

Correlation between Demographic Characteristics and Oxidized Low-Density Lipoprotein (oxLDL-IgM and oxLDL -IgG) Antibodies Levels in Patients with Systemic Lupus Erythematosus

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Abstract

Background: Systemic Lupus Erythematosus (SLE) may affect one or more organ systems; as time goes on, other manifestations may start to appear. Musculoskeletal, cutaneous, renal, and endocrine systems are all involved in SLE. The nervous system, hematological, vascular, pulmonary, gastrointestinal, and ocular imbalance of the immune response and the production of autoantibodies such as anti-oxidized Low-Density Lipoprotein LDL antibodies have a clear impact on the body's organs and the development of complications of the disease.

Objectives: To assess the levels of anti-oxLDL (IgM-Abs) and anti-oxLDL (IgG-Abs) as biomarkers for disease activity in SLE patients and their relationship to demographic characteristics.

Methods: The study comprised 100 SLE patients admitted to the Rheumatology Unit at Baghdad Teaching Hospital, age range (33.4 to 9.95) years, including 7 males and 93 females. An enzyme-linked immunosorbent Assay ELISA was used to measure the levels of serum oxLDL (IgM- Abs) and oxLDL (IgG-Abs).

Results: The results of the present study showed that there was a significant difference between the levels of anti-oxLDL IgM antibodies(Abs) in SLE patients in obese and non-obese groups since the levels of anti-oxLDL-IgM Abs in obese patients were (3.14 µg/L) and non-obese patients were (5.13 µg/L) (P=0.005), while in SLE patients with Diabetes Mellitus (D.M.), the levels of anti-ox LDL-IgM Abs were (3.80 µg/L) and in SLE patients with no DM were (5.13 µg/L). Also, the results showed that there were no significant differences between levels of anti-oxLDL IgG Abs in obese patients with SLE (6.28 µg/L) and non-obese patients with SLE (10.25µg/L) P > 0.05.

Conclusion: There was a significant difference between levels of anti-oxLDL IgM Abs in obese and non-obese patients with SLE, and no significant differences between the levels of anti-oxLDL IgG Abs in the same groups of patients.

Keywords: Immunoglobulins G; Immunoglobulins M; Oxidized Low-Density Lipoprotein antibody; Obesity; Systemic Lupus Erythematosus.

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune condition that can affect virtually any organ in the body and is relapsing-remitting. The result is tissue damage and systemic inflammation, which is marked by the creation of autoantibodies, the growth of immune complexes, and the deposition of autoantibodies (1). The development of lupus is strongly predisposed in females of reproductive age. In women between the ages of 15 and 44, the female-to-male ratio for the prevalence of lupus can reach 13:1, whereas in children and the elderly, it is only 2:1(2). Chronic Obstructive Pulmonary Disease (COPD), malignancies, and cardiovascular disorders are associated with smoking. Smoking condition and the effectiveness of available appears to be a significant risk factor for SLE in addition to its regular side effects, and it has a negative impact on both the

progression of the treatments (3). Despite the inherent heterogeneity and research design limitations, there are signs that smoking causes illnesses such as rheumatoid arthritis, Grave's disease, and multiple sclerosis (3, 4). Additionally, smoking increases comorbidities in lupus patients, such as Atherosclerosis, at a risk comparable to Diabetes mellitus (5). Obesity has been linked to the pathophysiology of SLE because it can create a systemic milieu that is low-gradely inflamed by increasing the production of cytokines such as tumor necrosis factor-alpha (TNF-) and interleukin 6 (IL-6) (6). SLE is also linked to a higher risk of developing Diabetes Mellitus (DM). Type 1 Diabetes and other autoimmune diseases were more likely to occur in SLE patients (7). The relationship was first demonstrated in the context of hypercholesterolemia, where the lowest risk of Coronary artery disease for a given degree of hypercholesterolemia was associated with the highest IgM levels. IgG and IgM have been

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demonstrated to be independent predictors of Coronary artery disease (CAD) development, as well as potential moderators of the CAD risk linked to rising levels of oxidative Biomarkers, in an epidemiological cohort of initially healthy individuals (8). The increased risk of Atherosclerosis and CVD in SLE cannot totally be accounted for by the known risk factors (9). Their significance must not be overlooked. The onset of CVD is significantly correlated with age. An increased risk of clinical CVD has been linked to male sex, hypertension, and dyslipidemia (10,11,12). Oxidized LDL (ox-LDL) is thought to be a major Atherosclerosis antigen. In both atherosclerotic lesions and human plasma, anti-OxLDL antibodies have been identified. It has not yet been conclusively determined whether the immune response is primarily pro- or antiatherogenic. The majority of research has demonstrated a link between Atherosclerotic disease and higher IgG titers against OxLDL. Although fewer studies have looked into IgM titers, the majority of studies appear to show an inverse link between IgM titers and Atherosclerotic disease. Immunization with oxLDL induces antibody formation (both IgG and IgM) and protects against Atherosclerosis development (13).

