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Research Article

High Prevalence of Metabolic Syndrome in South African Systemic Lupus Erythematosus Patients

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ABSTRACT

Introduction: Patients with systemic lupus erythematosus (SLE) are at increased risk of metabolic syndrome (MetS) and its complications. In absence of published studies from sub- Saharan Africa, we investigated the prevalence and associations of MetS amongst recent-onset SLE patients.

Methods: A cross-sectional study of recent onset (<5 years disease duration) SLE patients meeting the Systemic Lupus International Collaborating Clinics (SLICC) SLE classification criteria. MetS was defined by Joint Interim Statement criteria. Clinical, demographic data, a Functional Assessment of Chronic Illness Therapy score and the 36-Item Short-Form Healthy Survey were completed.

Results: 75 SLE patients were included in the study, 65 (86.7%) were female, and 68.0% were of mixed ethnic, the mean age was 37.1 (11.7) years and the mean disease duration was 30.8 (23.6) months. The mean Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score was 0.9 (1.6). Prevalence of MetS was 40.0%, age and body mass index were the only significant features associated with MetS (p=0.003 and 0.001 respectively). Increased waist circumference (WC) was the most frequently observed feature, present in 92.9% of patients with MetS patients. Patients with an elevated WC were 32.5 times more likely to have MetS.

Conclusion: This study shows a high prevalence of MetS amongst South Africans with recently diagnosed SLE. This calls for aggressive strategies to reduce the prevalence of MetS and atherosclerotic cardiovascular disease. Waist circumference is a useful and cost-effective screening tool to identify SLE patients at risk of MetS.

Keywords: Systemic Lupus Erythematosus; Metabolic Syndrome; Waist Circumference; Africa

BACKGROUND

Systemic lupus erythematosus (SLE) is a multi-systemic autoimmune disease, associated with an increased risk of atherosclerotic cardiovascular disease (ASCVD), with an incidence of myocardial infarction in women with SLE aged 35-44 years over 50 times greater than in women of similar age [1]. Recent studies have reported an increased risk of premature cardiovascular disease after adjustment for age and traditional vascular risk factors [2,3]. Metabolic syndrome (MetS) is a cluster of metabolic abnormalities associated with central adiposity and insulin resistance [4]. This syndrome leads to endothelial dysfunction, arterial stiffness and accelerated ASCVD [5-7]. Patients with SLE have been shown to have a higher burden of MetS than healthy controls, with particularly increased incidence in low and middle-income countries (Table 1).

At first glance, MetS is a disease of affluence, and was once uncommon in sub-Saharan Africa [8]. Over the last three decades, lifestyle changes as urbanisation have taken place and, despite widespread poverty, the prevalence of MetS is increasing and ASCV is emerging as a major cause of mortality [9]. Recently, a high prevalence of MetS was documented in an urban population of mixed ethnic ancestry in the Western Cape where 62.0% of adults over 31 years had MetS, with females particularly affected [10].

To date, there are no published studies on MetS prevalence in sub-Saharan Africans with SLE. This study was undertaken to determine the prevalence and associations of MetS in adults with recent onset SLE in the Western Cape, South Africa.

PATIENTS AND METHODS

This cross-sectional study of 75 SLE patients recruited between January 2017 and July 2017 from the rheumatology clinic in a state-sector academic hospital as part of the African Lupus Genetics Network, a prospective database of SLE patients [11]. All patients

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met the following inclusion criteria: adults (≥ 18 years); symptom onset within the last 5 years; and fulfilled the Systemic Lupus International Collaborating Clinics (SLICC) SLE criteria [12]. Approval for the study was obtained from the University of Cape Town Human Research Ethics Committee, and all patients signed an informed consent before participating in the study.

