Bionatura
Latin American Journal of Biotechnology and Life Sciences

Bionatura Issue 2 Vol 8 No 1 2023

Article

A comparison of VCAM-1 and ICAM-1 as atherosclerosis risk factors in patients with systemic lupus erythematosus from Iraq

Hajer Walid Khammas Jaafar[1,*], Ghid Hassan Abdulhadi[1], Mohammad Hadi Munshid[2]
[1]College of Medicine, University of Baghdad, Iraq.
[2]Baghdad Teaching Hospital, Iraq.
***Correspondence: Email: chemist.hajer@gmail.com**
Available from: http://dx.doi.org/10.21931/RB/CSS/2023.08.02.61

Abstract: All major organs may be impacted by the connective disease systemic lupus erythematosus, a separate risk factor for coronary artery disease (CAD). Adhesion molecules like intercellular adhesion molecules (ICAM) and vascular cell adhesion molecules (VCAM) can detect endothelial damage and dysfunction, which appear to play a crucial role. This study investigated whether people with SLE had elevated subclinical and clinical atherosclerosis risk factors. Traditional CAD risk factors such as smoking, hypertension, and hyperlipidemia cannot entirely explain this elevation. It is thought that immunological dysfunction also increases CAD risk in SLE patients. The study aimed to assess early endothelial changes in SLE Iraqi female patients without previous coronary artery lesions by exploring a potential relationship between circulating VCAM-1 and ICAM-1 as risk factors for atherosclerosis and the relationship of CAD with SLE disease and its severity; further, the study explained the effect of the hydroxychloroquine (HCQ) on the lipid profile levels of the patients. 92 female SLE patients were divided into mild, moderate, and severe, according to the SLE disease activity index 2000 (SLEDAI-2k), compared with 30 apparently healthy control individuals. All of them need a history of CAD. Serum VCAM-1, ICAM-1 level, VCAM-1/ICAM-1 ratio, TC, HDL, LDL levels TC/HDL and LDL/HDL ratios were measured. sVCAM-1, sICAM-1 levels and VCAM-1/ICAM-1 ratio were significantly and gradually increased in patient groups compared with control. Serum TC, HDL and LDL levels were significantly reduced in the SLE patients compared to the control. At the same time, the TC/HDL and LDL/HDL ratios were significantly elevated with the severity of the SLE disease. sVCAM-1, sICAM-1 level and VCAM-1/ICAM-1 ratio together with serum TC/HDL and LDL/HDL may improve coronary artery disease risk categorization in SLE patients without acute coronary syndromes. Furthermore, they were more sensitive in severe SLE instances than in moderate and mild ones, suggesting that they may be related to the extent of coronary lesions in SLE patients. VCAM-1 had a higher sensitivity than ICAM-1 in detecting and severity screening for CAD in SLE patients.

Keywords: VCAM-1, ICAM-1, SLE, Atherosclerosis

Introduction

Systemic Lupus Erythematosus (SLE) is a Chronic multisystemic autoimmune disease characterized by a propensity for flare-ups and complex and varied

immunological dysregulation [1,2]. More women than men are afflicted by SLE, which typically manifests in early or middle adulthood [3]. SLE symptoms include exhaustion, joint pain, fever, dyspnea, chest pain, and a recognizable facial butterfly rash. Occasionally, these symptoms deteriorate during flare episodes. The diagnosis of SLE is challenging due to symptoms that can present in various ways, and it frequently depends on distinct clinical findings in the blood, skin, joints, kidneys, and central nervous system [4,5]. The most significant cause of death worldwide is coronary artery disease (CAD) [6]. Premature atherosclerosis contributes to the nine times higher mortality risk for cardiovascular illnesses in SLE patients than in the general population [7].

