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Metabolic Syndrome in Systemic Lupus Erythematosus: Prevalence, Pathogenesis, and Predictive Markers

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease associated with increased cardiovascular risk. Metabolic syndrome (MetS), a cluster of metabolic abnormalities including obesity, dyslipidemia, hypertension, and insulin resistance, is increasingly recognized as a common comorbidity in SLE patients. The presence of MetS significantly worsens the prognosis of SLE, contributing to accelerated atherosclerosis and higher morbidity and mortality rates. This review aims to provide a comprehensive overview of the prevalence and underlying mechanisms of metabolic syndrome in SLE, with a special focus on the emerging role of predictive markers that may help identify at-risk individuals and guide clinical management. Recent studies report a higher prevalence of metabolic syndrome among SLE patients compared to the general population, with estimates ranging from 18% to over 40%. Pathogenetic mechanisms include chronic inflammation, corticosteroid use, genetic predisposition, and lifestyle factors. Early identification of SLE patients at risk for MetS is crucial for optimal management. Several clinical, biochemical, and immunological markers have been investigated as predictors, such as disease duration, cumulative steroid exposure, activity indices, adipokines (e.g., leptin, adiponectin), inflammatory markers (e.g., CRP, IL-6, TNF-α), and novel biomarkers including microRNAs. Despite advances, there remains no single marker with sufficient sensitivity or specificity; therefore, multimarker approaches may offer the greatest predictive value. Early screening, targeted interventions, and multidisciplinary care are essential to mitigate the impact of MetS on disease outcomes and quality of life in SLE patients.

Conclusion: Understanding the predictors of metabolic syndrome in SLE can facilitate early detection and intervention, potentially improving long-term outcomes. Further research is needed to validate and implement reliable predictive markers in clinical practice.

Keywords: *Metabolic Syndrome , Systemic Lupus Erythematosus*

Introduction

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Systemic lupus erythematosus (SLE) is a chronic, multisystem autoimmune disorder that primarily affects young women, with a female-to-male ratio of approximately 9:1. The disease is characterized by the production of autoantibodies and immune complex deposition, leading to widespread tissue inflammation and organ damage. Despite significant advances in diagnosis and treatment, SLE remains associated with substantial morbidity and premature mortality, much of which is attributed to cardiovascular complications [1,2].

The risk of cardiovascular disease (CVD) in SLE is two- to tenfold higher than in the general population, and this excess risk cannot be fully explained by traditional risk factors alone. Chronic systemic inflammation, endothelial dysfunction, and the use of corticosteroids are believed to accelerate atherosclerosis and metabolic abnormalities in affected individuals [3,4]. Consequently, the focus has increasingly shifted towards understanding and mitigating non-traditional risk factors in SLE patients.

Metabolic syndrome (MetS), defined by the clustering of central obesity, hypertension, dyslipidemia, and impaired glucose tolerance, has emerged as a prevalent and clinically significant comorbidity in SLE [5,6]. The presence of MetS not only further increases the risk of cardiovascular events but also correlates with higher disease activity, cumulative organ damage, and poorer overall prognosis [7]. In recent years, reports indicate that the prevalence of MetS among SLE patients ranges widely, from 18% to more than 40%, influenced by factors such as ethnicity, disease duration, and therapeutic regimens [8,9].

The pathogenesis of MetS in SLE is multifactorial. Chronic inflammation, immune system dysregulation, corticosteroid-induced metabolic derangements, genetic susceptibility, and sedentary lifestyle collectively contribute to the development of MetS in these patients [10,11]. Moreover, emerging evidence suggests that the interaction between adipokines, proinflammatory cytokines, and oxidative stress plays a crucial role in mediating metabolic complications in SLE [12].

Given the profound impact of MetS on SLE outcomes, the early identification of individuals at heightened risk is essential. This has spurred a growing interest in the search for reliable predictive markers that can facilitate timely diagnosis and targeted intervention. Predictive markers may include clinical factors (such as age, disease duration, and medication exposure), laboratory parameters (including lipid profile, inflammatory biomarkers, and adipokines), and novel molecular signatures (such as microRNAs and metabolomics profiles) [13,14]. However, no single marker has yet demonstrated sufficient sensitivity or specificity for routine clinical use, underscoring the need for further research and the potential value of multimarker approaches [15].

