Interleukin-6 (IL-6)) [6]. At the same time, TNF-α and IL-6 are associated with the activity of the disease in patients with SLE [1], therefore, it is believed that adipokines have an important role in the development of the metabolic syndrome and its relationship to the SLE disease activity [1, 7, 8].

This study aims to reveal the association between SLE and metabolic syndrome, its components, and its relationship with disease activity.

Methods

Study design and participants

This cross-sectional study was conducted on 70 SLE patients. The participants were recruited from the outpatient clinic of Al Mouwasat University Hospital between November 2021 and November 2022. The study was approved by the Ethical Committee of the Faculty of Medicine, Damascus University (NK: 42121/2021). The sample size was 70 patients with a confidence interval of 95% and a predictive value of 0.05. Inclusion criteria include SLE patients older than 18 years diagnosed according to the American College of Rheumatology/European League Against Rheumatism 2019 [9] after signing the confirmed consent. Exclusion criteria include patients with arthritis, rheumatic diseases, other connective tissue lesions, cancer patients, pregnant women, and postpartum periods less than six months. The metabolic syndrome was diagnosed if at least 3 of the five following factors were found: central (body mass index (BMI) > 30 kg/m2) and /or abdominal obesity (waist circumference > 102 cm for men and 88 cm for women, systemic arterial hypertension > 130×85 mmHg, fasting blood glucose > 100 mg/dl, hypertriglyceridemia > 150 mg/dl, and levels of HDL cholesterol < 35 mg/dl for men and 45 mg/dl for women, according to the definition of the National Cholesterol Education Program Adult Treats of the met Panel III [1, 2].

Questionnaire

The authors collected the data by administering a validated five-part questionnaire (Supplemental file 1). The first part gathered demographic information such as age, gender, medical and surgical history, and current treatments. It also included questions about the patient's main complaints, other symptoms, and the duration of the disease.

The second part involved a comprehensive physical examination and laboratory tests. Blood samples were taken after a 12-hour fast to analyze parameters such as fasting blood sugar, lipid profile, complete blood count, urea, creatinine, erythrocyte sedimentation rate, CRP, complements (C3 and C4), and Anti-ds DNA. These samples were analyzed using an automatic analyzer.

Anthropometric measurements were obtained in the third part. Height was measured using a SECA device, and BMI was calculated using height and weight values [10]. Waist circumference was measured using a non-stretching centimeter tape. Blood pressure was measured after a five-minute rest in a sitting position, and the mean of two measurements was recorded.

The fourth part utilized the ACR/EULAR2019 criteria to diagnose SLE. A positive ANA ≥ 1:80 and the presence of 10 points were required for diagnosis [9].

Lastly, the fifth part utilized SLEDAI to assess disease activity. Disease activity was classified based on the number of points, with remission/mild disease being 0–5 points, a moderate disease being 6–10 points, and severe disease being > 10 points. Patients were diagnosed with lupus nephritis if their renal SLEDAI score was > 8 [11].

The SLE patients were divided into two groups: SLE patients with metabolic syndrome and SLE patients without metabolic syndrome; then every group was divided according to the disease activity index into three subgroups: 1- patients with remission/mild disease: SLEDAI < 5, 2- patients with moderate activity: 6 ≤ SLEDAI ≤ 10, 3- patients with severe active disease: SLEDAI > 10.

Statistical analysis

The data was converted to a computer database using Excel 2016, and the data were analyzed using the SPSS statistical analysis program (version 25). Data analysis was performed using frequency, percentage, standard deviation, and mean. A descriptive study was conducted to assess the study's indicators. The data was represented in tables and charts, which facilitated their understanding. ACR/EULAR2019 criteria were calculated, where every SLEDAI was calculated. The Chi-Square independence test was used to test the independence of qualitative variables. The variable was considered statistically significant when the significance level *P* value was less than 0.05.

Results

Sample characteristics

The study sample consisted of 70 patients, with a mean age of 32.19±7.15 years, ranging from 19 to 45 years, and included 5 (7.1%) males and 65 (92.9%) females. The mean age when SLE was diagnosed was 27.79±4.98 years, ranging from 18 to 37 years. The disease duration was 4.4±2.96 years, ranging from 1 to 11 years. The musculoskeletal manifestations were the most frequent in SLE patients. 90% of patients were under steroid treatment, whereby 77.1% of patients took hydroxychloroquine (Table 1).