The current study aimed to assess the levels of oxLDL (IgM-Abs) and oxLDL (IgG-Abs) as Biomarkers for disease activity in SLE patients and their relationship to demographic characteristics.

Patients and Methods

The current study involved (100) patients (7 males, 93 females) with SLE and the age range was 33.4 ± 9.95 years for the patients admitted Rheumatology Unit in the Baghdad Teaching Hospital from 09/11/2021 to 18/01/2022.

The rheumatologist used the 2012 Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) [14] criteria and the 1997 updated Systemic Lupus Erythematosus (SLE) criteria of the American College of Rheumatology (ACR) [15], which are based on clinical examination and laboratory evaluation, to make the diagnosis.

Table (1): Demographic Characteristics of patients SLE

		Count	%
Disease activity	Active	50	69.4
	Inactive	22	30.6
Hypertension	Yes	32	33.3
	No	64	66.7
Obesity	Yes	17	17.7
	No	79	82.3
Anemia	Yes	54	56.2
	No	42	43.8
Hair loss	Yes	56	58.3
	No	40	41.7
DM	Yes	18	18.6
	No	79	81.4
Thyroid	Yes	25	25.8
	No	72	74.2
CVD	Yes	3	3.1
	No	94	96.9
Smoking	Yes	4	4.1
	No	93	95.9

The current study received approval from the College of Medicine scientific ethics committee at the University of Baghdad. Blood samples were collected, to get baseline information for each participant. After that, sera were kept at -20°C . Each serum sample underwent evaluation for detection of directed by the manufacturer (Sun Long Biotech Company, China). The absorbance was measured at 450 nm. All immunological tests were carried out in the Medical Research Unit at the College of Medicine, Al-Nahrain University.

Statistical analyses: The SPSS statistics software for Social Sciences was used to perform the statistical analysis (version 20.0 for Windows, SPSS, Chicago, IL, USA). Because of the non-normal distribution of the oxLDL (IgM) Abs and oxLDL- (IgG) Abs, median and IQR (Inter Quartile Range) were used to describe them (Kolmogorov-Smirnov test). Mann-Whitney test was used to study the difference between the two groups. Qualitative data is represented as count and percentage. The chi-squared test was used to test the relation of qualitative data. Pearson correlation test was used to test the relation between quantitative data. P- value of <0.05 was considered statistically significant.

Results

Table (1) shows some characteristics of SLE patients, such as active disease hypertension, obesity, hair loss, smoking, thyroid disease, anemia, diabetes, and CVD. The results showed that 50 (69.4%) of the SLE patients had disease activity, while 22 (30.6%) patients with inactive phases of SLE. Also, 33.3% of patients with SLE had hypertension, compared to 66.7% of patients with SLE who did not have hypertension, while 82% of SLE patients had no obesity, and 17.7% of SLE patients were obese. Anemia was seen in 56.2% of SLE patients, compared to 43.8% of SLE did not have anemia. The percentage of SLE patients who had hair loss was 58.3%, compared to 41.7% of those who did not have. While 25.8% of patients had thyroid disease compared with 74.2% of SLE patients who did not have.

Figure (1) showed that there were significant differences between obese patients with SLE(5.13%) and non- obese patients with SLE (3.14%)for oxLDL IgM-Abs, *P*- value ($P<0.005$) and significant

differences between SLE patients with DM for anti oxLDL IgM Abs (5.13%) and patients with SLE non-diabetic (3.8%) ($P<0.005$).