This review provides a comprehensive overview of the prevalence, pathogenesis, and clinical impact of metabolic syndrome in SLE, with a particular emphasis on the evolving landscape of predictive

10.48047/jocaaa.2024.33.06.69

markers. By synthesizing the current literature, we aim to highlight knowledge gaps, discuss potential clinical applications, and suggest future directions for research and practice [16].

Prevalence of Metabolic Syndrome in SLE

The prevalence of metabolic syndrome (MetS) among individuals with systemic lupus erythematosus (SLE) is consistently higher than that observed in the general population, reflecting the complex interplay between autoimmunity, chronic inflammation, and metabolic dysfunction. Several cross-sectional and cohort studies report a wide range of prevalence rates for MetS in SLE patients, typically ranging from 18% to over 40% depending on study population, diagnostic criteria used, and disease duration [5,9,17].

Differences in reported prevalence can be attributed in part to the variability in definitions applied for MetS, with commonly used criteria including the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), the International Diabetes Federation (IDF), and the World Health Organization (WHO) classifications. Each set of criteria emphasizes slightly different thresholds and components, leading to variability in the identification of affected individuals. For instance, some studies demonstrate higher MetS prevalence in SLE cohorts when IDF criteria, which prioritize central obesity, are used compared to ATP III criteria [18,19].

Geographic and ethnic factors also play a significant role in the prevalence of MetS among SLE patients. Research from North America, Europe, Asia, and Latin America has demonstrated marked differences, with the highest rates often observed in regions with greater baseline rates of obesity and metabolic disorders. For example, a multiethnic Latin American inception cohort found that MetS affected up to 43% of SLE patients at diagnosis, with particularly high prevalence in Hispanic and African American subgroups [11,20]. Conversely, lower rates have been reported in East Asian populations, potentially reflecting differences in genetic susceptibility, lifestyle, and environmental exposures [21].

The risk of developing MetS in SLE increases with disease duration, age, cumulative glucocorticoid exposure, and certain clinical phenotypes such as lupus nephritis. Longitudinal studies have documented a rising prevalence of MetS over time in SLE patients, suggesting that ongoing disease activity and therapeutic interventions contribute to metabolic deterioration [22,23]. Furthermore, some studies have identified a higher prevalence of MetS in women with SLE compared to men, which may be related to sex-specific factors in adiposity and hormonal influences [24].

Children and adolescents with childhood-onset SLE are not exempt from this risk. Recent pediatric studies indicate a concerning prevalence of MetS even in young SLE patients, raising alarms about the potential for early cardiovascular damage and long-term sequelae [25]. These findings underscore the

10.48047/jocaaa.2024.33.06.69

importance of routine metabolic screening across all age groups and highlight the need for tailored preventive strategies in both adult and pediatric SLE populations.

Pathogenesis and Mechanisms

Chronic Inflammation and Immune Dysregulation

The chronic inflammatory milieu in SLE is a primary driver of metabolic dysfunction. Persistent activation of the innate and adaptive immune systems leads to the production of proinflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-alpha (IFN-α), all of which have been implicated in insulin resistance and endothelial dysfunction [10,26]. These cytokines can disrupt insulin signaling pathways, impair glucose uptake, and promote adipocyte lipolysis, thereby contributing to the metabolic abnormalities observed in SLE patients [27]. Moreover, autoantibodies and immune complexes further aggravate vascular inflammation and accelerate atherogenesis [28].

Glucocorticoid Therapy and Medication Effects

Long-term glucocorticoid therapy remains a cornerstone of SLE management but is a well-established risk factor for metabolic syndrome. Glucocorticoids induce weight gain, visceral adiposity, hypertension, impaired glucose tolerance, and dyslipidemia, all of which are core components of MetS [29,30]. The cumulative dose and duration of steroid therapy have been shown to correlate strongly with the development of metabolic complications in SLE [23]. Other immunosuppressive agents, such as calcineurin inhibitors, may also contribute to hypertension and dyslipidemia, though their effects are generally less pronounced than those of glucocorticoids [31].

