FREQUENCY OF METABOLIC SYNDROME IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING AT A PUBLIC SECTOR TERTIARY CARE HOSPITAL OF LAHORE: A CROSS- SECTIONAL STUDY

Saima Nouman Khan,[1] Ahmed Hassan,[2] Amina Umer,[3] Aneela Chaudhary,[4] Sadia Salman,[5] Muhammad Ijaz Bhatti,[6] Shehryar Aamer[7]

Abstract

Background and Objective: Metabolic syndrome is characterized by central obesity, deranged lipid profile, high blood pressure and abnormally high levels of blood sugar. It is an independent risk factor for cardiovascular disease. Systemic Lupus Erythematosus (SLE) is an autoimmune disease that can affect joints, skin, brain, lungs, kidneys, and blood vessels. The extent to which metabolic syndrome is frequent in our population is less known. The objective of this study was to assess the frequency of metabolic syndrome amongst SLE patients.

Methods: This cross-sectional study was undertaken in a public sector tertiary care hospital of Lahore from February 2021 through August 2021, including 110 confirmed SLE cases. After institutional approval and taking an informed consent, blood pressure, fasting and random blood sugar levels and fasting lipid profile were measured. Central obesity was assessed using waist circumference. Data were transferred to SPSS 21 for descriptive and inferential analyses. Frequencies were determined using numbers and percentages.

Results: Of 110 SLE patients, 14 (12.3%) were males and 96 (87.7%) were females. Mean age of SLE patients was 42.9± 9.9 years. Mean BMI was 28.7±4.7 kg/m2. The frequency of metabolic syndrome in studied SLE patients was 37/110 (33.6%).

Conclusion: Systemic lupus erythematosus patients had abnormally high serum triglyceride and cholesterol levels, diabetes mellitus, central obesity, high levels of fasting plasma glucose and hypertension. Therefore, one-third of SLE patients may have metabolic syndrome in our population.

Key Words: Dyslipidemia, Frequency, Metabolic Syndrome, Systemic Lupus Erythematosus.

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Systemic Lupus Erythematosus (SLE) is an autoimmune disease with wide spread chronic inflammatory which effects multiple organs including skin, joints, kidneys, lungs, nervous system and serous membranes. Abnormal immune response owing to the generation of antinuclear antibodies may result in organ damage with resultant malfunction and metabolic derangement. Etiological basis of SLE is still unknown; there may be genetic, environmental or hormonal factors involved in its pathogenesis.[1-3] There are reports of an association of SLE with COVID-19 vaccination.[4] Although there is no clear pattern of inheritance, there is evidence to suggest that genetics play a significant "high concordance rates" among identical twins. The great majority of people's genetic propensities are carried in the major histocompatibility complex (MHC) locus. Antigen-presenting molecule coding genes are

1,3. *Department of Medicine, Allama Iqbal Medical College/Jinnah Hospital Lahore*
2. *Department of Medicine, Jinnah Hospital Lahore*
4. *Department of Pulmonology, Allama Iqbal Medical College /Jinnah Hospital Lahore*
5. *Department of Endocrinology, Allama Iqbal Medical College /Jinnah Hospital Lahore*
6. *Department of Cardiology, Al-Aleem Medical College/ Gulab Devi Teaching Hospital Lahore*
7. *Department of Medicine, Jinnah Hospital Lahore*

Correspondence:
Dr Saima Nouman Khan ; *Assistant Professor of Medicine, Jinnah Hospital Lahore ; Email: samnouman@gmail.com*

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found in MHC class I and II HLA (human leukocyte antigens) regions.[5-9] Female gender and hormonal factors are major contributors to the development of SLE[10,11]. Additionally, estrogens and prolactin contribute to the development of autoimmunity, as well as to boost the synthesis of B-cell activation factor and affect the activation of lymphocytes and plasmacytoid dendritic cells (pDC). Patients diagnosed with SLE are more likely to experience flares of their disease because of using contraceptive medications that contain estrogen and hormone replacement therapy taken once menopause ensues; both of which have been linked to a higher incidence of SLE as well as pregnancy.[12] Androgens are known to suppress the immune system.[13] Environmental factors can also trigger this condition further deteriorating patient's quality of life.[14] Since SLE is associated with inflammatory damage to major organs, therefore, they are probably more likely than other individuals to develop metabolic dysfunction, such as sugar control, fat metabolism and changes in vasculature.