Genetic, environmental, and inter-factor interactions all have a role in the development of CAD. Numerous risk factors for CAD have been discovered, including smoking, high blood pressure, dyslipidemia, obesity, and diabetes [8,9]. Atherosclerosis development is linked to the majority of CVDs [10]. Atherosclerosis is a long-term inflammatory condition that affects the medium and large arteries. Inflammation-driven plaque development is characterized by the buildup of lipids and immune cells in the sub-endothelial artery wall. In early-stage atherosclerosis, inflammation, hemodynamic damage, and aberrant lipid metabolism are the main culprits. SLE patients had a higher risk of atherosclerosis than non-SLE patients, according to several studies [13]. Dyslipidemia, a common disorder in SLE patients with long-term negative consequences, is indeed one of the traditional risk factors for atherosclerosis. It elevates the risk of coronary artery disease (CAD). It impacts other pathological changes in SLE patients, such as accelerating the progression of chronic kidney disease and resulting in brain damage. Autoantibodies influence the prevalence of dyslipidemia in the metabolism of lipoproteins, renal involvement, disease activity, and high lipid profile levels brought on by medicines [16]. In the current era of rheumatic disease management, there is increased interest in analyzing the effect of disease-modifying therapies on traditional cardiac risk factors. There is a growing interest in how hydroxychloroquine (HCQ) affects cardiac risk factors because it has been shown to lessen disease activity when used to treat SLE [17]. According to recent studies, HCQ reduces the traditional cardiac risk factors associated with SLE problems [18]. Results have been described as less atherogenic lipid profiles, a decreased risk of diabetes, and antithrombotic properties [19]. Endothelial dysfunction is strongly linked to the development of atherosclerosis [20], and since many SLE patients have reduced endothelium-dependent vasorelaxation and increased arterial stiffness, they have endothelial dysfunction [20,21]. Endothelial dysfunction is the term used to describe a number of functional phenotypic deviations that significantly affect the regulation of hemostasis and thrombosis, local vascular tone and redox homeostasis, and the sensitivity of acute and chronic inflammatory responses within the arterial wall [20]. Subclinical atherosclerosis must be identified to prevent atherosclerosis from developing and minimize early mortality and morbidity in SLE patients.

Finding biomarkers with a high predictive value for subclinical atherosclerosis in chronic inflammatory disorders is crucial. Leukocyte adherence and rolling along endothelial cell surfaces are enabled by cell adhesion molecules, which also govern leukocyte migration into inflamed tissues. According to previous research, patients with systemic lupus erythematosus (SLE) had higher amounts of adhesion molecules. Increased amounts of adhesion molecules have also been linked to disease activity [22]. Adhesion molecules such as intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule (VCAM) could be used to quantify endothelial damage [23] reliably. Increased sVCAM-1 and sICAM-1 levels in SLE patients have been linked to coronary artery disease, coronary artery calcium score, and carotid plaque development [24,25]. When employing a continuous scale, the Receiver Operating Characteristic (ROC) curve has been widely used in medical research to

evaluate the precision of a diagnostic test or biomarker in disease screening and diagnosis. The binary test rule is generated at each potential threshold point, and the ROC curve shows the relationship between sensitivity and 1-specificity [26].

Materials and Methods

This case-control study included 92 female SLE patients aged between (14-58) divided into i. Mild group (n = 33), ii. Moderate group (n=27), iii. Sever group (n=32) and healthy female controls (n= 30), their age between (14-52). All patients that met four or more of the 1982 updated American College of Rheumatology Criteria for categorization of SLE at the Department of Rheumatology, Baghdad Hospital/Medical City [27]. Systemic Lupus Erythematosus Disease Activity Index 2000 assessed their clinical disease activity (SLEDAI-2K). SLEDAI-2K is based on the existence of 24 descriptors during the past 10 days in nine organ systems. With the following definition: 0 to 4: (no activity disease); 5 to 9: (mild activity disease); 10 to 14: (moderate activity disease); ≥15: severe activity disease [28-31]. A specialist rheumatologist identified the diagnosis of each SLE patient, Dr. Mohamed Hadi, by their clinical examinations supported with laboratory tests.

Exclusion criteria

Both patients and healthy controls were free from CAD (acceptable within six months), hematological diseases, endocrine diseases, acute infections and tumors.

VCAM-1 and ICAM-1

VCAM-1 and ICAM-1 were measured using enzyme-linked immunosorbent assay (ELISA) kits from The Picokine™ Human VCAM1. The Sandwich-ELISA concept is used in the Pre-Coated ELISA kit, a solid phase immunoassay explicitly created to test Human VCAM1 using a 96-well strip plate pre-coated with an antibody specific for VCAM1.

Blood and Biochemistry analysis

Total Serum Cholesterol, High-density lipoprotein (HDL), low-density lipoprotein (LDL),(cobas c111, ROSH, Germany).

Results and Discussion

Serum ICAM-1 and VCAM-1 levels and ROC analysis

This study compared serum (VCAM-1 and ICAM-1) levels among SLE patients divided into (mild, moderate and severe). As shown in Table 1, the VCAM-1 mean ± SD were (87.59±19.89), (199.45±46.65), (239.07±51.95) and (329.78±59.87) in control, mild, moderate and severe, respectively. The ICAM-1 mean ± SD were (1.806±0.218), (2.63±0.84), (2.95±0.75) and (3.06±0.82) in control, mild, moderate and severe, respectively. The VCAM-1/ICAM-1 mean ± SD were (48.76±11.09), (80.87±25.17), (84.25±23.57) and (113.38±33.04) in control, mild, moderate and severe, respectively. The values were increased gradually when the activity of the disease was increased.