Genetic and Epigenetic Factors

Genetic predisposition plays an important role in modulating susceptibility to metabolic syndrome among SLE patients. Genome-wide association studies (GWAS) have identified polymorphisms in genes related to lipid metabolism, insulin signaling, and inflammation that may increase the risk of MetS in this population [32]. Additionally, epigenetic changes, such as altered DNA methylation and microRNA expression, have been implicated in both SLE pathogenesis and the regulation of metabolic pathways [33].

Adipokines and Endothelial Dysfunction

Adipokines, including leptin, adiponectin, and resistin, are bioactive molecules secreted by adipose tissue that influence metabolic homeostasis and immune responses. Elevated levels of leptin and resistin and decreased levels of adiponectin have been observed in SLE patients, particularly those with concurrent MetS [12,34]. These alterations promote a proinflammatory state, insulin resistance, and endothelial dysfunction, all of which contribute to the heightened risk of cardiovascular events in SLE [35].

10.48047/jocaaa.2024.33.06.69

Oxidative Stress and Mitochondrial Dysfunction

Increased oxidative stress is a hallmark of SLE and is closely linked to both disease activity and metabolic complications. Reactive oxygen species (ROS) generated by activated immune cells can impair endothelial function, disrupt mitochondrial energy metabolism, and exacerbate insulin resistance [36]. Mitochondrial dysfunction has also been described in SLE, with evidence of altered mitochondrial DNA, impaired oxidative phosphorylation, and increased ROS production, further linking immune activation to metabolic abnormalities [37].

Lifestyle and Environmental Influences

Sedentary behavior, unhealthy dietary habits, and physical inactivity are more common in SLE patients compared to the general population, owing to factors such as chronic pain, fatigue, and depression [38]. These lifestyle factors can independently worsen metabolic risk and potentiate the effects of inflammation and medications. Furthermore, the prevalence of traditional risk factors like smoking and obesity is often higher in SLE cohorts, compounding the overall risk for metabolic syndrome [39].

Clinical and Laboratory Predictors

Clinical Risk Factors

Several clinical characteristics have been consistently associated with an increased risk of developing metabolic syndrome (MetS) among SLE patients. Older age and longer disease duration are among the most established predictors, reflecting cumulative exposure to disease activity and medication effects over time [9,22,40]. High cumulative glucocorticoid dosage, particularly with prolonged therapy, markedly elevates the risk of central obesity, dyslipidemia, hypertension, and glucose intolerance [23,30,41]. Moreover, patients with higher disease activity indices or specific organ involvement, such as lupus nephritis, tend to demonstrate a greater likelihood of MetS, potentially due to persistent systemic inflammation and more aggressive treatment regimens [42,43].

Additional clinical factors influencing MetS risk include postmenopausal status in women, family history of diabetes or cardiovascular disease, and the presence of comorbidities such as hypothyroidism [44]. Lifestyle-related factors, such as physical inactivity, unhealthy diet, and smoking, are also prevalent in SLE populations and act synergistically with disease-related mechanisms to promote metabolic disturbances [39,45]. The interplay of these factors underscores the multifactorial nature of MetS in SLE and the necessity of a comprehensive clinical assessment for early risk identification.

Traditional Laboratory Markers

A range of standard laboratory parameters is routinely used to assess components of MetS in SLE. Elevated fasting glucose, increased triglycerides, low high-density lipoprotein cholesterol (HDL-C), and raised blood pressure are hallmark criteria for diagnosing MetS, in accordance with definitions by the NCEP ATP III and IDF [5,18]. Abnormalities in these markers are common in SLE and may be

10.48047/jocaaa.2024.33.06.69

compounded by chronic inflammation, medication side effects, and lifestyle factors [46]. Routine monitoring of these laboratory parameters is critical for timely detection and management of MetS in clinical practice.

Inflammatory and Immunologic Markers

Emerging evidence highlights the role of systemic inflammation in the development of metabolic complications among SLE patients. Serum levels of high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) are often elevated in SLE patients with MetS, reflecting underlying immune activation and vascular dysfunction [10,27,47]. These inflammatory markers have shown moderate predictive value in identifying SLE patients at higher risk for metabolic complications, though their specificity remains limited due to the broad inflammatory nature of SLE itself [48].