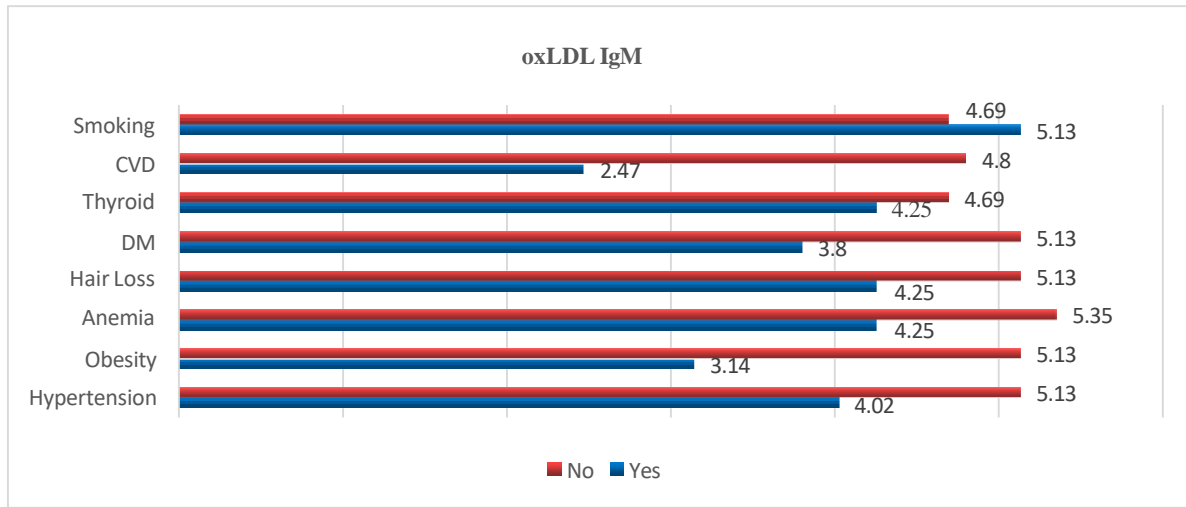


Figure 1: The percentages of oxLDL-IgM Abs in SLE patients according to demographic characteristics of SLE patients

Also, the results showed in Figure (2) that there were no significant differences in oxLDL IgG Abs levels

in Diabetic patients with SLE(10.82%) and non-DM patients with SLE(5.45%) ($P< 0.005$).

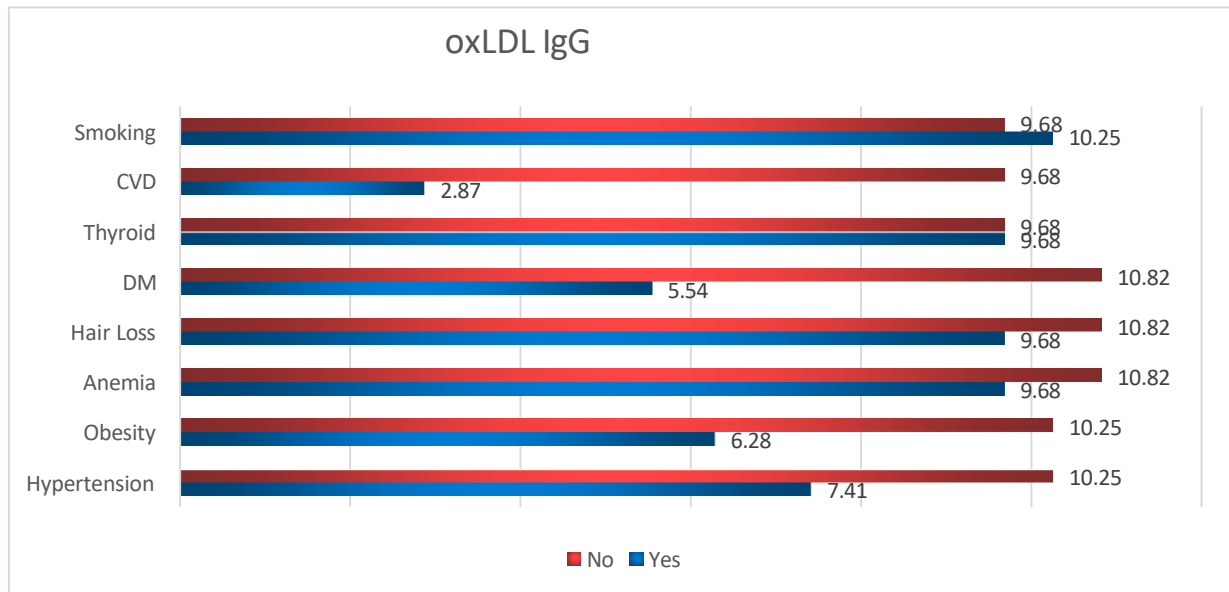


Figure 2: The percentages of oxLDL-IgG Abs in SLE patients according to demographic characteristics of SLE patients.