parameters	Control (n=32)	SLE patient	P values		
		Mild (n=33)	Moderate (n=27)	Sever (n=32)	
VCAM-1	87.59±19.89	199.45±46.65			<0.001
	87.59±19.89		239.07±51.95		<0.001
	87.59±19.89			329.78±59.87	<0.001
		199.45±46.65	239.07±51.95		0.002

		199.45±46.65		329.78±59.87	<0.001
			239.07±51.95	329.78±59.87	<0.001
ICAM-1	1.806±0.218	2.63±0.84			<0.001
	1.806±0.218		2.95±0.75		<0.001
	1.806±0.218			3.06±0.82	<0.001
		2.63±0.84	2.95±0.75		0.088
		2.63±0.84		3.06±0.82	0.018
			2.95±0.75	3.06±0.82	0.577
VCAM/ICAM	48.76±11.09	80.87±25.17			<0.001
	48.76±11.09		84.25±23.57		<0.001
	48.76±11.09			113.38±33.04	<0.001
		80.87±25.17	84.25±23.57		0.603
		80.87±25.17		113.38±33.04	<0.001
			84.25±23.57	113.38±33.04	<0.001

n Number of individuals placed in parentheses.
ICAM: intercellular adhesion molecule,
VCAM: vascular cell adhesion molecule Continuous variables are presented as the mean ± standard deviation and compared using the post hoc test or ANOVA.
P-values of 0.05 were considered statistically significant.

Table 1. Serum ICAM-1 and VCAM-1 levels in SLE patients and control.

Receiver operating characteristic (ROC) curve analysis was constructed for serum VCAM-1 and ICAM-1 level to detect SLE patients at risk of CAD and its severity. As shown in Table 1 and Figures 1, the cut-off point of ICAM-1 was 1.97, VCAM-1 was 117, and VCAM-1 / ICAM-1 ratio was 61.15, so ICAM-1 level > 1.97, VCAM-1 level > 117, and VCAM-1 / ICAM-1 ratio > 61.15.

Marker	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
ICAM	1.97	90.2%	86.4%	96.5%	67.9%	89.5%
VCAM	117	97.8%	100%	100%	91.7%	98.2%
VCAM/ICAM	61.15	84.8%	95.5%	98.7%	60%	86.8%

Table 2. Diagnostic accuracy of markers as a predictor for CAD in SLE.

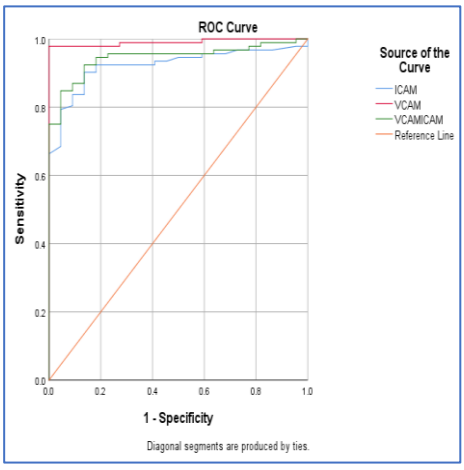

Figure 1. ROC curve for VCAM, ICAM, and VCAM/ICAM in predicting CAD in SLE patients.

To evaluate the accuracy of serum VCAM, ICAM, and VCAM/ICAM ratio levels in detecting CAD in SLE in each patient group, a ROC test was done, as presented in Table 3. Serum VCAM-1 has AUC (0.982), (0.990), and (1.000) in mild, moderate and severe, respectively. With sensitivity (97%), (96%) and (100%) in mild, moderate and severe, respectively. With specificity (100%) and p-value < 0.0001 in all the SLE patient groups Figures 2, 3, and 4. Serum ICAM-1 has AUC (0.866), (0.928), and (0.977) in mild, moderate, and severe, respectively. With sensitivity (81%), (92%), and (100%) in mild, moderate and severe, respectively. With specificity (87%), (91%) and (82%) in mild, moderate, and severe, respectively. P-value < 0.0001 in all the SLE patient groups Figures 2, 3, and 4. Serum VCAM-1/ICAM-1 ratio has AUC (0.898), (0.946), and (0.993) in mild, moderate, and severe, respectively. With sensitivity (90%), (96%), and (96%) in mild, moderate, and severe respectively. With specificity (80%), (87%) and (100%) in mild, moderate and severe, respectively. P-value < 0.0001 in all the SLE patient groups as described in 2, 3, and 4.

SLE groups	Marker	Area	Asymptotic Sig. [b]	Sensitivity	Specificity	Accuracy
Mild	VCAM	.982	.000	97%	100%	98.2%
	ICAM	.866	.000	81%	87%	86.6%
	VCAM/ICAM	.898	.000	90%	80%	89.8%
Moderate	VCAM	.990	.000	96%	100%	99%
	ICAM	.928	.000	92%	91%	92.8%
	VCAM/ICAM	.946	.000	96%	87%	94.6%
Sever	VCAM	1.000	.000	100%	100%	100%
	ICAM	.977	.000	100%	82%	97.7%
	VCAM/ICAM	.993	.000	96%	100%	99.3%

Table 3. Diagnostic accuracy of markers as a predictor for CAD in SLE patients groups.

