# Determination the Role of Anti Oxidized Low Density Lipoprotein Antibodies in Systemic Lupus Erthematosus Patients

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**Abstract**

Background: Systemic lupus erythematosus (SLE) is an autoimmune, inflammatory disease, that can affect virtually every organ. Imbalance of the immune response and the production of autoantibodies as anti Anti Oxidized LDL (anti oxLDL) antibodies has a clear impact on the body's organs and the development of complications of the disease, including cardiovascular diseases . Patients and Methods;The study included 100 SLE patients 7 males (7%) and 93 (93%) females with age range of 33.4±9.95 years attending Rheumatology Unit, Baghdad Teaching Hospital and 38 matched controls was 6 (15.8%) males and 32 (84.2%) females their mean age 34.2 + 9.1 years.. Serum oxLDL (IgM) and oxLDL (IgG) levels were assessed using an enzyme-linked immunosorbent assay (ELISA). RESULTS;The present study showed that, there was a significant differences between levels of OxLDL IgM between patients and controls groups, whereas the levels of oxLDL IgM in controls (11.56 µg/L) was higher than in patient with SLE (4.80 µg/L). P value was (0.005), while the results showed that there was a significant differences between levels of oxLDL IgG between patients and controls groups, whereas the levels of oxLDL IgG in control groups (19.91 µg/L) was higher than in patient SLE which was (9.68 µg/L), P value was (0.005).Conclusion:When compared to SLE patients, control groups had higher concentrations of the markers oxLDL IgM and oxLDL IgG . Further studies are. Needed to be implement and illustrate the role of OxLDL IgM in the process of the acceleration of atherosclerosis in SLE patients.

Keywords: SLE; oxLDL (IgM); oxLDL (IgG); CVD

## 1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune condition that has a relapsing-remitting history and can affect virtually any organ in the body. Systemic inflammation and tissue damage are the outcome, and it is characterized by the production of autoantibodies, the development of immune complexes, and the deposition of autoantibodies [1]. The development of lupus is strongly predisposed in females of reproductive age. The female-to-male ratio for the occurrence of lupus among women between the ages of 15 and 44 is as high as 13:1, although it is only 2:1 in youngsters and the elderly [2]. SLE has been linked to an increased risk of cardiovascular disease (CVD) development and a greater likelihood of cardiovascular mortality. One of the causes of the increased cardiovascular risk in SLE is the quicker development of atherosclerosis. Additionally, it appears that inflammatory and immunologic factors contribute to atherosclerosis in SLE patients [3] The link was first shown in the context of hypercholesterolemia, where the highest IgM levels were associated with the lowest risk of coronary artery disease for a given amount of hypercholesterolemia. An epidemiological cohort of initially healthy individuals found that IgG and IgM are not only independent predictors of coronary artery disease (CAD) occurrences but may also modify the CAD risk associated with increasing levels of oxidative biomarkers [4] Interest in type I interferons as potential causes of SLE has increased. Additionally, it has been suggested that IFN-a contributes to the development of atherosclerosis.by causing a disproportion between endothelial repair and restoration, resulting in aberrant vasculogenesis [5,6] Although the elevated risk for atherosclerosis and CVD in SLE cannot entirely be explained by the established risk factors [7] Their importance cannot be understated. Age itself is a significant risk factor for the development of CVD. Male sex, hypertension, and dyslipidemia have all been linked to an elevated risk for clinical CVD [8, 9-10]

The objective of the present work was to evaluate the usefulness of oxLDL (IgM) and oxLDL (IgG) a biomarker for the activity of disease in SLE patients and its relation with the of pathogenesis of CVD.

## 2. Patients and Methods

The current study involved a (100) patient with range of age was 33.4±9.95 years for the patient's subjects. (Rheumatologist at Rheumatology Unit) from Baghdad Teaching Hospital during the period November 2021 to January 2022.

The rheumatologist according to the 1997 revised criteria for Systemic lupus erythematosus (SLE) of

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the American College of Rheumatology (ACR) and the criteria for SLE of Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) 2012, which are based on clinical examination and laboratory evaluation, made the diagnosis.

The scientific ethics committee of the College of Medicine, University of Baghdad, approved the study. For all participants, baseline information were collected from blood tests and self-reported histories including gender and age.