Demographic data, clinical details including comorbidities, therapy and bio-morphometric details were collected. Disease duration was defined as the time from diagnosis of SLE to enrolment in the study, and ethnicity was self-reported by the patients. The SLE disease activity index (SLEDAI) and Systemic Lupus International Collaborating Clinics damage index (SLICC-DI) were calculated at enrolment to assess disease activity and damage respectively [13,14]. Serum lipid lipogram results including total cholesterol, triglyceride (TG), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) were documented. In addition, patients completed a Functional Assessment of Chronic Illness Therapy (FACIT) score measuring fatigue and the 36-Item Short-Form Health Survey (SF-36) as a general measure of health-related quality of life (HRQoL) [15]. MetS was defined according to the Joint Interim Statement (JIS) criteria, using WC cut-offs of male>94 cm, female>80 cm [16].

Statistical methods

The Students t-test was applied to compare continuous variables between groups, except where the data showed a non-normal distribution, in which case the Wilcoxon rank sum test was used. The Chi-square test, or when it is indicated, the 2-tailed Fishers' exact test was used in case of categorical variables. A bivariate logistic regression model was constructed to assess the association between specific variables (socio-demographic, clinical and treatment) and MetS. Significant variables found in the univariate analyses and chi-square contingency tests were entered the logistic regressions. A p-value of 0.05 was considered significant. Statistical analyses were done using SPSS version 24.

RESULTS

Of 75 patients, 86.7% were female, and of these 58.5% were premenopausal, the mean (SD) age was 37.1 (11.7) years and disease duration was 30.8 (23.6) months (Table 2).

In terms of ethnicity, 68.0% were of mixed ethnic ancestry and 29.3% were black Africans. Patients were of poor socio-economic backgrounds: the mean (SD) highest level of schooling was 10.0 (2.6) years and 30.7% were unemployed. Disease activity and damage scores were low (SLEDAI 0.9 (1.6) and SLICC-DI 0.3 (0.7) respectively). The mean (SD) body mass index (BMI) was (30.3-23.6) kg/m^2, and 36.0% were smokers. Two thirds of patients had been exposed to corticosteroids. The SF-36 scores showed poor physical and mental health, with low FACIT scores suggesting a high burden of fatigue. The prevalence of MetS in this cohort was 40.0%, and patients with MetS were significantly older than patients without MetS (mean age 41.9 vs. 33.8 years, p=0.003), and had a higher BMI (mean BMI 30.3 vs. 25.7 kg/cm^2, p=0,001) (Table 2). More patients in the MetS group were unemployed (47.8% vs. 26.7%), although this did not reach statistical significance.

The feature of the MetS most commonly encountered was an elevated WC, present in 92.9% of those with MetS (Table 3).

Elevated TG and low HDL-C were also significantly associated with the MetS (p<0.001 and 0.008 respectively). Multivariate analysis showed that elevated waist circumference, hypertension, and low HDL-C were independently associated with the MetS, encountered in 74.1% of MetS patients (p<0.001, Nagelkerke R^2=0.74).

DISCUSSION AND CONCLUSION

This study, the first to our knowledge assessing MetS in sub-Saharan African SLE patients, shows that 40.0% of patients with recent-onset SLE fulfilled criteria for the MetS. This high prevalence of the MetS is similar to that reported in low and middle-income countries in patients with SLE with disease duration less than 10 years, with a lower prevalence reported in higher income European countries. While these differences may reflect different diagnostic criteria for MetS, genetic susceptibility or environmental factors including sedentary lifestyle and a high calorie diet may be important [17,18]. Elevated WC was the most common component of the MetS. In our study 57.3% of patients with elevated WC had MetS, and patients with an elevated WC were 32.5 times more likely to have MetS than those with a normal WC. Elsewhere, studies of SLE patients have shown WC to be an important feature of the MetS [19-21]. In a US cohort of patients, elevated WC was a better predictor than BMI of ASCVD risk in the general population [22]. Hence, WC could be a useful and cost-effective screening tool to identify those at risk of MetS.

Dyslipidaemia, specifically a reduced HDL-C, was the second most frequent feature of the MetS in our study, again similar to the findings

Table 1: Global prevalence of Metabolic syndrome in patients with recent-onset SLE (disease duration less than 10 years).