Metabolic syndrome is a condition characterized by a waist circumference of greater than 35 inches for women and 40 inches for men, elevated triglycerides of 150 mg/dL or more, high-density lipoprotein cholesterol (HDL) of less than 40 mg/dL in men or 50 mg/dL in women, fasting glucose of 100 mg/dL or more, and/or blood pressure readings of 130/85 mmHg or more.[15,16] Three out of these five criteria is usually considered sufficient to label a case as having metabolic syndrome. Insulin resistance, oxidative injury and cardiovascular risk are all exacerbated by metabolic syndrome, which is now understood to be a chronic condition that is both pro-inflammatory and prothrombotic over time. Systemic lupus erythematosus is closely associated with instability of the adipokines and cytokines, which is a common trait of metabolic syndrome as well as SLE. This suggests a complex relationship among autoimmunity, atherosclerosis, inflammatory processes and being overweight.[17-20] There is lack of evidence regarding the frequency of metabolic syndrome among patients with SLE in our population. The aim of this study is to assess the frequency of metabolic syndrome in patients with SLE and identify the factors associated with concomitant presence of both these conditions in a patient.

METHODS

This cross-sectional study was conducted from February 2021 through August 2021 in Jinnah Hospital Lahore, which is a public sector tertiary care centre in metropolitan city of Lahore. Ethical approval for this study was obtained from institutional Ethical Review Board. We included 110 SLE patients using non-probability convenient, consecutive sampling technique. This sample size was calculated using WHO sample size calculator version 1.1 assuming confidence level of 95% with absolute precision of 7% and anticipated population proportion of 16% using a formula of $n=[Z^2 \times P(1-P)/d^2]$.

Our inclusion criteria included the patients aged 15-60 years, either male or female, diagnosed as a case of SLE on presence of 4/11 criteria of the "American College of Rheumatology" for at least one year prior to inclusion in study. Patients who had history of SLE < 1 year, history of coronary artery disease, diabetes mellitus (DM), hypertension (HTN) and/or dyslipidemia and taking medications for it were excluded. Prior to recruitment, patients were provided written consent after being informed of the benefits of the study. Baseline demographic information age, gender, blood pressure and central obesity (defined as "waist >102 cm in men and >88 cm in women measured midway at the level of umbilicus) were recorded. After an overnight fast, early morning blood sample of about 5 ml was taken by venipuncture using aseptic technique for triglyceride level, HDL cholesterol levels and serum fasting blood sugar level and was sent to hospital laboratory. Results were collected the next day were noted. Presence of metabolic syndrome was then recorded which was defined by presence of 3/5 WHO criterion: (1), fasting plasma glucose >110 mg/dl; (2), serum triglyceride > 150 mg/dl; (3), Serum cholesterol < 40 mg/dl in males and < 50 mg/dl in females; (4), mean Blood pressure > 130/85 mmHg obtained by two reading 15 minutes apart on both arms measured by

mercury sphygmomanometer in lying position or patients already taking antihypertensive medication; (5), Central obesity. Data were transferred to SPSS version 21 for cleaning, coding and for descriptive and inferential analyses. Quantitative data were described using mean± standard deviation and qualitative data were presented as frequency and percentages. Data on age, gender, duration of SLE, body mass index (BMI), and family history of diabetes mellitus, hypertension and dyslipidemia were stratified using reasonable cut off points. We used Pearson's Chi-squared test to examine the difference of proportions to be significantly significant. A p-value of $p < 0.05$ was considered as statistically significant difference in proportions.