Blood samples were collected in gel tubes and the serum was removed by centrifugation at 1000-3000 rpm for 10 minutes. Samples were then frozen at -20°C. Each serum sample was analyzed for oxLDL (IgM) and oxLDL (IgG) levels using an enzyme-linked immunosorbent assay (ELISA) (Sun Long Biotech Company, China), according to the manufacturer's instructions. The absorbance was measured at 450 nm using a plate reader. Blood samples were collected from patients attending the Baghdad Teaching Hospital Rheumatology Unit and immunological tests were performed in the Medical Research Unit at the College of Medicine, Al-Nahrain University.

Statistical analyses: were performed using SPSS statistical package for Social Sciences (version 20.0 for windows, SPSS, Chicago, IL, USA).Quantitative data are represented as mean, standard deviation and range. To test differences between the patient and control groups Student's t-test was used.Median and IQR (Inter Quartile Range) were used to describe oxLDL (IgM), oxLDL (IgG), as their distribution was non-normal (Kolmogorov-Smirnov test). Mann Whitney test was used to study the difference between the two groups.Qualitative data are represented as count and percentage. Chi-square 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.

## 3. Results and Discussion

The present study included 100 patients and 38 controls subjects. Their age ranges mean, S.D. were (33.4 + 9.95) years for the patients and (34.2 + 9.1) years for the control subjects. The result showed that there was no significant difference in age mean between SLE patients and healthy control groups. There were seven males, (7%) and 93 (93%) females in the patient group and 6 (15.8%) males, and 32 (84.2%) females in the control group. The current study showed that the number of women diagnosed with SLE in the samples under study was 93 (93%), while the number of men was 7% (7%). This shows a significant superiority in the number of women diagnosed with SLE compared to the number of men; these results were in agreement with most studies reported by, [12-14] who mentioned in their studies [15-17] that the majority of SLE patients under their studies were women. According to the majority of earlier studies, women are more likely than men to develop autoimmune disorders like SLE. This is because of the impact of female sex hormones, particularly estrogens. While testosterone serves as a suppressant for an overactive immune response, these hormones increase the effectiveness of the immune system.

The Characteristics of the patients and control are presented in Table 1. There was a significant difference between patients and control for the markers oxLDL IgM and oxLDL IgG with higher values in the control group (P<0.05).

While patient with SLE levels of oxLDL (IgM) (4.8 µg/L) were lower than controls (11.56 µg/L), P value was (0.005), and the results showed that there were significant variations in oxLDL (IgG) levels between the patient and control groups, with the control groups having oxLDL (IgG) levels that were greater than those of the SLE patients which were (9.68 µg/L).

**Table 1:** Difference between patients and control for oxLDL IgM and IgG markers

| | Group | | | | | | | | Pvalue |
|---|---|---|---|---|---|---|---|---|---|
| | Patient | | | | Control | | | | |
| | Median | IQR | Min | Max | Median | IQR | Min | Max | |
| OxLDL IgM | 4.80 | 2.44 | 1.58 | 36.17 | 11.56 | 6.43 | 5.58 | 53.47 | 0.005 |
| OxLDL IgG | 9.68 | 10.51 | 0.60 | 91.46 | 19.91 | 16.47 | 4.00 | 76.70 | 0.005 |

In systemic lupus erythematosus, the immune system targets body tissues, resulting in extensive inflammation and tissue destruction in the organs that are affected. The skin, joints, lungs, brain, blood vessels, and kidneys can all be impacted. Although there is no known treatment for lupus, medical procedures and dietary modifications can assist to lessen and control its side effect [11] in the current study, an evaluation study for a few immunological markers (Anti OxLDL IgM & IgG) was undertaken for SLE patients and healthy individuals. In order to determine their relationship to the effectiveness of the disease and the emergence of its consequences, various essential features and hematological parameters were also investigated. According to the results of the current study, there were 93 (93% of the samples) of women who had been diagnosed with SLE and 7% (of the samples) of men. The results were consistent with the majority of studies that were reported by [12, 13-14] and this reveals a considerable superiority in the number of women diagnosed with SLE compared to the number of men. They noted in their studies that women made up the majority of their SLE patients.

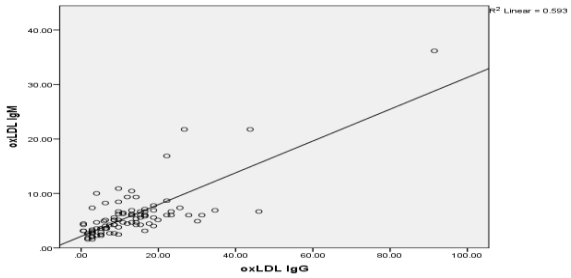
A considerably higher level of (OxLDL IgM) and (OxLDL IgG) was found in the control group in the comparison analyses between the study groups, with a significance level of =0.005(P>0.05).