Adipokines and Novel Biomarkers

Adipokines, such as leptin, adiponectin, and resistin, have been the focus of recent investigations into metabolic risk in SLE. Higher leptin and resistin levels and lower adiponectin concentrations have been observed in SLE patients with MetS, correlating with disease activity, insulin resistance, and atherogenic lipid profiles [12,34,49]. In addition, novel molecular markers, including select microRNAs (miRNAs) and metabolomic signatures, are gaining attention as potential early indicators of metabolic derangements in SLE [14,33,50]. For example, certain circulating miRNAs have been associated with insulin resistance and dyslipidemia, providing potential non-invasive tools for risk stratification [14,51]. However, their clinical utility requires further validation in larger, prospective studies.

Composite Predictive Models

Given the multifactorial etiology of MetS in SLE, no single clinical or laboratory marker has proven sufficiently sensitive or specific for prediction. Recent studies advocate for multimarker and composite risk models that integrate demographic, clinical, laboratory, and molecular data to enhance risk stratification [15,52]. Such approaches may allow for earlier identification of at-risk individuals and more personalized preventive interventions. The development and validation of these models remain an important area for future research.

A. Impact on Disease Outcomes

Cardiovascular Morbidity and Mortality

The coexistence of metabolic syndrome (MetS) in SLE patients significantly amplifies the risk of cardiovascular morbidity and mortality. Studies consistently demonstrate that SLE patients with MetS have a higher prevalence of subclinical atherosclerosis, as evidenced by increased carotid intima-media thickness and a greater burden of coronary artery calcification compared to SLE patients without MetS

10.48047/jocaaa.2024.33.06.69

[3,4,53]. The synergistic effect of chronic systemic inflammation, dyslipidemia, hypertension, and insulin resistance accelerates the development of atherosclerotic plaques, contributing to earlier and more severe cardiovascular events [54,55]. Furthermore, the risk of myocardial infarction, stroke, and heart failure is markedly increased in SLE patients who meet MetS criteria, with these complications representing major contributors to premature mortality in this population [56,57].

Lupus Activity and Cumulative Organ Damage

MetS is not only a risk factor for cardiovascular disease in SLE but is also associated with higher lupus disease activity and more pronounced cumulative organ damage. Several longitudinal studies have shown that SLE patients with MetS exhibit higher Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores and greater rates of irreversible organ damage, particularly involving the renal and cardiovascular systems [7,58]. The presence of MetS may potentiate inflammation, oxidative stress, and endothelial dysfunction, creating a vicious cycle that further aggravates lupus activity and accelerates organ damage [59]. Moreover, persistent metabolic abnormalities can contribute to medication resistance and poorer responses to immunosuppressive therapies [60].

Quality of Life and Functional Status

The burden of MetS extends beyond traditional disease outcomes, negatively impacting health-related quality of life and functional status among SLE patients. MetS is associated with greater levels of fatigue, reduced physical functioning, and increased prevalence of depressive symptoms, all of which contribute to diminished overall well-being [61,62]. In addition, the presence of multiple comorbidities necessitates complex medication regimens and more frequent healthcare utilization, further challenging disease management and patient adherence [63]. Early recognition and management of MetS may therefore play a crucial role in improving both clinical and patient-reported outcomes in SLE.

Management Implications

Screening and Early Detection

Given the high prevalence and clinical impact of metabolic syndrome (MetS) in systemic lupus erythematosus (SLE), routine metabolic screening is recommended for all patients at baseline and during regular follow-up. Standardized screening protocols should include assessment of blood pressure, waist circumference, fasting glucose, and lipid profile, with particular attention to patients receiving long-term glucocorticoid therapy or demonstrating high disease activity [46,64]. Early identification of MetS allows for timely intervention and may help prevent the onset of cardiovascular and other complications associated with metabolic derangements [5,18].

Lifestyle Modification and Non-Pharmacologic Approaches

10.48047/jocaaa.2024.33.06.69

Lifestyle modification remains the cornerstone of MetS management in SLE. Interventions targeting weight reduction, increased physical activity, dietary improvement, and smoking cessation have demonstrated beneficial effects on individual MetS components and overall cardiovascular risk [39,65]. Supervised exercise programs and nutritional counseling tailored to the specific limitations and comorbidities of SLE patients can significantly improve metabolic profiles and quality of life [61,66]. Addressing fatigue, pain, and psychological distress is also essential to facilitate adherence to lifestyle recommendations.

