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BRIEF REPORT

The impact of obesity on SLE disease activity: findings from the Southern California Lupus Registry (SCOLR)

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Abstract

The role of obesity in systemic lupus erythematosus (SLE) remains controversial. Studies have linked adiposity with a heightened risk of clinical complications including neurocognitive decline, renal impairment, dampened physical activity, and depressed quality of life—but not disease activity. We aimed to reexamine whether obesity in SLE patients independently associates with higher disease activity. Adult patients with SLE were recruited from the longitudinal, multi-ethnic Southern California Lupus Registry (SCOLR). Disease status was ascertained by calculating SLE Disease Activity Index (SLEDAI), which was then statistically analyzed for association with increased body mass index (BMI) by univariable and multivariable regression analyses. One hundred and thirty-seven patients were included in the study; 37% were obese (BMI ≥ 30 kg/m^2). Obesity was significantly associated with SLEDAI ($P = 0.026$) and current steroid use ($P = 0.029$). Multivariable regression analysis demonstrated that obesity remained independently associated with lupus activity (OR 2.335, $P = 0.026$). In a representative sample of patients with SLE, obesity independently associated with worse SLE disease activity. Obesity may therefore be an important target for improving SLE outcomes.

Keywords Cardiovascular diseases · Disease activity index · Obesity · Systemic lupus erythematosus

Introduction

Obesity, defined by a body mass index (BMI) ≥ 30 kg/m^2, remains a major health problem in the USA and other Western countries. According to the National Health and Nutrition Exam Survey (NHANES), the prevalence of obesity has continued to increase over the past decades at 22.5% in 1988–1994, 30.6% in 1999–2002, and 37.9% in 2013–2014 [1].

Increased adiposity has long been associated with a state of altered immune function and chronic low-grade inflammation [2]. The discovery of adipokines, soluble inflammatory mediators produced by adipocytes, has shed some understanding to the mechanistic link between obesity and autoimmune diseases [3]. In systemic lupus erythematosus (SLE) specifically, the adipokine leptin promotes the survival of autoreactive T lymphocytes while reducing T_{reg} cells in mice models [4–7].

Despite these findings, however, the role of obesity in SLE remains controversial. Clinical studies have linked obesity with a heightened risk of renal impairment (lupus nephritis), amplified burden of atherosclerosis, worsened neurocognitive capacities, decreased physical activity, more fatigue, and worsened quality of life in SLE patients [8–12]. These findings are particularly important not only because there is a higher prevalence of obesity observed in SLE [13], but also because cardiovascular disease (CVD) remains the major cause of mortality in SLE [14]. However, studies that specifically evaluated the relationship between increased adiposity and SLE disease activity found no association between the two [8, 15]. One study was notably limited by observing only a small number of participants from a single ethnic population [8].

The aim of our present study is to reevaluate the impact of obesity in SLE disease activity and damage accrual by

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utilizing data from the Southern California Lupus Registry (SCOLR).

Materials and methods

SCOLR is a population-based, longitudinal, multi-ethnic cohort of patients with SLE. Patient recruitment began in June 2016 to include individuals greater than 18 years of age with SLE as defined by the Systemic Lupus International Collaborating Clinics (SLICC) [16]. The participant population is representative of San Bernardino and Riverside counties of Southern California, accounting for greater than four million individuals. The institutional review board at Loma Linda University approved this study and all patients provided written informed consent for participation.

Sociodemographic and clinical variables were collected via review of medical records, office visits, and laboratory findings. Sociodemographic variables included age, gender, and ethnicity; clinical variables included disease duration, BMI calculated from height and weight, steroid use, and SLE disease manifestations. Obesity was defined as patients having a BMI ≥ 30 kg/m^2. SLE Disease Activity Index (SLEDAI) was calculated and defined as low and high activity if less than 6 or greater than or equal to 6, respectively.

Statistical analyses

All statistical analyses were performed using SPSS V.24 (Chicago, IL). Patients were grouped into non-obese and obese groups based on their BMI. Differences in baseline socio-demographic and clinical variables between the two groups were assessed using the Student *t* test and Chi square analyses. Subsequently, a multivariate linear regression model was utilized to evaluate the association between obesity and SLEDAI while controlling for potential confounders (age, gender, current steroid use, disease duration, and presence of nephritis).

Results

At the time of data analysis, 157 SLE patients were enrolled in SCOLR. Of these, 137 patients had complete data sets for SLEDAI calculation and were included in the study: 48 Caucasian (35%), 49 Hispanic (36%), 17 Asian (12%), and 23 African American (17%). Mean age and disease duration were 42.1 ± 15.4 years and 9.4 ± 9.3 years, respectively. As expected, 92% of patients were women. Obesity criteria were met in 37% of patients.

Baseline sociodemographic and disease pertinent characteristics of study participants are presented in Table 1. Increased BMI was significantly associated with higher SLEDAI ($P = 0.026$). However, increased BMI was also associated with current steroid use ($P = 0.029$). To correct for influence of confounders, a multivariate regression model was utilized. After adjusting for age, gender, current steroid use, disease duration, and presence of nephritis, obesity remained independently associated with lupus activity (odds ratio 2.335, $P = 0.026$) (Table 2). Clinical manifestations of study participants were also evaluated in Table 3. A statistical difference is noted in the prevalence of mucocutaneous ($P = 0.028$) and musculoskeletal ($P = 0.003$) involvement between the non-obese and obese groups.