Table 1 Sample characteristics

		Number of patients (%)	Per cent %
Gender	Male	5 (7.1)	7.1%
	Female	65 (92.9)	92.9%
Smoker	Male	4 (80)	80
	Female	40 (49.23)	40
Parent's history of obesity	Male	3 (6.25)	
	Female	45 (93.75)	
SLE Manifestation	Musculoskeletal involvement	53 (75.75)	75.75
	Mucocutaneous involvement	44 (62.9)	62.9%
	Renal involvement	39 (55.7)	55.7%
	Nervous system involvement	21 (30)	30%
	Hematologic involvement	29 (41.4)	41.4%
	Serositis	17 (24.3)	24.3%
Treatment	Steroids	63 (90)	90%
	Hydroxychloroquine	54 (77.1)	77.1%
	Cyclophosphamide	22 (31.4)	31.4%
	Azathioprine	20 (28.6)	28.6%
	Mycophenolate mophetil	20 (28.6)	28.6%
	Cyclosporine	7 (10)	10%
Age	Ranging	19–45 years	
	Mean	32.19	
	SD	±7.15	
Age when SLE was diagnosed	Ranging	18–37 years	
	Mean	27.79	
	SD	4.98	
Disease duration	Ranging	1–11 years	
	Mean	4.4	
	SD	2.96	

The average systolic pressure in the sample patients was 133.43±20.21 mm Hg, and the average diastolic pressure was 82.71±11.12 mm Hg. While the average waist circumference of the research sample was 87.76±5.57 cm, and the values ranged between 79 and 104 cm. The number of patients with metabolic syndrome in the research was 32 patients, with a prevalence of 45.7%. Regarding SLEDAI, 21(30%) of patients had remitted disease, and 33(47.1%) patients had moderate activity disease (Table 2).

Characteristics of metabolic syndrome among SLE patients

By using the student t-test, there was a statistically significant difference (*P*-value<0.001) in the mean age of 32 SLE patients with metabolic syndrome (36.09±6.02 years) and 38 SLE patients without metabolic syndrome (28.89±6.37). In addition, 62.5% of SLE patients with metabolic syndrome had a positive history of parents with obesity. In comparison, 37.5% of SLE patients without metabolic syndrome had a positive history of parents with obesity (*P*<0.001). In the clinical manifestations of SLE, there was a statistically significant difference between renal injury and the presence of metabolic syndrome (*P*=0.012) by using Pearson Chi-Square. Whereas renal injury was found in 71.9% of patients with metabolic syndrome, compared to 42.1% in patients without metabolic syndrome, confirmed with renal biopsy that related the renal injury to SLE, according to glomerulonephritis. As for the rest of the clinical manifestations, there was no statistically significant difference between the presence and absence of metabolic syndrome (Table 3).

For most treatments, there was no statistically significant difference between the presence and absence of metabolic syndrome (Table 4).

An independent test was conducted to determine the statistical significance of these differences in each part of the metabolic syndrome. Thus, using the Independent Samples T- Test, there are statistically significant differences between the two groups in all components of the metabolic syndrome (Table 5).

Multivariate logistic regression

There was a statistically significant indication that factors including age, age when SLE was diagnosed, renal involvement, GLU, TG, HDL, and BMI can predict metabolic syndrome with *p*-values 0.002, 0.002, 0.04, 0.018, 0.002, 0.005, and 0.019 respectively; in contrast, Cyclophosphamide did not have a significant relationship with metabolic syndrome with a *p*-value of 0.93 (Table 6).

Table 2 The presence of metabolic syndrome and distribution of SLEDAI among patients

		Number (*N*)	Per cent (%)
Metabolic Syndrome	No	38	54.3%
	Yes	32	45.7%
SLEDAI	Remission/mild disease activity	21	30%
	Moderate disease activity	33	47.1%
	Severe disease activity	16	22.9%

Table 3 Clinical manifestations of systemic lupus erythematosus between 2 groups

Clinical manifestation	SLE patients without MS (*N* = 38 patients)	SLE patients with MS (*N* = 32 patients)	*P*-value
MSK manifestation	29(76.3%)	24(75%	0.898
Mucocutaneous manifestation	25(%65.8)	19(%59.4)	0.580
Renal manifestation	16(%42.1)	23(%71.9)	**0.012***
Nervous system manifestation	10(%26.3)	11(%34.4)	0.464
Hematologic manifestation	17(%44.7)	12(%37.5)	0.540
Serositis	9(%23.7)	8(%25)	0.898

*; significant, MSK; musculoskeletal manifestation

Table 4 Treatment in SLE with MS group and SLE without MS group

Treatment	SLE patients without MS (*N* = 38 patients)	SLE patients with MS (*N* = 32 patients)	*P*-value
Steroids	35(92.1%)	32(%87.5)	0.695
Hydroxychloroquine	30(%78.9)	24(%75)	0.695
Cyclophosphamide	8(%21.1)	14(%43.8)	**0.042***
Azathioprine	12(%31.6)	8(25%)	0.445
mycophenolate mophetil	10(%26.3)	10(%31.3)	0.649
Cyclosporine	3(%7.9)	4(12.5%)	0.695