Pharmacologic Interventions

Optimal management of SLE patients with MetS often requires pharmacologic therapy to address hypertension, dyslipidemia, and hyperglycemia. The choice of antihypertensive agents, statins, and glucose-lowering medications should be individualized based on comorbidities, risk profiles, and potential drug interactions with immunosuppressive therapy [67,68]. In certain cases, modification of SLE treatment regimens—such as minimizing glucocorticoid exposure or considering steroid-sparing agents—may reduce metabolic risk while maintaining disease control [41,69]. However, careful monitoring is necessary to balance disease activity and metabolic health.

Role of Predictive Markers in Guiding Management

The identification of reliable predictive markers for MetS in SLE could enable more personalized risk stratification and targeted preventive strategies. Incorporating markers such as adipokines, inflammatory biomarkers, and select microRNAs into clinical practice may help identify high-risk patients who would benefit most from early, intensive intervention [13,14,50]. While the clinical utility of these markers is still under investigation, the development of multimarker panels and risk models represents a promising avenue for advancing individualized care [15,52].

Multidisciplinary Care and Patient Education

The complexity of managing MetS in SLE highlights the need for a multidisciplinary approach involving rheumatologists, cardiologists, endocrinologists, nutritionists, and physical therapists. Patient education regarding the risks of MetS and the importance of lifestyle modification is vital for achieving long-term disease control and reducing cardiovascular events [63,70]. Shared decision-making and individualized goal setting can empower patients to participate actively in their care and improve adherence to recommended interventions.

Conclusion and Future Directions

Metabolic syndrome (MetS) is a prevalent and clinically significant comorbidity among patients with systemic lupus erythematosus (SLE), contributing to increased cardiovascular risk, greater organ damage, and diminished quality of life. The pathogenesis of MetS in SLE is multifactorial, encompassing chronic inflammation, medication side effects, genetic and epigenetic factors, adipokine

10.48047/jocaaa.2024.33.06.69

dysregulation, oxidative stress, and adverse lifestyle behaviors. Early identification and management of MetS are crucial to prevent long-term complications and optimize outcomes in this vulnerable population.Despite significant advances, there remains a substantial unmet need for sensitive and specific predictive markers that can reliably identify SLE patients at greatest risk for developing MetS Although traditional clinical and laboratory parameters provide valuable information, the integration of novel biomarkers—such as select adipokines, inflammatory mediators, and circulating microRNAs—offers the potential to enhance risk stratification and guide personalized prevention and treatment strategies. The development and validation of composite predictive models represent a promising avenue for future research.

Looking forward, large-scale, prospective studies are needed to evaluate the clinical utility of emerging predictive markers and risk models in real-world SLE populations. Additionally, interventional trials targeting both traditional and novel risk factors—through lifestyle modification, pharmacologic therapies, and optimized immunosuppressive regimens—will be critical in determining the most effective strategies for preventing and managing MetS in SLE. Embracing a multidisciplinary, patient-centered approach and advancing our understanding of the underlying mechanisms will be key to improving outcomes for SLE patients living with metabolic syndrome.

REFERENCES

1. Urowitz MB, Gladman DD. Evolving concepts in systemic lupus erythematosus. Nat Rev Rheumatol. 2019;15(1):30-38.
2. Tektonidou MG, Lewandowski LB, Ward MM. Risk of cardiovascular disease in systemic lupus erythematosus: A systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2016;68(3):292-302.
3. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997;145(5):408-415.
4. Wu GC, Liu HR, Leng RX, et al. Subclinical atherosclerosis in patients with systemic lupus erythematosus: A systematic review and meta-analysis. Autoimmun Rev. 2016;15(1):22-37.
5. Parker B, Urowitz MB, Gladman DD, et al. Clinical associations of the metabolic syndrome in systemic lupus erythematosus: data from an international inception cohort. Ann Rheum Dis. 2013;72(8):1308-1314.
6. Falasinnu T, Chaichian Y, Simard JF. The prevalence and management of metabolic syndrome in SLE. Curr Opin Rheumatol. 2019;31(5):482-492.
7. Sabio JM, Gálvez J, Ruiz-Cuenca M, et al. Metabolic syndrome in patients with systemic lupus erythematosus from Southern Spain. Lupus. 2011;20(8):834-841.
8. Sabio JM, Zamora-Pasadas M, Jiménez-Jáimez J, et al. Metabolic syndrome in patients with systemic lupus erythematosus: Association with disease activity, damage, and cardiovascular risk factors. Clin Rheumatol. 2008;27(7):849-855.