Table 1 Relationship between obesity and baseline sociodemographic and clinical variables

	Non-obese ($n = 87$)	Obese ($n = 50$)	*P* value
Age	41.8 ± 16.9	41.8 ± 12.8	0.690
Male	8 (9.2%)	3 (6.0%)	0.508
Ethnicity			0.270
White, non-Hispanic	32 (36.8%)	16 (32.0%)	
Hispanic	30 (34.5%)	20 (40.0%)	
Asian	13 (14.9%)	3 (6.0%)	
African American	12 (13.8%)	11 (22.0%)	
SLE duration	10 ± 10	8 ± 9.3	0.426
Current steroid use	24 (27.6%)	23 (46.0%)	*0.029*
Prednisone (< 10 mg/day)	16 (69.6%)	10 (43.5%)	0.186
Prednisone (10–15 mg/day)	5 (21.7%)	8 (34.8%)	
Prednisone (> 15 mg/day)	2 (8.7%)	5 (21.7%)	
Lupus nephritis	31 (35.6%)	12 (24.0%)	0.158
SLEDAI			*0.026*
SLEDAI (< 6)	52 (59.8%)	20 (40.0%)	
SLEDAI (≥ 6)	35 (40.2%)	30 (60.0%)	

Obesity = BMI > 30 kg/m^2; *SLEDAI* Systemic Lupus Erythematosus Disease Activity Index

Table 2 Multivariable analysis against high lupus disease activity index (SLEDAI ≥ 6)

	OR	*P* value	95% CI	
			Lower bound	Upper bound
Age	1.019	0.111	0.996	1.043
Female	0.648	0.511	0.178	2.363
SLE duration	0.879	0.634	0.516	1.496
Current steroid use	1.292	0.506	0.607	2.752
Lupus nephritis	1.740	0.162	0.801	3.782
Obesity*	2.335	*0.026*	1.109	4.919

Obesity = BMI > 30 kg/m^2; *OR* odds ratio; *CI* confidence interval

*Adjusted for age, gender, lupus duration, current steroid use, and presence of nephritis

Table 3 Clinical manifestations among systemic lupus erythematosus (SLE) patients according to body mass index

	Non-obese ($n = 87$)	Obese ($n = 50$)	P value
Musculoskeletal	26 (29.9%)	25 (50.0%)	*0.019*
Mucocutaneous	17 (19.5%)	22 (44.0%)	*0.002*
Renal	37 (42.5%)	22 (44.0%)	0.867
Serositis	3 (3.4%)	2 (4.0%)	0.868
Hematologic	17 (19.5%)	6 (12.0%)	0.256

Obesity = BMI > 30 kg/m^2

Musculoskeletal = arthritis, myositis; Mucocutaneous = new rash, alopecia, mucositis; Renal = casts, hematuria, proteinuria, pyuria, lupus nephritis; Serositis = pleurisy or pericarditis; Hematologic = leukopenia and thrombocytopenia

Discussion

With improved management of the classical manifestations of SLE, cardiovascular disease has emerged as the most prominent cause of disease morbidity and mortality [17]. Increased disease activity further increases the risk of CVD in individuals with SLE [18, 19]. Therefore, variables affecting SLE disease activity serve as modifiable factors that may improve long-term outcomes in SLE.

We sought to investigate the relationship between SLE disease activity and obesity, an area that remains controversial. By reviewing patient data from our multi-ethnic cohort and utilizing a multivariate regression model, we found that obesity is independently associated with SLEDAI.

Our results are in contrast with the findings of Chaiamnuay et al. and Rizk et al., who demonstrated an association of obesity with fibromyalgia and decreased quality of life, but not disease activity [8, 15]. Factors that might be responsible for the discrepant results include the different types of disease activity index utilized and our more heterogeneous and representative participant base. Rizk et al. used the same activity index (SLEDAI) whereas Chaiamnuay et al. used Systemic Lupus Activity Measure-Revised (SLAM-R). Findings from Rizk et al. are limited by their sample size that looked at only one ethnic group with a total of only 60 patients [8].

We acknowledge that our study also has some limitations. First, not all patients were included in our analysis due to missing data points needed for SLEDAI calculation. However, the 137 patients included in the study were representative of the entire cohort. Second, our conclusion may be limited by non-inclusion of other potential confounders such as socioeconomic status and the presence of medical comorbidities such as diabetes, hypertension, hyperlipidemia, and fibromyalgia. Finally, our cross-sectional study design limits us by simply showing an association between obesity and SLEDAI but not causality. Prospective studies in the future are needed to further evaluate causality.

In conclusion, we have shown that increased BMI is independently associated with worse SLE disease activity. This is a finding with important clinical implications as it suggests that increased adiposity may be a potential target and/or adjuvant preventive approach for improving SLE outcomes.

Compliance with ethical standards

The institutional review board at Loma Linda University approved this study and all patients provided written informed consent for participation.

Disclosures None.

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