Discussion

The demonstrates the various characteristic features of SLE patients such as the disease activity, and this may be due to the failure of SLE patients to adhere to their treatment, whereas patients who undergo customized treatment have shown good results in reducing SLE activity and these results in agreement with that reported by Petri et al (16), that primary and secondary prevention strategies directed at hypertension, hypercholesterolemia, and obesity, as well as other known CAD risk factors, should be

routinely employed in the management of patients with SLE(16). According to the results of the represented study, 32 (33.3%) SLE patients were suffering from hypertension, this result was in agreement with that reported by Nived, et al (17); who revealed that 15% of SLE patients had high blood pressure while Mungu-Realpozo reported that cardiovascular disease had a higher prevalence in people with systemic lupus erythematosus (SLE) (CVD), which was partly due to traditional vascular

risk factors like hypertension. was found that 66.7% of SLE patients had high blood pressure. According to WHO, hypertension affects 14% to 60% of SLE patients, making it more common than it is in the general population (18). The current study found that the number of SLE patients was 17 (17.7%) who suffering from obesity and had high body mass index, these results were in agreement with that reported by (Patterson, et al (19); that although the exact function that obesity plays role in disease activity is unknown, it has been linked to the accumulation of SLE damage, particularly lupus nephritis, as well as other risk factors such as disease duration, aging, and higher steroid use. The risk of atherosclerosis rises with increasing waist size. According to earlier research on SLE-affected women, obesity is independently linked to the disease's negative consequences, such as depression, disease activity, exhaustion, and pain. Obesity reduction is a crucial objective for patients' health (20). The study shows that there were 58.3% of SLE patients had hair loss, these results were in agreement with that reported by Segura et al,2020 that there are several complications that result in SLE patients as a result of the long period of disease, including the period of taking steroid medications, and as a result, it leads to exposure to several complications, including diabetes, thyroid disorders, anemia, and hair loss due to the exposure of various parts of the body to damage (21,22).

There were 18.6% of SLE patients had D. M. and there were 81.4% did not have D.M., these results in agreement with that reported by Masztalewicz et al, that cardiovascular disease is more likely to be the reason for death in those with SLE who had it longer than five years (CVD) Epidemiological findings in inflammatory disorders like SLE, additional processes (atypical/disease-specific factors) accelerate atherosclerosis when combined. Age, hypertension, diabetes mellitus, dyslipidemia, a history of a vascular event, such as ischemic heart disease or cerebrovascular accident, menopause, and smoking are all traditional causes of cardiovascular disease risk factors, with more conventional risk elements. [23].The results of the present study showed that the levels of ox-LDL IgM Abs in diabetic patients with SLE were 5.13µg/L, and 10.82 µg/L of ox LDL-IgG Abs, and these results were in agreement with that reported by Omer et al,2017and Van den berg et al, that many studies showed that the high levels of (ox-LDL)antibodies in people who suffer from various diseases such as diabetes, hypertension, thyroid disease, Atherosclerosis Rheumatoid arthritis, in addition to other autoimmune diseases [24,25,26,27] Furthermore, there were 5.13% of OxLDL IgM Abs and 10.28% of OxLDL IgG Abs, in non-diabetic patients with SLE Conversely, the percentage of oxLDL- IgM Abs and OxLDL -IgG Abs was (3.8%, and 5.54%) in diabetic patients with SLE respectively. Additionally, the levels of OxLDL-IgM Abs and OxLDL- IgG Abs in non-obes patients with SLE were (5.13% and 10.26%) respectively.

Furthermore, the percentage of obese patients with SLE in both OxLDL IgM and OxLDL IgG Abs were 3.14% and 6.28% respectively. In addition, the results of the present study showed that SLE patients with D.M. had higher levels of ox LDL- IgG Abs which were 10.82µg/L than oxLDL- IgM Abs which were 5.54 µg/L and these results agreed with that reported by Maria et al.,2011 that human-modified LDL, Abs are predominantly of the IgG Abs isotype easily across the endothelial barrier (28).

Conclusion

The results of the present study showed that SLE patients with D.M. had higher levels of ox LDL- IgG Abs than oxLDL- IgM Abs. Also, there was a significant difference between levels of OxLDL- IgM Abs in obese patients with SLE and non-obese patients with SLE, and no significant differences between the levels of OxLDL- IgG Abs.

Authors' declaration

We confirm that all the Figures and Tables in the manuscript belong to the current study. Besides, the Figures and images, which do not belong to it have been given permission for re-publication attached to the manuscript. Authors sign on ethical consideration's approval- Ethical Clearance: This study was approved by the Scientific Ethics Committee of Communicable Clinical Infectious Diseases Research Unit. It is also approved by the Iraqi Ministry of Health and the Ministry of Education and Scientific Research according to the code number (88 IN 25/10/2021)

Conflicts of interest: None.