Since the concentration of OxLDLIgM and OxLDLIgG Abs were (4.80) and (9.68), respectively, the results of the present investigation demonstrated that the concentrations of anti-OxLDL IgM (11.56) & IgG (19.91) in the samples of healthy people in the present study were greater than the results of SLE patients. [15]. Reported in

their study that the concentrations of OxLDLIgM and OxLDLIgG antibodies had increased in the sera of SLE patients compared to healthy controls, and it was concluded that there is a positive correlation between high levels of antibodies and OxLDL levels. These results were in conflict with previous studies. The findings of the current study were in disagreement with some recent studies that discovered that (OxLDL) antibodies are present in higher concentrations in the sera of lupus patients than in those of healthy control individuals [16, 17, 18-19].

Whereas [17] found that the risk of atherosclerosis decreased when the level of (OxLDL) antibodies in SLE patients was lower. They also found that the levels of (OxLDL) antibodies were higher in the blood of lupus patients who were suffering from atherosclerosis.

Since the healthy control of the current study may have other diseases that cause their levels of (oxLDL) antibodies to rise, the discrepancy between the results of the current study of Abs levels and the results of the previous studies may be caused by the different conditions of the current experiment with the rest of the experiments. Numerous studies have shown that individuals with autoimmune disorders such as rheumatoid arthritis, diabetes, high blood pressure, thyroid disease, atherosclerosis, and other diseases have high levels of (oxLDL) antibodies[20, 21, 22-23]




Acording the Figure-1 found the There were a significant correlation between oxLDLIgM and oxLDLIgG (P<0.05) while, there was no significant correlation with disease activity. The correlation between studied markers and SLE activity conflicted with previous studies that reported the correlation between the activity of SLE disease and some biomarkers and immune complexes, including anti-oxLDL antibodies and circulating immune complexes [27]

Conclusion: The current study showed that there is a substantial difference in serum OxLDLIgM Abs between healthy control groups and SLE patients. The serum of healthy control groups had higher significant differences in OxLDLIgG Abs positive tests than did the serum of SLE patients. The levels of OxLDL IgM and OxLDIgG did not significantly correlate with SLE disease activity.

## References

Gustafsson JT, Svenungsson E: Definitions of and contributions to cardiovascular disease in systemic lupus erythematosus. Autoimmunity. 2014; 47:67-76.

Danchenko N, Satia JA, Anthony MS: Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. Lupus. 2006; 15:308-18.

Hermansen, M.-L., S6andholt, B., Fuchs, A., Sillesen, H., Køber, L., Kofoed, K. F. . . . Jacobsen, S. (2018). Atherosclerosis and renal disease involvement in patients with systemic lupus erythematosus: a cross-sectional cohort study. Rheumatology, 2018;57(11), 1964-1971.

Li, H., Li, D.-q., Li, X.-x., & Wang, L.-q. (2016). The association between oxidized low-density lipoprotein antibodies and hematological diseases. Lipids in health and disease, 2016;15(1), 1-10.

Ronnblom, L., G. V. Alm, and M. L. Eloranta. 2011. The type I interferon system in the development of lupus. Semin. Immunol. 23: 113–121

Kaplan, M. J. (2009. Premature vascular damage in systemic lupus erythematosus. Autoimmunity 2009;42: 580–586.

. Esdaile, J. M., M. Abrahamowicz, T. Grodzicky, et al. 2001. Traditional Framingham risk factors fail to fully account for accelerated atherosclerosis in systemic lupus erythematosus. Arthritis Rheum. 2001;44: 2331–2337

Manzi, S., E. N. Meilahn, J. E. Rairie, et al. 1997. 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: 408–415.

Pons-Estel, G. J., L. A. Gonzalez, J. Zhang, et al. 2009. Predictors of cardiovascular damage in patients with systemic lupus erythematosus: data from LUMINA (LXVIII), a multiethnic US cohort. Rheumatology (Oxford) 2009;48: 817–822

Petri, M., S. Perez-Gutthann, D. Spence, and M. C. Hochberg. 1992. Risk factors for coronary artery disease in patients with systemic lupus erythematosus. Am. J. Med. 1992;93: 513–519.

Signorini, V., Elefante, E., Zucchi, D., Trentin, F., Bortoluzzi, A., &Tani, C. (2020). One year in review 2020: systemic lupus erythematosus. ClinExpRheumatol, 2020;38(4), 592-601.