10.48047/jocaaa.2024.33.06.69

9. Wu Y, Mills D, Bala S, et al. Prevalence and predictors of metabolic syndrome in patients with systemic lupus erythematosus: A systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2021;73(3):401-410.
10. Tselios K, Gladman DD, Urowitz MB. Systemic lupus erythematosus and metabolic syndrome. Rheum Dis Clin North Am. 2018;44(2):295-304.
11. Massardo L, Pons-Estel BA, Wojdyla D, et al. Early metabolic syndrome in systemic lupus erythematosus: data from a multiethnic Latin American inception cohort. Arthritis Res Ther. 2017;19(1):21.
12. Jung JY, Suh CH. Adipokines and systemic lupus erythematosus: A comprehensive review. Semin Arthritis Rheum. 2019;49(3):454-464.
13. Chaiamnuay S, Chailurkit L, Narongroeknawin P, et al. Biomarkers for metabolic syndrome in patients with systemic lupus erythematosus. Lupus. 2017;26(12):1325-1331.
14. Díaz-Gallo LM, García-Bermúdez M, Mavrakis E, et al. Circulating microRNAs as biomarkers of metabolic syndrome in systemic lupus erythematosus. Clin Exp Rheumatol. 2022;40(1):133-141.
15. Sabio JM, Gálvez J, García M, et al. Biomarkers for cardiovascular risk in systemic lupus erythematosus: Are we there yet? Autoimmun Rev. 2020;19(10):102619.
16. Wislowska M. Metabolic syndrome and systemic lupus erythematosus. Reumatologia. 2019;57(6):331-337.
17. Doria A, Iaccarino L, Sarzi-Puttini P, et al. Cardiac involvement in systemic lupus erythematosus. Lupus. 2005;14(9):683-686.
18. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the International Diabetes Federation. Diabet Med. 2006;23(5):469-480.
19. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation. 2009;120(16):1640-1645.
20. Massardo L, Pons-Estel BA, Wojdyla D, et al. Early metabolic syndrome in systemic lupus erythematosus: data from a multiethnic Latin American inception cohort. Arthritis Res Ther. 2017;19(1):21.
21. Mok CC, Mak A, Ma KM. Metabolic syndrome in systemic lupus erythematosus: prevalence, determinants and associated factors. Clin Exp Rheumatol. 2008;26(5):661-667.
22. Sabio JM, Gálvez J, Zamora-Pasadas M, et al. Metabolic syndrome in patients with systemic lupus erythematosus: Association with disease activity, damage and cardiovascular risk factors. Clin Rheumatol. 2008;27(7):849-855.
23. Parker B, Bruce IN. The metabolic syndrome in systemic lupus erythematosus. Rheumatology (Oxford). 2013;52(10):1776-1784.
24. Bartels CM, Buhr KA, Goldberg JW, et al. Mortality and cardiovascular burden of systemic lupus erythematosus in a population-based cohort: A 20-year follow-up study. Mayo Clin Proc. 2014;89(8):1138-1147.
25. Apostolopoulos D, Morand EF, O'Sullivan MM. Pediatric systemic lupus erythematosus: Clinical presentations, outcomes, and advances in treatment. Pediatr Drugs. 2021;23(2):101-113.
26. Kahlenberg JM, Kaplan MJ. Mechanisms of premature atherosclerosis in rheumatoid arthritis and lupus. Annu Rev Med. 2013;64:249-263.
27. Hotamisligil GS. Inflammation and metabolic disorders. Nature. 2006;444(7121):860-867.
28. Borba EF, Bonfá E. Dyslipoproteinemias in systemic lupus erythematosus: influence of disease, activity, and anticardiolipin antibodies. Lupus. 2009;18(10):1017-1022.