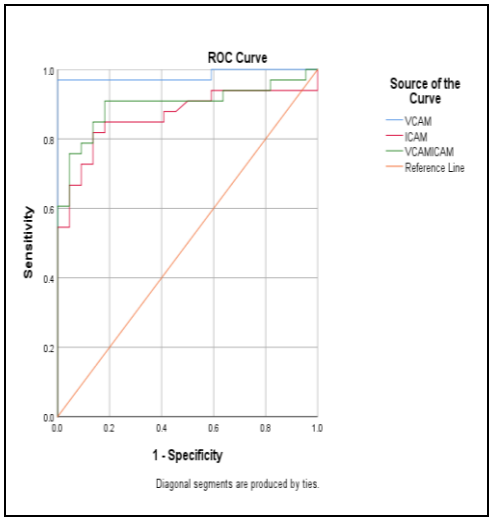

Figure 2. ROC curve for VCAM, ICAM and VCAM/ICAM in mild SLE.

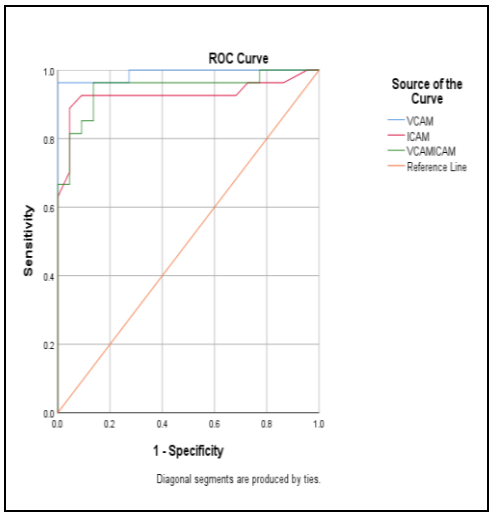

Figure 3. ROC curve for VCAM, ICAM and VCAM/ICAM in moderate SLE.

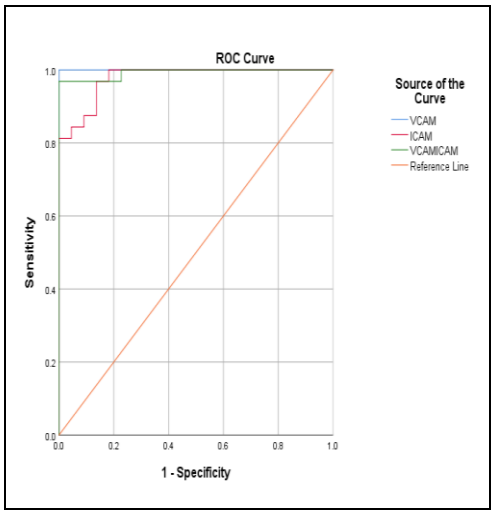

Figure 4. ROC curve for VCAM, ICAM and VCAM/ICAM in severe SLE.

A study found revealed that lupus-prone mice developed vascular dysfunction in their aortas. Comparatively to age-matched control mice, the melatonin nuclear receptor ROR expression was reduced in the aortas of lupus-prone animals. Human umbilical vein endothelial cells' ROR protein levels were downregulated by cell media containing SLE patient sera (HUVECs). In HUVECs treated with melatonin, the expression of anti-oxidant molecules increased, whereas pro-inflammatory factors and adhesion molecules (VCAM and ICAM) decreased. Patients with SLE may be more at risk for vascular damage due to various autoimmune manifestations, such as altered cytokine levels and innate immune responses, autoantibodies, oxidative stress, and dysregulated lipids. Melatonin levels in SLE patients have reportedly been lower than those of healthy people. Melatonin treatment in female MRL/MpJ-Faslpr lupus-prone mice reduced pro-inflammatory cytokines (IL-1, IL-2, IL-6, IFN-, and TNF-). Endothelium highly expresses several types of adhesion molecules, including ICAM-1, VCAM-1, MCP-1, and E-selectin, which can attract monocytes, T cells, and dendritic cells and encourage these cells to adhere to endothelial cells when pro-inflammatory cytokines like IL-1 and TNF- are stimulated in the blood of patients with SLE. ROR's ability to reduce TNF-induced VCAM-1 and ICAM-1 expression in human endothelial cells has also been demonstrated. As shown in Table 4, the result shows a significant decrease in serum (TC, HDL, LDL) between the control and the mild, moderate, and severe groups. The percentage of TC/HDL ratio (mean ± SD) was (4.71±1.8), (5.07±1.7), (5.43±1.4),

(6.13±3.07) in control, mild, moderate and severe, respectively. as well as the percentage of LDL/HDL ratio (mean ± SD) was (3.327±1.56), (3.857±2.11), (3.945±1.6) and (4.615±3.04) in control, mild, moderate and severe respectively. The TC/HDL and LDL/HDL ratios were significantly increased in the severe group compared with the control group. The TC/HDL ratio in the severe group significantly increased compared to the mild group. However, the LDL/HDL ratio had no significant changes between the patient groups (mild, moderate, severe).