RESULTS

Demographic characteristics and disease profile of 110 SLE patients is presented in Table 1. The mean age of these SLE patients was 42.9± 9.9 years with age range between 23 to 60 years. Mean duration of disease was 8.4±2.2 years, duration of disease ranges between 5-12 years. Of these 110 SLE patients, 14 (12.7%) were males and 96(87.3%) were females. On examination of criteria for labelling SLE patients for presence of metabolic syndrome, we found that 54(49.1%) SLE patients had blood pressure more than 130/85 mm Hg, 50 (45.5%) had fasting blood sugar level of more than 110 mg/dl, 47 (42.7%) had serum cholesterol level of 40mg/dl and 51(46.4%) had central obesity. In addition, more than half of these participants had family history of hypertension, diabetes mellitus and dyslipidemia. Based on the WHO criteria, of 110 SLE patients, 37(33.6%) were labelled as having metabolic syndrome (Figure 1). Therefore, one-third of SLE patients had metabolic syndrome in our sample.

To answer the question whether presence of metabolic syndrome in these SLE patients is associated with age, gender, fasting blood sugar, serum cholesterol and family history of hypertension, diabetes mellitus, dyslipidemia our bivariate analyses show that there was no statistical association between age, gender, BMI > 28 kg/m2, and family history of dyslipidemia and presence of metabolic syndrome in SLE patients ($p > 0.05$), whereas, family history of diabetes, hypertension, baseline mean blood pressure >130/85, central obesity, baseline fasting plasma glucose level >110 mg/dl, serum triglyceride > 150mg/dl and serum cholesterol level > 40mg/dl had significant association with the presence of metabolic syndrome ($p > 0.05$) (Table 2).

Table 1: Baseline demographic characteristics of SLE patients with disease profile (n=110)

Characteristics	Mean ± SD
Quantitative	
Age (years)	42.9 ± 9.9
Duration of SLE (years)	8.4 ± 2.2
Body Mass Index (Kg/m^2)	28.7 ± 4.7
Qualitative	**Number (%)**
Gender	
Male	14 (12.7%)
Female	96 (87.3%)
Blood Pressure (systolic/diastolic)	
>130/85	54 (49.1%)
<130/85	56 (50.9%)
Fasting plasma glucose (mg/dl)	
>110	50 (45.5%)
<110	60 (54.5%)
Serum Triglycerides (mg/dl)	
> 150	60 (54.5%)
< 150	50 (45.5 %)
Serum Cholesterol (mg/dl)	
> 40	47 (42.7%)
< 40	63 (57.3%)
Central obesity (Yes)	51 (46.4%)
Family history of hypertension (Yes)	66 (60.0%)
Family history of Diabetes Mellitus (Yes)	59 (53.6%)
Family history of dyslipidemia (Yes)	73 (66.4%)

Abbreviations: SD, standard deviation;

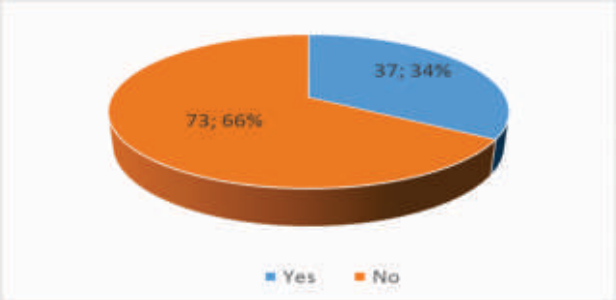

Figure 1. *Frequency of Metabolic Syndrome in Patients with SLE based on WHO Criteria (n=110)*

DISCUSSION

Table 2: *Association between demographic and disease profile with presence of metabolic syndrome in SLE patients (n=110)*