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Author Contributions

Study conception & design: (Suha A. Al-Fakhar, Muhammed H. Al-Asami). *Literature search:* (Nusaibah Kh. Al-Zubaidi). *Data acquisition:* (Nusaibah Kh. Al-Zubaidi & Suha A. Al-Fakhar). *Data analysis & interpretation:* (Nusaibah Kh. Al-Zubaidi & Suha A. Al-Fakhar). *Manuscript preparation:* (Nusaibah Kh. Saddam Suha A. Al-Fakhar). *Manuscript editing & review:* (Nusaibah Kh. Al-Zubaidi & Suha A. Al-Fakhar, Muhammed H. Al-Asami).

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العلاقة بين الخصائص الديموغرافية لمرضى داء الذئبة الحمامي المجموعي مع مستوى الاضداد المناعية المضادة للاكسدة OxLDL-IgM و OxLDL-IgG.

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الخلاصة:

داء الذئبة الحمامي المجموعي (SLE) قد يؤثر على واحد أو أكثر من أجهزة الجسم، ومع مرور الوقت، قد تبدأ المظاهر الأخرى بالظهور. الجهاز العضلي الهيكلي، والجلد، والكلية، وأنظمة الغدد الصماء كلها متورطة في مرض داء الذئبة الحمامي المجموعي. إن اختلال توازن الجهاز العصبي، الدم، الأوعية الدموية، الرئوي، الجهاز الهضمي، والعين في الاستجابة المناعية وإنتاج الأجسام المضادة الذاتية كأجسام مضادة للاكسدة LDL (مضادات oxLDL) لها تأثير واضح على أعضاء الجسم وتطور مضاعفات المرض.

الهدف من الدراسة: تقييم مستويات اضداد oxLDL (IgM) و اضداد oxLDL (IgG-Abs) كمؤشرات حيوية لنشاط المرض لدى مرضى داء الذئبة الاحمامي المجموعي وعلاقتها بالخصائص الديموغرافية.

طرق العمل: اشتملت الدراسة على 100 مريض بمرض داء الذئبة الحمامي المجموعي 7 ذكور (7%) و 93 إناث تتراوح أعمارهم بين 33.4 ± 9.95 سنة والذين دخلوا وحدة المفاصل بمستشفى بغداد التعليمي. تم تقييم مستويات اضداد oxLDL IgM و oxLDL IgG باستخدام المقايسة الامتصاصية المناعية بالإنزيم المرتبط (ELISA).

النتائج: أظهرت الدراسة الحالية أن هناك فرقا معنويا بين مستويات الأجسام المضادة OxLDL IgM في مرضى داء الذئبة الحمامي المجموعي الذين يعانون من السمنة المفرطة ومجموعات غير البدنين، حيث أن مستويات اضداد oxLDL-IgM في المرضى الذين يعانون من السمنة كانت (3.14 ميكروغرام / لتر) والمرضى غير البدنين كانت (5.13 ميكروغرام / لتر). كانت قيمة P 0.005 بينما مرضى داء الذئبة الحمامي المجموعي كانت مستويات اضداد oxLDL-IgM (3.80 ميكروغرام / لتر) وفي مرضى داء الذئبة الحمامي المجموعي الذين ليس لديهم مرض السكري كانت (5.13 ميكروغرام / لتر)، بينما أظهرت النتائج عدم وجود فروق ذات دلالة إحصائية. بين مستويات اضداد oxLDL IgG في مرضى داء الذئبة الحمامي المجموعي الذين يعانون من السمنة المفرطة وغير البدنين. ومرضى داء الذئبة الحمامي المجموعي مع مرض داء السكري. كانت قيمة P>0.05.

الاستنتاجات: عند مقارنة مرضى داء الذئبة الحمامي المجموعي، تم العثور على فروق ذات دلالة إحصائية بين مستويات اضداد oxLDL IgM في المرضى البدناء والمصابين بداء الذئبة الحمامي المجموعي وغير البدناء وعدم وجود فروق ذات دلالة إحصائية بين مستويات اضداد oxLDL IgG. **الكلمات المفتاحية:** داء الذئبة الحمامي المجموعي، الاضداد المضادة للاكسدة OxLDL (IgM) و OxLDL (IgG)، مرض السمنة مع داء الذئبة الحمامي المجموعي، التهاب المفاصل الرئوي، امراض المناعة الذاتية.