Test	Control (n=30)	SLE patient			P values
		Mild (n=33)	Moderate (n=27)	Sever (n=32)	
TC	200.19±36	153.36±48.35			<0.001
	200.19±36		161±28.14		<0.001
	200.19±36			161.31±33	<0.001
HDL	45.61±13.31	33.52±15.37			0.001
	45.61±13.31		31.8±8.27		<0.001
	45.61±13.31			31.2±16.67	0.001
LDL	134.26±24	109.56±36.49			0.001
	134.26±24		113.42±24.25		0.009
	134.26±24			117.28±34.4	0.024
TC/HDL	4.71±1.8	5.07±1.7			0.510
	4.71±1.8		5.43±1.4		0.227
	4.71±1.8			6.13±3.07	0.015
LDL/HDL	3.327±1.56	3.857±2.11			0.351
	3.327±1.56		3.945±1.6		0.322
	3.327±1.56			4.615±3.04	0.034

n Number of individuals placed in parentheses.
TC, total cholesterol;
HDL-C, high-density lipoprotein cholesterol;
LDL-C, low-density lipoprotein cholesterol.

Table 4. Lipid profile in SLE patients and control.

Continuous variables are presented as the mean ± standard deviation and compared using the post hoc test or ANOVA. P-values of 0.05 were considered statistically significant.

Twenty-four individuals with moderate to severe disorders who had never received therapy participated in the cross-sectional prospective trial; 15 had rheumatoid arthritis (RA), and 9 had SLE. The patients' cardiovascular risk was evaluated using the atherogenic index of plasma (AIP). Spearman's correlation was used to confirm the connection between inflammatory and metabolic measures. For all analyses, a two-tailed P 0.05 was regarded as statistically significant. The ratio of total cholesterol (TC) to high-density lipoprotein (HDL) cholesterol may reveal information not included in more widely used single cholesterol assays. Assessing the effect of such extra information on the risk of atherosclerotic cardiovascular disease may be made more accessible by analyzing the discrepancy between lipid measurements. Research determined how the TC/HDL cholesterol ratio compared to non-HDL and low-density lipoprotein (LDL) cholesterol predicts the risk of developing atherosclerotic cardiovascular disease.

Discussion

A study of Framingham, QRISK2 and QRISK3 scores was calculated in 109 patients with SLE and 29 healthy controls. Endothelial microvesicles (EMVs), triglycerides, vascular cell adhesion molecule (VCAM), and high-sensitivity C reactive protein (hsCRP) were measured using markers of inflammation and endothelial dysfunction. Measures of endothelial dysfunction, such as EMVs and systolic blood pressure, are associated with SLE patients' elevated 10-year risk of developing CAD, significantly captured by QRISK3. Compared to low-risk individuals, newly discovered patients had substantially higher systolic blood pressure, glucocorticoid usage, CKD, BMI, and type 2 diabetes. While blood levels of VCAM-1 were substantially more significant in all of the high-risk vs. low-risk new QRISK3 groups, serum levels of TG and CRP were higher in the new QRISK3 group compared to the low-risk group. The study showed that VCAM improves CAD risk identification in SLE patients with overt atherosclerotic symptoms [32]. In the current study, melatonin reduces the expression of ICAM-1 and VCAM-1 in SLE medium-treated HUVECs, which reduces the Number of peripheral blood monocytes that adhere to the endothelial monolayer. When the ROR gene was silenced in HUVECs, the levels of the proteins ICAM-1 and VCAM-1 increased, demonstrating that melatonin inhibits the expression of adhesion molecules by activating the nuclear receptor ROR [33]. In a study of 66 female patients with premenopausal symptoms who fit the American College of Rheumatology (ACR) SLE categorization criteria, 20 of them with metabolic syndrome (Met.S), 46 of them without Met.S, and 28 healthy females control. Subclinical atherosclerosis was screened by measuring serum ICAM-1, Liptin, and CRP levels. They noticed that ICAM-1 was significantly increased in both patient groups, so it is helpful to discover the SLE patients who do not have symptoms predictive of CAD, reversal of Met.S patients [34]. The levels of uric acid, very low-density lipoprotein cholesterol, total cholesterol/high-density lipoprotein cholesterol ratio (TC/HDL-C), and the logarithmic ratio of triglycerides to HDL-cholesterol (log[TG/HDL-C]) were all higher in SLE patients than in RA. However, the former group had lower total lymphocyte count, lipoprotein (a), and low-density lipoprotein cholesterol than the RA group. Compared to RA patients, most SLE patients showed higher cardiovascular disease risk (> 0.24 AIP score) [35]. 14,403 individuals in the Atherosclerosis Risk in Communities (ARIC) study who had no history of atherosclerotic cardiovascular disease at the start of the study were examined. At five visits, the discordance of TC/HDL cholesterol with LDL cholesterol (calculated using the innovative Martin/Hopkins approach) and non-HDL cholesterol was evaluated and was defined as being at or above the median for each lipid parameter. Using a time-varying methodology, they created Cox proportional hazard models to calculate the risk for incident atherosclerotic cardiovascular disease events linked to each lipid concordance/discordance category. A clinically significant discrepancy exists between the commonly used non-HDL and LDL cholesterol and the TC/HDL cholesterol accessible from the standard lipid profile. Such discordance, especially in those with diabetes where discordance is more prevalent, may aid in informing atherosclerotic cardiovascular disease risk management.