*; statically significant

Table 5 Comparison of the characteristics of the components of the metabolic syndrome between the two groups of patients

MS components	SLE patients without MS (*N* = 38 patients)	SLE patients with MS (*N* = 32 patients)	*P*-value
Systolic blood pressure (mmHg)	125.53 ± 19.69	142.81 ± 16.70	**< 0.001**
Diastolic blood pressure (mmHg)	78.42 ± 11.92	87.81 ± 7.51	**< 0.001**
Blood sugar (mg/dL)	96.87 ± 20.90	118.78 ± 48.38	**0.022**
TG (mg/dL)	127.61 ± 31.17	159.88 ± 36.08	**< 0.001**
HDL, mg/dl	54.50 ± 10.53	159.88 ± 36.08	**< 0.001**
BMI, (Kg/m^2)	24.29 ± 2.45	28.13 ± 2.59	**< 0.001**
Waist circumference (cm)	85.11 ± 4.24	90.91 ± 5.35	**< 0.001**

MS; Metabolic Syndrome, TG; triglyceride, HDL; high density lipoprotein, BMI; body mass index

The only statistically significant value in the table (*P*-value is less than 0.05)

Table 6 Multivariate logistic regression

Factor	Odds ratio (95% CI)	*p*-value
Age	1.71 (1.22–2.41)	**0.002**
Age when SLE was diagnosed	1.30 (1.10–1.54)	**0.002**
Disease duration	0.71 (0.43–1.16)	0.172
Renal involvement	7.93 (1.10-56.89)	**0.04**
Cyclophosphamide	1.09 (0.17–7.08)	0.93
Systolic Pressure	1.05 (0.97–1.14)	0.248
Diastolic pressure	1.03 (0.89–1.20)	0.663
GLU	1.04 (1.01–1.07)	**0.018**
TG	1.05 (1.02–1.09)	**0.002**
HDL	0.71 (0.56–0.90)	**0.005**
BMI	3.91 (1.25–12.27)	**0.019**
Waist Circumference	1.04 (0.74 0 1.48)	0.815
SLEDAI	1.23 (0.98–1.55)	0.081

The bold values indicate statistically significant values in the table (*p*-value is less than 0.05)

Association between MS and SLEDAI

The SLEDAI score in both groups is determined by the presence of the metabolic syndrome. To find out the statistical significance of these differences, a chi-square test (X2-test) was performed, and a statistically significant relationship was found between the metabolic syndrome and SLEDAI, where SLE patients with the metabolic syndrome had a greater frequency of highly active disease compared to SLE patients without the metabolic syndrome. *P*-value = 0.025 < 0.05.

Discussion

The prevalence of metabolic syndrome among SLE patients was 45.7%, which is higher compared to other studies conducted in China (34.2%), Egypt (36.9%), and Australia (29%) [12–14]. These differences in prevalence rates can be attributed to various factors such as racial diversity, genetic factors, lifestyle, and dietary habits, as well as variations in the criteria used to diagnose metabolic syndrome [8]. In addition, the bordering nations of Syria have varying rates of metabolic syndrome prevalence. Jordan has the highest percentage (51%) [15], followed by Iraq (39.4%) [16], Lebanon (31.2%) [17], Palestine (23%), and Turkey being the lowest one with (17.9%) [18]. In terms of the components of metabolic syndrome, low HDL and hypertension were the most frequent components among SLE patients, 84% and 72%, respectively [19]. These findings were consistent with the Egyptian study but differed from the Australian and Turkish studies, where hypertension was the most common component at 59% and 38.6%, respectively [14, 20].

This study revealed a significant association between metabolic syndrome in SLE patients and older age, later age at diagnosis, and increased disease duration. These associations may be explained by the increased risk of diabetes and hypertension with age, as well as chronic exposure to inflammatory mechanisms and SLE therapies

[19, 21]. Hammam et al. study showed that metabolic syndrome is associated with advanced age and later age at diagnosis but without a significant association with the duration of the disease [19]. Contrary to the above, the study of Jin et al. did not find any statistically significant relationship between metabolic syndrome, age, and disease duration [22].

Furthermore, our study showed a significant association between metabolic syndrome and renal injury, which was consistent with other studies. Patients with metabolic syndrome have a high risk of developing renal injury and renal insufficiency, even in the absence of diabetes. This may be due to increased connective tissue growth and the secretion of adipokines in metabolic syndrome, which can contribute to microvascular damage and fibrosis in the kidney [23, 24]. Jin et al. showed a significant association between metabolic syndrome and renal injury in addition to arthritis [22]. However, Hammam et al. did not find a significant association with renal injury, but they did find that neuropsychiatric manifestations were associated with metabolic syndrome [18].