Country, year of publication (reference)	MetS criteria	Age (yrs) (Mean, SD)	Disease duration- mean (yrs)	Prevalence MetS n (%)
Iran, 2018 Mobini et al. [31]	NCEP/ATPIII IDF	41.0 (12.2)	6.5	33/73 (45.2) 34/73 (46.6)
Italy, 2017 Margiotta et al. [30]	IDF	47.5 (14.1)	9.9	34/100 (34.0)
Multinational, 2015 Parker et al. [32]	JIS	34.9 (13.6)	0.5	439/1150 (38.2)
Egypt, 2015 Baraka et al. [33]	(NCEP/ ATP III)	32.9 (8.5)	3.4	12/30 (40.0)
Peru,2014 Ugarte-Gil et al. [34]	JIS	44.6 (12.9)	7.6	42/117 (44.4)
China,2013 Liu et al. [35]	JIS	34.1 (11.1)	2.9	40/116 (34.2)
Egypt, 2013 Gheita et al. [36]	(ATP III)	30.2 (8.3)	5.8	34/92 (36.9)
UK, 2011 Parker et al. [17]	JIS	48.0 (42-58)	8.5	60/200 (30.0)
Netherlands, 2008 Bultink et al. [37]	AHA/NHLB	39.0 (12)	6.6	22/14 (16.0)

MetS: Metabolic Syndrome; IDF: International Diabetes Federation; NCEP ATP III: National Cholesterol Education Program Adult Treatment Panel III; JIS: Joint Interim Statement on MetS; AHA/NHLB: American Heart Association /National Heart, Lung ,and Blood Institute

Table 2: Demographic and clinical characteristics of patients with SLE according to the presence or absence of metabolic syndrome.

Features	Overall cohort (n=75)	MetS (n=30)	No MetS (n=45)	p value*	OR (95% CI)**
Age (years)(mean, SD)	37.1 (11.7)	41.9 (10.1)	33.8 (11.6)	0.003	-
Female n (%)	65 (86.7)	28 (93.3)	37 (56.9)	ns	3.0 (0.6 -15.3)
Postmenopausal n (%)	5 (7.7)	4 (16.0)	1 (2.5)	ns	-
Ethnicity (self-reported)- n (%)	-	-	-	-	-
Black African	22 (29.3)	7 (23.3)	15 (33.3)	ns	-
Mixed ancestry	51 (68.0)	22 (73.3)	29 (64.4)	ns	-
White	2 (2.7)	1 (3.3)	1 (2.2)	ns	-
Disease duration (months)(mean, SD)	30.8 (23.6)	29.9 (18.8)	31.5 (27.0)	ns	-
Highest level schooling (years) (SD)	10.0 (2.6)	9.9 (2.7)	10.1 (2.6)	ns	-
Unemployed n (%)	23 (30.7)	11 (47.8)	12 (26.7)	0.1	1.6 (0.6 – 4.3)
Body Mass Index (kg/cm^2) (mean, SD)	27.6 (5.9)	30.3 (4.7)	25.7 (6.1)	0.001	-
Cigarette smoking (current) n (%)	27 (36.0)	12 (40.0)	15 (34.1)	ns	1.3 (0.5 – 3.4)
SLEDAI score (mean, SD)	0.9 (1.6)	0.7 (1.1)	1 (1.8)	ns	-
SLICC damage index (mean, SD)	0.3 (0.7)	0.3 (0.5)	0.3 (0.8)	ns	-
Corticosteroids ever prescribed n (%)	50 (66.6)	20 (66.6)	30 (66.6)	ns	0.9 (0.3 – 2.4)
Corticosteroid dose n (%)	-	-	-	-	0.7 (0.2 – 2.7)
Low (≤ 10 mg)	37/48 (77.1)	17/20 (85.0)	20/28 (71.4)	ns	-
High (>10 mg)	11/48 (22.9)	4/20 (20.0)	7/28 (25.0)	ns	-
SF-36 PCS (mean score) (mean, SD)	39.1 (19.8)	39 (20.1)	39.2 (19.9)	ns	-
SF-36 MCS (mean score) (mean, SD)	43.1 (24.7)	41.1 (26.9)	44.5 (23.3)	ns	-
FACIT score (mean, SD)	28.1 (12.4)	26.5 (12.8)	29.2 (12.2)	ns	-

*Comparing patients with MetS to those without MetS ; **Odds Ratio only reported for categorical variables; ns: Not Significant; MetS: Metabolic Syndrome; SLEDAI: SLE Disease Activity Index; SLICC: Systemic Lupus International Collaborating Clinics; MCS Mental Composite Score; PCS: Physical Composite Score; FACIT: Functional Assessment of Chronic Illness Therapy

Table 3: Frequency of the different components of metabolic syndrome in SLE patients.