Conclusions

Our findings demonstrated that as disease activity increased, serum levels of VCAM-1, ICAM-1, and VCAM-1/ICAM-1 ratio were also elevated and greater than apparently healthy control subjects. They were significantly elevated with severe SLE than the moderate ones, moderately higher than mild SLE patients, and all higher than apparently healthy control subjects. Therefore, they could act as detecting markers for atherosclerosis in SLE patients and as differentiating markers for its activity in patients because their levels were positively related to SLE

disease activity. In SLE patients at risk for developing CAD, levels of VCAM-1, ICAM-1, and VCAM-1/ICAM-1 ratio may be related to the size of coronary lesions, but sVCAM-1 level was more sensitive than sICAM-1 level in our study, making it more helpful in detecting and screening the prognosis of CAD in SLE patients than sICAM-1. Also, our results show that (TC, TG, HDL, VLDL and LDL), the most risk factors for CAD were significantly lower than the healthy control subjects. They were within the normal range, and that happened because of the uses of CQ or HCQ, which can be associated with lowering serum lipid profile independently of the other variables. Despite this decrease in serum lipid profile, the TC/HDL and LDL/HDL ratios remained high. Therefore, the serum lipid profile levels cannot be adopted alone in the detection of CAD in SLE patients, and the use of serum VCAM-1, ICAM-1 and VCAM-1/ICAM-1 ratio levels together with TC/HDL and LDL/HDL ratios is necessary to promote early detection of CAD in SLE patients. Another study found revealed that lupus-prone mice developed vascular dysfunction in their aortas. Comparatively to age-matched control mice, the melatonin nuclear receptor ROR expression was reduced in the aortas of lupus-prone animals. Human umbilical vein endothelial cells' ROR protein levels were downregulated by cell media containing SLE patient sera (HUVECs)

References

1. Soliman MI, Esawy AM, Khashba SA. Role of prolactin in activity of systemic lupus erythematosus. *Egyptian Journal of Dermatology and Venerology*. **2018** Jan 1;38(1):23.
2. Gregory Katz, Nathaniel R. Smilowitz, Ashira Blazer, Robert Clancy, Jill P. Buyon, Jeffrey S. Berger, Systemic Lupus Erythematosus and Increased Prevalence of Atherosclerotic Cardiovascular Disease in Hospitalized Patients, Mayo Clinic Proceedings, Volume 94, Issue 8, **2019**, Pages 1436-1443, ISSN 0025-6196.
3. Justiz Vaillant AA, Goyal A, Bansal P, Varacallo M. Systemic Lupus Erythematosus (SLE). StatPearls. Treasure Island (FL): StatPearls Publishing Copyright. **2020**.
4. Kuhn A, Bonsmann G, Anders HJ, Herzer P, Tenbrock K, Schneider M. The diagnosis and treatment of systemic lupus erythematosus. Dtsch Arztebl Int. **2015**;112(25):423–32.
5. Mayo Clinic Staff. Lupus: Symptoms and causes **2021**, Jan 27 [Available from: https://www.mayoclinic.org/diseases-conditions/lupus/symptoms-causes/syc-20365789.
6. Szarpak, L., Mierzejewska, M., Jurek, J., Kochanowska, A., Gasecka, A., Truszewski, Z., Pruc, M., Blek, N., Rafique, Z., Filipiak, K.J. and Denegri, A., **2022**. Effect of Coronary Artery Disease on COVID-19—Prognosis and Risk Assessment: A Systematic Review and Meta-analysis. Biology, 11(2), p.221.
7. Blazer, A., Parikh, K., Fudman, D.I. and Garshick, M.S., **2021**. Dietary and Lifestyle Cardiometabolic Risk Reduction Strategies in Pro-inflammatory Diseases. In Prevention and Treatment of Cardiovascular Disease (pp. 179-191). Humana, Cham.
8. Krist, Alex H., Karina W. Davidson, Carol M. Mangione, Michael J. Barry, Michael Cabana, Aaron B. Caughey, Katrina Donahue. Behavioral counseling interventions to promote a healthy diet and physical activity for cardiovascular disease prevention in adults with cardiovascular risk factors: US Preventive Services Task Force recommendation statement." Jama 324, no. 20 (**2020**): 2069-2075.
9. Tektonidou MG. Cardiovascular disease risk in antiphospholipid syndrome: Thrombo-inflammation and atherothrombosis. *Journal of Autoimmunity*. **2022** Apr 1;128:102813.
10. Pardali, E., Dimmeler, S., Zeiher, A.M. and Rieger, M.A., **2020**. Clonal hematopoiesis, aging, and cardiovascular diseases. Experimental Hematology, 83, pp.95-104.

11. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med **2005**; 352(16): 1685-95. http://dx.doi.org/10.1056/NEJMra043430 PMID: 15843671
12. iang, Shuang & Zhang, Jingyi & Ning, Ruihong & Du, Zhou & Liu, Jiangyan & Batibawa, Joe & Duan, Junchao & Sun, Zhiwei. **2020**. The critical role of endothelial function in fine particulate matter-induced atherosclerosis. Particle and Fibre Toxicology. 17. 10.1186/s12989-020-00391-x.
13. M. Frieri, H. Stampfl, Systemic lupus erythematosus, and atherosclerosis: a literature review, Autoimmun. Rev. 15 (**2016**) 16–21, https://doi.org/10.1016/j. autrev.2015.08.007.
14. Spannella F, Di Pentima C, Giulietti F, Buscarini S, Ristori L, Giordano P, Sarzani R. Prevalence of subclinical carotid atherosclerosis and role of cardiovascular risk factors in older adults: atherosclerosis and aging are not synonyms. High Blood Pressure & Cardiovascular Prevention. **2020** Jun;27(3):231-8.
15. Tselios K, Koumaras C, Gladman DD, Urowitz MB. Dyslipidemia in systemic lupus erythematosus: just another comorbidity? InSeminars in arthritis and rheumatism **2016** Apr 1 (Vol. 45, No. 5, pp. 604-610). WB Saunders.
16. Tao CY, Shang J, Chen T, Yu D, Jiang YM, Liu D, Cheng GY, Xiao J, Zhao ZZ. Impact of antimalarial (AM) on serum lipids in systemic lupus erythematosus (SLE) patients: a systematic review and meta-analysis. Medicine. **2019** Jun;98(14).
17. Dima A, Jurcut C, Chasset F, Felten R, Arnaud L. Hydroxychloroquine in systemic lupus erythematosus: an overview of current knowledge. Therapeutic advances in musculoskeletal disease. **2022** Feb;14:1759720X211073001.
18. Floris A, Piga M, Mangoni AA, Bortoluzzi A, Erre GL, Cauli A. Protective effects of hydroxychloroquine against accelerated atherosclerosis in systemic lupus erythematosus. Mediators of inflammation. **2018** Feb 18.
19. Babary H, Liu X, Ayatollahi Y, Chen XP, Doo L, Uppaluru LK, Kwak MK, Kulaga C, Modjinou D, Olech E, Yoo JW. Favorable effects of hydroxychloroquine on serum low-density lipid in patients with systemic lupus erythematosus: A systematic review and meta-analysis. *International journal of rheumatic diseases*. **2018** Jan;21(1):84-92.
20. Al-Tamimi, H. .; Al-Qaraghouli, A. A. .; Khudair, Z. .; Jbara, A. A. . Effect Of Different Concentrations Of Nano-Magnesium And Nano-Titanium Oxide On The Cumulative Mortality Of Larvae Of Two Species Of Cucurbit Fruit Fly Affiliated With The Dacus In Iraq. JLSAR 2021, 2, 9-13..
21. Hasni, S.A., Gupta, S., Davis, M., Poncio, E., Temesgen-Oyelakin, Y., Carlucci, P.M., Wang, X., Naqi, M., Playford, M.P., Goel, RR and Li, X. Phase 1 double-blind, randomized safety trial of the Janus kinase inhibitor tofacitinib in systemic lupus erythematosus. Nature Communications, **2021,** 12(1), pp.1-11.
22. Guo Liu, Run-Nan, Qian-Yao Cheng, Hao-Yue Zhou, Bao-Zhu Li, and Dong-Qing Ye. "Elevated blood and urinary ICAM-1 is a biomarker for systemic lupus erythematosus: a systematic review and meta-analysis." Immunological Investigations 49, no. 1-2 **2020**: 15-31.
23. Nowak K, Gumkowska-Sroka O, Kotyla P. Adhesion molecules: a way to understand lupus. Reumatologia/Rheumatology. 2022;60(2):133-141. doi:10.5114/reum.**2022**.115664.
24. Gustafsson J, Gunnarsson I, Borjesson O, et al. Predictors of the first cardiovascular event in patients with systemic lupus erythematosus - a prospective cohort study. Arthritis Res Ther **2009**; 11: R186.
25. Run-Nan Guo Liu, Qian-Yao Cheng, Hao-Yue Zhou, Bao-Zhu Li & DongQing Ye. Elevated Blood and Urinary ICAM-1 is a Biomarker for Systemic Lupus Erythematosus: A Systematic Review and Meta-Analysis, Immunological Investigations, **2019**.