No significant association was observed between the use of cyclophosphamide, a treatment for SLE, and the presence of metabolic syndrome. SLE patients with metabolic syndrome were more likely to receive cyclophosphamide compared to those without metabolic syndrome. This finding was in contrast with studies conducted in Brazil and Egypt [19, 23]. The higher incidence of kidney injury in SLE patients with metabolic syndrome may explain the increased use of cyclophosphamide in this group, as this medication is commonly used to treat acute lupus nephritis, a kidney complication associated with SLE.

Even though antimalarials have lipid-lowering and anti-inflammatory properties [25], our study did not find any statistically significant difference in their usage between the two groups of patients. This finding is consistent with some previous studies [19, 21]. However, a study by Medeiros et al. found that using antimalarials has a protective effect against the development of metabolic syndrome [23].

The same applies to corticosteroids despite their known role in increasing cholesterol levels, obesity, and high arterial tension. Our study did not find a significant association between their use and the development of metabolic syndrome, which is consistent with some studies [14, 19] but different from others that found a significant association only when prednisolone was given in a daily dose greater than 10 mg [21, 23]. A study by Demir et al. also found no significant association between metabolic syndrome and the treatments used for SLE. (20) Some studies suggest that the relationship between the effects of prednisolone and the protective effects of hydroxychloroquine on metabolic disorders is complex, as an increase in the lipid-lowering effect of hydroxychloroquine was observed in SLE patients receiving corticosteroid treatment and a lower cholesterol-raising effect of corticosteroids was observed in SLE patients receiving antimalarial treatment [13].

The study also found a significant relationship between metabolic syndrome and disease activity in SLE patients. Those with metabolic syndrome had a higher frequency of highly active disease than those without, which is consistent with some studies [19, 22–24]. However, one study found no correlation between disease activity and metabolic syndrome [21].

Study's limitations

The study had several limitations, including its cross-sectional design, which only suggests correlations rather than establishing causality. Additionally, the study was limited to participants from one center, which may restrict the generalizability of the findings. Furthermore, due to the small sample size of the subgroups, the study did not analyze environmental factors such as socioeconomic status, nutrition, and sedentary lifestyle between the two groups.

Strengths of the study

This study's insights on the connection between SLE and metabolic syndrome in a limited geographical setting are significant. A cross-sectional approach was adopted, which helps to understand existing within-patient associations and the prevalence of metabolic syndrome among SLE patients accessing healthcare services in Syria. The research also applies a stringent methodology encompassing well-defined diagnostic tools and a comprehensive assessment of metabolic aspects, making the results trustworthy. Moreover, this study focuses on an underrepresented group of individuals in previous research, providing new insights into the health risks experienced by people with lupus in Syria and thus necessitating tailored strategies for managing autoimmune illnesses and obesity. Eventually, this investigation is expected to lead to better public health policies and clinical practices due to improved outcomes for patients in this area.

Conclusion

The prevalence of metabolic syndrome among SLE patients was 45.7%. The most frequent components of metabolic syndrome among SLE patients were Low HDL and hypertension. This study found a significant relationship between metabolic syndrome and age, age at diagnosis, hyperglycemia, and mainly having renal affection in SLE patients; in contrast, Cyclophosphamide did not have a significant relationship with metabolic syndrome. Our research findings highlight the importance of assessing and managing metabolic syndrome and its

components in individuals with SLE in order to regulate disease activity.

Abbreviations

SLE	Systemic lupus erythematosus
SLEDAI	The SLE disease activity index
WHO	World Health Organization
TG	Triglycerides
HDL	High-density lipoprotein
TNF	Tumor necrosis factor
CRP	C-reactive protein
IL-1	Interleukin-1
IL-6	Interleukin-6
BMI	Body mass index

Supplementary Information

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Supplementary Material 1

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Author contributions
Noura Mallouhi: Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; writing—original draft. Ahmad Nabil Alhouri: Methodology; project administration; resources; validation; visualization; writing—original draft; writing— review and editing. Naram Khalayli: Data curation; investigation; writing—original draft. Hasan Al Houri: Methodology; validation; visualization; writing—original draft; writing— review and editing. Mayssoun Kudsi: Supervision. Younes Kabalan: Supervision.

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Data availability
The data supporting this study's findings are available from the Corresponding author upon reasonable request.

Declarations

Ethical approval
Ethical approval was obtained from the Institutional Review Board (IRB: DB,7683,2022), Faculty of Medicine, Damascus University. Informed consent was obtained from the patients who agreed to participate in the study.

Consent for publication
Not Applicable.

Competing interests
The authors declare no competing interests.

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