Features	Overall cohort n=75	MetS patients n=30	Non MetS patients n=45	Uni variate analysis*		Multi variate analysis*	
				OR (95% CI)	p value	OR (95% CI)	p-value
Elevated waist circumference n (%)	43 (57.3)	26/28 (92.9)	10/35 (28.6)	32.5 (6.5-163.3)	<0.001	0.01 (0.01-0.61)	0.03
Elevated triglycerides or on drug therapy n (%)	18/74 (24.3)	15/29 (51.7)	5/39 (12.8)	7.3 (2.2-23.9)	<0.001	0.07 (0.01-1.36)	0.08
Reduced HDL-C or on drug therapy n (%)	35 (46.5)	18/26 (69.2)	14/39 (35.9)	4.0 (1.4-11.6)	0.008	0.04 (0.0.1-0.85)	0.04
Elevated blood pressure or on drug therapy n (%)	20 (26.9)	15 (50.0)	9/44 (20.5)	3.9 (1.4-10.8)	0.008	0.04 (0.01-1.03)	0.05
Elevated fasting glucose or drug therapy n (%)	3 (4.3)	3 (10.0)	1/44 (2.3)	4.8 (0.5-48.3)	ns	-	-

*Comparing patients with MetS to those without; MetS: Metabolic syndrome; HDL-C: High Density Lipoprotein Cholesterol; SLE: Systemic Lupus Erythematosus

of other studies. Of concern, HDL can lose its anti-inflammatory properties in states of chronic inflammation, and instead become pro-inflammatory (piHDL). In a study in California, 45.0% of women with SLE were found to have the dysfunctional piHDL, increasing the risk of subclinical atherosclerosis [23]. Most of the patients in this study were young women of poor socioeconomic status, with almost a third unemployed. Several studies have shown that low socioeconomic status is associated with MetS [24,25]. The high prevalence of smoking in this cohort is of concern, and an area for intervention. A recent South African study demonstrated a high smoking prevalence (51.5% of females in the 35-44 year age group) and a 50% higher overall smoking-related mortality in patients of mixed ethnic ancestry compared to other race groups, with ASCVD a major cause of death [26]. Many studies have looked at

the factors that predispose SLE patients to MetS. The present study found only age and BMI to be significant, with no association with disease duration, activity, damage scores nor therapy. Similarly, in a recent study in South India, no association was found between the MetS, SLE disease activity nor damage scores [27]. Several studies have shown no association with steroid use [19-28]. In contrast, a Brazilian study of premenopausal SLE women showed that MetS was associated with a higher cumulative dose of steroids [29]. In addition, the present study found no association between MetS and HRQoL or fatigue. A recent Italian study demonstrated that SLE patients with MetS report low mood and physical inactivity, and have a poor HRQoL in both mental and physical components [30]. Limitations of this study include the cross-sectional design, the small number of patients included, and the lack of a healthy control group. In addition, we were unable 7 calculate patients cumulative prednisone dose. We plan to expand and follow this cohort for the development of ASCVD. In conclusion, we have shown a high prevalence of MetS amongst South Africans with recently diagnosed SLE. This, together with the high prevalence of cigarette smoking, and SLE disease itself, infers a particularly significant risk of ASCVD. Future interventional studies addressing modifiable risk factors such as weight loss, smoking cessation and physical activity in this population are planned. Waist circumference is a useful screening tool for identifying those at risk of MetS and should be incorporated into the routine assessment of SLE patients.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

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