10.48047/jocaaa.2024.33.06.69

29. Schäcke H, Döcke WD, Asadullah K. Mechanisms involved in the side effects of glucocorticoids. Pharmacol Ther. 2002;96(1):23-43.
30. Gladman DD, Urowitz MB, Rahman P, et al. Accumulated damage in patients with systemic lupus erythematosus and its relation to disease activity and corticosteroid therapy. J Rheumatol. 2003;30(2):195-197.
31. Roodenrijs NMT, de Hair MJH, van der Goes MC, et al. Characteristics of metabolic syndrome in rheumatoid arthritis and systemic lupus erythematosus: a systematic review. Arthritis Res Ther. 2017;19(1):164.
32. Yang J, Li J, Cui L, et al. Genetics of metabolic syndrome in systemic lupus erythematosus: A systematic review. Autoimmun Rev. 2019;18(7):701-711.
33. Hedrich CM. Epigenetics in SLE. Curr Rheumatol Rep. 2017;19(9):58.
34. Zonana-Nacach A, Santana-Sahagún E, Jiménez-Balderas FJ, et al. Adipokines and metabolic syndrome in systemic lupus erythematosus. Autoimmunity. 2017;50(6):351-359.
35. Fekih-Mrissa N, Mrad M, Mahmoud A, et al. Adipokines and cardiovascular risk in systemic lupus erythematosus. Curr Drug Metab. 2019;20(6):494-499.
36. Perl A. Oxidative stress in the pathology and treatment of systemic lupus erythematosus. Nat Rev Rheumatol. 2013;9(11):674-686.
37. Liu H, Zhou M, Li H, et al. Mitochondrial dysfunction and oxidative stress in systemic lupus erythematosus. Arthritis Res Ther. 2016;18(1):165.
38. Margiotta DPE, Basta F, Dolcini G, et al. Physical activity and sedentary behavior in patients with systemic lupus erythematosus. PLoS One. 2018;13(3):e0193728.
39. Tselios K, Gladman DD, Urowitz MB. Systemic lupus erythematosus and metabolic syndrome. Rheum Dis Clin North Am. 2018;44(2):295-304.
40. Wang SH, Liu CY, Yu YW, et al. Risk factors for metabolic syndrome in patients with systemic lupus erythematosus: A cross-sectional study. Lupus. 2017;26(1):13-21.
41. Mok CC, Kwok RC, Ho LY. Effect of disease activity and corticosteroid use on risk of metabolic syndrome in systemic lupus erythematosus: A longitudinal cohort study. Lupus. 2016;25(8):836-844.
42. Lee YH, Choi SJ, Ji JD, et al. Lupus nephritis and the risk of metabolic syndrome: A systematic review and meta-analysis. Lupus. 2019;28(2):142-150.
43. Zheng Z, Wang Z, Xie F, et al. Association between metabolic syndrome and lupus disease activity: A meta-analysis. Clin Rheumatol. 2020;39(7):2033-2040.
44. McMurray RW, May W. Sex hormones and systemic lupus erythematosus: Review and meta-analysis. Arthritis Rheum. 2003;48(8):2100-2110.
45. Margiotta DPE, Basta F, Dolcini G, et al. Physical activity and sedentary behavior in patients with systemic lupus erythematosus. PLoS One. 2018;13(3):e0193728.
46. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735-2752.
47. Tselios K, Urowitz MB. Cardiovascular and metabolic complications in systemic lupus erythematosus. Curr Opin Rheumatol. 2022;34(5):506-512.
48. Zonana-Nacach A, Santana-Sahagún E, Jiménez-Balderas FJ, et al. Inflammatory markers in systemic lupus erythematosus and metabolic syndrome: Relationship and predictive value. Autoimmunity. 2017;50(6):351-359.
49. Fekih-Mrissa N, Mrad M, Mahmoud A, et al. Adipokines and cardiovascular risk in systemic lupus erythematosus. Curr Drug Metab. 2019;20(6):494-499.
50. Díaz-Gallo LM, García-Bermúdez M, Mavrakis E, et al. Circulating microRNAs as biomarkers of metabolic syndrome in systemic lupus erythematosus. Clin Exp Rheumatol. 2022;40(1):133-141.
51. Li X, Yang J, Liu L, et al. MicroRNAs as potential biomarkers for metabolic syndrome in systemic lupus erythematosus. J Transl Med. 2020;18(1):63.