Nobee, A., Vaillant, A. J., Akpaka, P. E., & Poon-king, P. (2015). Systemic Lupus Erythematosus (SLE): A 360 Degree. American Journal of Clinical Medicine Research, 2015;3(4), 60-63.

Margery-Muir, A. A., Bundell, C., Nelson, D., Groth, D. M., &Wetherall, J. D. (2017). Gender balance in patients with systemic lupus erythematosus. Autoimmunity reviews, 2017;16(3), 258-268.

Singh, R. P., & Bischoff, D. S. (2021). Sex hormones and gender influence the expression of markers of regulatory T cells in SLE patients. Frontiers in Immunology, 2921;12, 619268.

Moulton, V. R. (2018). Sex hormones in acquired immunity and autoimmune disease. Frontiers in Immunology, 2018;9, 2279.

Xing, E., Billi, A. C., & Gudjonsson, J. E. (2021). Sex bias and autoimmune diseases. Journal of Investigative Dermatology.

diseases, 2021;15(3), 261-6267.

17.Ryan, L., & Mills, K. H. (2022). Sex differences regulate immune responses in experimental autoimmune encephalomyelitis and multiple sclerosis. European Journal of Immunology, 2022;52(1), 24-33.
18. Ganjali, S., Shirmoham]madi, L., Read, M. I., &Sahebkar, A. (2020). High-density lipoprotein functionality in systemic lupus erythematosus. Paper presented at the Seminars in Arthritis and Rheumatism2020; 769-775
19. Kostopoulou, M., Nikolopoulos, D., Parodis, I., &Bertsias, G. (2020). Cardiovascular disease in systemic lupus erythematosus: recent data on epidemiology, risk factors and prevention. Current Vascular Pharmacology, 2020;18(6): 549-565
20. Masztalewicz, M., Nowacki, ]P, Kotlęga, D., Bajer-Czajkowska, A., &Drechsler, H. (2014). Anti-oxLDL antibodies are clinically insignificant for stroke patients. Neurological Research,2014;36(1): 86-91.
21.Conti, F., Spinelli, F. R., Alessandri, C., Pacelli, M., Ceccarelli, F., Marocchi, E, Profumo, E. (2014). Subclinical atherosclerosis in systemic lupus erythematosus and antiphospholipid syndrome: focus on β2GPI-specific T cell response. Arteriosclerosis, thrombosis, and vascular biology, 2014;34(3):661-668.
22.Mattisson, I. Y., Rattik, S., Björkbacka, H., Ljungcrantz, I., Terrinoni, M., Lebens, M,.Bengtsson, A. A. (2021). Immune responses against oxidized LDL as possible targets for prevention of atherosclerosis in systemic lupus erythematosus. V6ascular Pharmacology, 2021;140: 106863.
23.Masztalewicz, M., Nowacki, ]P., Kotlęga, D., Bajer-Czajkowska, A., &Drechsler, H. (2014). Anti-oxLDL antibodies are clinically insignificant for stroke patients. Neurological Research, 2014;36(1): 86-91.
24.van den Berg, V. J., Vroegindewey, M. M., Kardys, I., Boersma, E., Haskard, D., Hartley, A., &Khamis, R. (2019). Anti-oxidized LDL antibodies and coronary artery disease: a systematic review. Antioxidants, 2019;8(10):484.
25.Omar, N. N., Hefnawy, M. H. E., Mohamed, F., Heider, N. M., &Hamed, H. (2017). Assessment of oxLDL, anti-oxLDL antibodies and lipoprotein-associated phospholipa]se A2 as cardiovascular risk markers in obese adolescents with and without T1DM. Bulletin of Faculty of Pharmacy, Cairo University, 2017;55(2): 325-331.
26.Shiri-Sverdlov, R., Dos Reis, I. M., Oligschlaeger, Y., Hendrikx, T., Meesters, D. M., Vanclooster, A., ...&Houben, T. (2021). The influence of a conjugated pneumococcal vaccination on plasma antibody levels against oxidized low-density lipoprotein] in metabolic disease patients: a single-arm pilot clinical trial. Antioxidants, 2021;10(61): 129.
27. Theodorou, E., Nezos, A., Antypa, E., Ioakeimidis, D., Koutsilieris, M., Tektonidou, M., ... & Mavragani, C. P. (2018). B-cell activating factor and related genetic variants in lupus related atherosclerosis. Journal of autoimmunity,2018; 92:87-92.