26. Wang D, Cai X. Smooth ROC curve estimation via Bernstein polynomials. PLoS One. 2021;16(5):e0251959. Published **2021** May 25.
27. Tan, E.M., Cohen, A.S., Fries, J.F., Masi, A.T., Mcshane, D.J., Rothfield, N.F., Schaller, J.G., Talal, N. and Winchester, R.J. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis & Rheumatism: *Official Journal of the American College of Rheumatology* **1982,** *25(11)*, pp.1271-1277.
28. InterYang H, Xie X, Song Y, Nie A, Chen H. Self-care agency in systemic lupus erythematosus and its associated factors: a cross-sectional study. Patient Prefer Adherence. **2018**;*12*:607-613. doi:10.2147/PPA.S162648.
29. Wang J, Niu R, Jiang L, et al. The diagnostic values of C-reactive protein and procalcitonin in identifying systemic lupus erythematosus infection and disease activity. Medicine (Baltimore). **2019**;98(33):e16798.
30. TANG, Yamei, et al. Changes of serum IL-6, IL-17, and complements in systemic lupus erythematosus patients. *Journal of Interferon & Cytokine Research*, **2019**, *39.7*: 410-415.
31. Huang X, Su G, Wang Z, Shangguan S, Cui X, Zhu J, Kang M, Li S, Zhang T, Wu F, Wang L. Hypomethylation of long interspersed nucleotide element-1 in peripheral mononuclear cells of juvenile systemic lupus erythematosus patients in China. *International Journal of Rheumatic Diseases*. **2014** Mar;*17(3)*:280-90.
32. Edwards N, Langford-Smith AW, Parker BJ, Bruce IN, Reynolds JA, Alexander MY, McCarthy EM, Wilkinson FL. QRISK3 improves detection of cardiovascular disease risk in patients with systemic lupus erythematosus. Lupus science & medicine. **2018** Aug *1;5(1)*:e000272.
33. Huang H, Liu X, Chen D, Lu Y, Li J, Du F, Zhang C, Lu L. Melatonin prevents endothelial dysfunction in SLE by activating the nuclear receptor retinoic acid-related orphan receptor-α. International Immunopharmacology. **2020** Jun *1;83*:106365.
34. Salwan M. Abdulateef, Ahmad A. Majid, Mohammed A. Al-Bayer, Srwd S. Shawkat, Ahmad Tatar, Thafer T. Mohammed, Firas M. Abdulateef, Mohammed Q. Al-Ani. Effect of aromatase inhibitors on sex differentiation and embryonic development in chicks. *Veterinary Medicine and Science*, **2021**, *7(6)*, pp. 2362–2373.
35. AL- Shamary, W. A. .; Alkhateb, B. A. A. H. .; Abdel, E. T. . Role Of Perlite Quantity And Intervals Of Irrigation On Potatoes (Solanum Tuberosum L.) Grown In Gypsiferous Soil. Journal of Life Science and Applied Research. 2020, 1, 31-39.
36. Quispe, R., Elshazly, M.B., Zhao, D., Toth, P.P., Puri, R., Virani, S.S., Blumenthal, R.S., Martin, S.S., Jones, S.R. and Michos, E.D. Total cholesterol/HDL-cholesterol ratio discordance with LDL-cholesterol and non-HDL-cholesterol and incidence of atherosclerotic cardiovascular disease in primary prevention: The ARIC study. *European Journal of Preventive Cardiology*, **2020** 27(15), pp.1597-1605.

Received: May 15, 2023/ Accepted: June 10, 2023 / Published: June 15, 2023

Citation: Jaafar, H. W.; Abdulhdi. G. H.; Munshid, M., H. A comparison of VCAM-1 and ICAM-1 as atherosclerosis risk factors in patients with systemic lupus erythematosus from Iraq. Revis Bionatura 2023;8 (2) 61. http://dx.doi.org/10.21931/RB/CSS/2023.08.02.61