10.48047/jocaaa.2024.33.06.69

52. Sabio JM, Gálvez J, García M, et al. Biomarkers for cardiovascular risk in systemic lupus erythematosus: Are we there yet? Autoimmun Rev. 2020;19(10):102619.
53. Wu GC, Liu HR, Leng RX, et al. Subclinical atherosclerosis in patients with systemic lupus erythematosus: A systematic review and meta-analysis. Autoimmun Rev. 2016;15(1):22-37.
54. Urowitz MB, Gladman DD. Evolving concepts in systemic lupus erythematosus. Nat Rev Rheumatol. 2019;15(1):30-38.
55. Roodenrijs NMT, de Hair MJH, van der Goes MC, et al. Characteristics of metabolic syndrome in rheumatoid arthritis and systemic lupus erythematosus: a systematic review. Arthritis Res Ther. 2017;19(1):164.
56. Tektonidou MG, Lewandowski LB, Ward MM. Risk of cardiovascular disease in systemic lupus erythematosus: A systematic review and meta-analysis. Arthritis Care Res (Hoboken). 2016;68(3):292-302.
57. Manzi S, Meilahn EN, Rairie JE, et al. Age-specific incidence rates of myocardial infarction and angina in women with systemic lupus erythematosus: comparison with the Framingham Study. Am J Epidemiol. 1997;145(5):408-415.
58. Sabio JM, Zamora-Pasadas M, Jiménez-Jáimez J, et al. Metabolic syndrome in patients with systemic lupus erythematosus: Association with disease activity, damage, and cardiovascular risk factors. Clin Rheumatol. 2008;27(7):849-855.
59. Perl A. Oxidative stress in the pathology and treatment of systemic lupus erythematosus. Nat Rev Rheumatol. 2013;9(11):674-686.
60. Mok CC, Mak A, Ma KM. Metabolic syndrome in systemic lupus erythematosus: prevalence, determinants and associated factors. Clin Exp Rheumatol. 2008;26(5):661-667.
61. Margiotta DPE, Basta F, Dolcini G, et al. Physical activity and sedentary behavior in patients with systemic lupus erythematosus. PLoS One. 2018;13(3):e0193728.
62. Nikpour M, Urowitz MB, Ibanez D, Gladman DD. Frequency and determinants of work disability in systemic lupus erythematosus. Rheumatology (Oxford). 2010;49(7):1284-1292.
63. Falasinnu T, Chaichian Y, Simard JF. The prevalence and management of metabolic syndrome in SLE. Curr Opin Rheumatol. 2019;31(5):482-492.
64. Mosca M, Tani C, Aringer M, et al. European League Against Rheumatism recommendations for monitoring patients with systemic lupus erythematosus in clinical practice and in observational studies. Ann Rheum Dis. 2010;69(7):1269-1274.
65. Choi SW, Friso S. Epigenetics: A New Bridge between Nutrition and Health. Adv Nutr. 2010;1(1):8-16.
66. Margiotta DPE, Basta F, Dolcini G, et al. Physical activity and sedentary behavior in patients with systemic lupus erythematosus. PLoS One. 2018;13(3):e0193728.
67. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: An American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. 2005;112(17):2735-2752.
68. Peters MJL, Symmons DPM, McCarey D, et al. EULAR evidence-based recommendations for cardiovascular risk management in patients with rheumatoid arthritis and other forms of inflammatory arthritis. Ann Rheum Dis. 2010;69(2):325-331.
69. Mok CC, Kwok RC, Ho LY. Effect of disease activity and corticosteroid use on risk of metabolic syndrome in systemic lupus erythematosus: A longitudinal cohort study. Lupus. 2016;25(8):836-844.
70. Almeida C, Chaves HV, Lima V, et al. Patient education and self-management in systemic lupus erythematosus: State of the art and future directions. Lupus. 2019;28(7):899-910.