Characteristics	Metabolic Syndrome		*p-value**
	Yes (n=37) N (%)	No (n=73) N (%)	
Age (years)			
20-35	07 (18.9)	23 (31.5)	0.471
36-50	16 (43.3)	31 (42.4)	
> 50	14 (37.8)	19 (26.1)	
Gender			
Male	8 (21.6)	06 (8.7)	0.05
Female	29 (78.4)	67 (91.3)	
BMI > 28kg/m2			
Yes	11 (29.7)	25 (34.3)	0.633
No	26 (70.3)	48 (65.7)	
Family history of dyslipidemia			
Yes	28 (75.7)	45 (61.6)	0.141
No	09 (24.3)	28 (38.4)	
Family history of diabetes mellitus			
Yes	29 (76.0)	30 (41.1)	<0.001
No	09 (24.0)	43 (58.9)	
Family history of hypertension			
Yes	18 (48.6)	43(58.9)	0.005
No	19 (51.4)	30 (41.1)	
Baseline Blood Pressure (> 130/85)			
Yes	29 (78.4)	25 (34.3)	<0.001
No	08 (21.6)	48 (65.7)	
Central obesity			
Yes	25 (67.6)	26 (35.6)	<0.001
No	12 (32.4)	47 (64.4)	
Fasting glucose level (>110mg/dl)			
Yes	29 (78.4)	21 (28.7)	<0.001
No	08 (21.6)	52 (71.3)	
Serum triglycerides (>150mg/dl)			
Yes	26 (70.3)	34 (46.6)	0.018
No	11 (29.7)	39 (53.4)	
Serum Cholesterol (>40mg/dl)			
Yes	28 (75.7)	35 (47.9)	0.005
No	09 (24.3)	38 (52.1)	

Abbreviations: BMI, body mass index; Pearson's Chi-Squared test was used to calculate p value

The purpose of this study was to assess the frequency of metabolic syndrome among SLE patients attending a public sector tertiary care hospital of Lahore. We found that almost one-third of SLE patients had concomitant metabolic syndrome. Being female and with family history of hypertension and with higher baseline triglycerides was found to be associated with occurrence of metabolic syndrome. Main strength of this study is that there are very few studies conducted on this subject and there is inconsistent evidence about the concurrence of SLE and metabolic syndrome. Results of this study should be interpreted after considering few limitations. This is a cross sectional study and its domain was in a single centre. Moreover, the sample size was also small to comment on precise estimate. Further, our analyses was restricted to univariable and bivariate analyses and we commented on the statistical significance without conducting regression analyses for adjusting confounding factors.

Mean age of SLE patients and duration of disease differs from other studies.[21,22] For instance, 35.2 ± 13.4 years and their mean duration of disease was 24.1 ± 18.0 years[22], whereas in our study mean age was 42 yers.

Previous studies showed that among patients with SLE, hypertension was found in 45.62% patients, diabetes mellitus was observed in 2.5% patients, dyslipidemia was noticed in 42.5 % patients, obesity was observed in 13.75% patients and there were 7.5% patients in which hyper-triglyceridemia was detected.[23] These findings are more or less consistent with our results. Frequency of metabolic syndrome was reported by previous studies ranges from 16% to 20%, which is lower than what we found. This may be due to smaller sample size, variation of study population as we used only one centre.[22,23], yet, some other reports showed the frequency of metabolic in SLE patients as 32.4% which is consistent with our findings.[24,25]

In present study, it was observed that gender and age groups were not significantly associated with presence of metabolic syndrome. Family history of HTN and DM was strongly associated with presence of metabolic syndrome but there was no significant association between family history of dyslipidemia and BMI > 28 kg/m^2 and presence of metabolic syndrome. Significant association was found between mean blood pressure and metabolic syndrome. There was significant association between central obesity and metabolic syndrome. Fasting plasma glucose level

was found to be significantly associated with metabolic syndrome. There was significant association between serum triglyceride level and metabolic syndrome. There was significant association between serum cholesterol level and metabolic syndrome. Our findings are consistent with some of these studies but there are variations observed about these results, which may be due to the reasons explained in limitations of this study. Some studies with multivariate analyses, serum triglycerides and HDL-cholesterol were significantly associated with metabolic syndrome ($p<0.001$).[23] We suggest a replication of this study protocol with larger sample size and recruiting participants from different Centres with varied socio-economic groups, genetic background and people living in urban and rural areas. Occupational environment may be considered as a risk factor as well. Use of corticosteroid for treating SLE may be another risk factor for concurrence of SLE with metabolic syndrome.

CONCLUSION

One-third of SLE patients had metabolic syndrome and these patients had a family history of hypertension, diabetes mellitus, had baseline higher blood pressure, central obesity, higher baseline fasting plasma glucose; triglyceride and cholesterol levels were significantly associated with presence of metabolic syndrome in SLE patients.

Conflict of Interest: *None*

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