Section: Physiology

Original Research Article

STUDY OF DYSLIPIDEMIA IN SYSTEMIC LUPUS ERYTHEMATOSUS

Rakesh Kumar[1], Sheela Kumari[2]

[1]PG Student, Department of Physiology, DMCH, Laheriasarai, Darbhanga, Bihar, India
[2]Professor, Department of Physiology, Darbhanga Medical College, Laheriasarai, Darbhanga, Bihar, India

Received : 24/01/2023
Received in revised form : 04/08/2023
Accepted : 23/08/2023

Keywords:
SLE, Dyslipidemia, Cholesterol, TG.

Corresponding Author:
Dr. Rakesh Kumar,
Email: rkjhadmch2k12@gmail.com

DOI: 10.47009/jamp.2024.6.2.219

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (2); 1087-1091

Abstract

Background: Patients with SLE have higher mortality and morbidity rate compared to the general population. The major causes of death remain to be infection, lupus nephritis (LN), and cardiovascular disease (CVD) (3). There is increased cardiovascular mortality in SLE. Accelerated atherosclerosis leading to coronary artery disease (CAD) and other cardiac manifestations have increasing importance for the management and outcome of SLE. **Materials and Methods:** The presented study included 50 SLE adult patients (46 females and 4 males) selected from Internal Medicine Departments, Darbhanga Medical College and Hospital, from January 2022 to December 2022. Patients were subjected to full medical history taking, clinical examination, as well as laboratory investigations. The revised criteria of the American College of Rheumatology were used for diagnosis of SLE. Assessment of Disease Activity of SLE Patients: The Systemic Lupus Activity Measure (SLAM) index was recorded for each patient. Receiver operator characteristic (ROC) curve was used and sensitivity and specificity for various cut off points were plotted. P was considered non-significant if >0.05, significant if were expressed as number and percentage of the total. The mean and standard deviation. **Result:** Cholesterol, LDL, and TG levels were elevated in the active group compared to that in the inactive group and healthy controls. This elevation was significant (P< 0.001). But HDL level decreased in the active group compared to the inactive and healthy controls groups. The decrease of HDL was the active group is significant (P< 0.001). **Conclusion:** The elevated levels of Total cholesterol, LDL, and TG and decreased level of HDL in SLE patients are considered an independent risk factor for cardiovascular disease. The dyslipidemia and inflammatory process predispose to premature atherosclerosis and disease activity contribute to dyslipidemia and hence cardiovascular risk associated with SLE.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune, chronic, relapsing, inflammatory, and often multi-systemic disorder of connective tissue, characterized by involvement of the skin, joint, kidney and serosal membranes.[1] Patients with SLE have higher mortality and morbidity rate compared to general population. The major causes of death remain to be infection, lupus nephritis (LN), and cardiovascular disease (CVD).[2] CVD in autoimmune rheumatic diseases is caused by traditional (increasing age, male gender, hypertension, smoking, hypercholesterolemia, diabetes) and the so called non-traditional risk factors.[3] There are statistically significant increases in coronary heart disease and stroke in SLE patients that cannot be fully explained by Framingham risk factors.[3] These non-traditional factors are disease related, such as disease activity, glucocorticoid, hydroxychloroquine (HCQ) used to control disease activity, impaired renal function, presence of antiphospholipid antibodies, and immune cell activation. A modification of Framingham risk score, where each item is multiplied by two, estimates more accurately the risk for coronary artery disease in lupus patients.[3] Additional mortality in SLE patients shows a bimodal pattern, with an early peak due to the consequence of active lupus and a later peak attributable mainly to atherosclerosis.[4] Abnormal plasma concentration of lipids is common in patients with SLE. Dyslipidemia usually refers to elevated total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL), and decreased high density lipoprotein (HDL) level.[4] Lupus nephritis (LN), a common and potentially life-threatening manifestation of SLE, occurs in almost half of the

ISSN (O): 2687-5365; ISSN (P): 2753-6556

lupus patients.[5] Patients with LN have a higher TC, TG, and LDL and lower HDL and apolipoprotein B levels, than patients without renal manifestation.[6] Dyslipidemia is more severe in lupus nephritic patients than those with a similar degree of chronic kidney disease despite disease inactivity, low level of Proteinuria, and low dose steroid usage.[7] Hyperlipidemia can affect all parts of the nephron causing endothelial cell injury, glomerular filtration defect with hyper filtration and tubule interstitial lipid deposition.[7] If other systemic disorders such as diabetes mellitus and thyroididtis are also present, they can also cause changes in lipid metabolism. Age-related and postmenopausal changes also matter.[8]

Several mechanisms have been proved or suggested among factors that may increase risk of dyslipidemia in SLE and by turn increase risk of CVD. Interestingly, immune and inflammatory reactions seem to have a role in the pathogenesis of atherosclerotic vascular damage.[9]

This raises the exciting possibility that SLE itself may be atherogenic through chronic activation of the immune system and inflammatory process. In fact, autoantibodies such as anti-phospholipids, antib2-glycoprotein1, anti-ox- LDL-c and antilipoprotein lipase and elevated inflammatory markers such as CRP and IL-6 are common finding of SLE. It is therefore reasonable to postulate that the interaction of disease associated factors induce specific alteration in lipoprotein metabolism which is aggravated by drugs and associated conditions frequently observed in lupus patients.[9]

MATERIALS AND METHODS

The presented study included 50 SLE adult patients (46 females and 4 males) selected from Internal Medicine Departments, Darbhanga Medical College and Hospital, from January 2022 to December 2022. Twenty healthy subjects with matched age, sex and BMI were included as healthy controls. Patients were classified according to disease activity into the following groups: Active Lupus: Comprised 25 lupus patients. Inactive Lupus: Comprised 25 lupus patients.

Patients were subjected to full medical history taking, clinical examination, as well as laboratory investigations. The revised criteria of the American College of Rheumatology,[10] were used for diagnosis of SLE. Assessment of Disease Activity of SLE Patients: The Systemic Lupus Activity Measure (SLAM) index was recorded for each patient. This scoring system is based on a comparative study done by Liang and his colleagues.[10]

The Lupus Activity Index is a concise measure comprised of a 0-3 visual analog scale for 4 symptoms (fatigue, rash, joint involvement, serositis) and 4 signs (neurologic, renal, pulmonary, and hematologic involvement). All subjects were subjected to A- Detailed history taking. B- Full clinical examination. C- Routine laboratory investigations; erythrocyte sedimentation rate (ESR), Creactive protein (CRP), fasting and 2 hours postprandial blood glucose, complete blood count (CBC), complete urine analysis, and liver and kidney function test. D- Measurement of proteins in 24 hour urine (g/24hrs). E- Antinuclear antibodies (ANA) and Antidouble stranded deoxyribonucleic acid antibodies (anti-dsDNA. Done by immunofluorescence technique. Titter of 1/40 or more is considered positive. (Done for SLE patients only). F-Serum complements levels (C3, C4). Done by nephelometry (Normal level of C3 is 84- 160 mg /dl and for C4 12- 36 mg /dl): (Done for SLE patients only) G-Total cholesterol in mg/dl by enzymatic colometric assay. H-Total triglyceride in mg/dl by enzymatic colometric assay. J-LDL cholesterol by mg/dl by enzymatic colometric assay. K-HDL in mg/dl by enzymatic colometric assay. Sample collections: After 12 hours fast 8 ml venous blood was obtained from all participate. They were divided into; 1 ml on EDTA (1 mg/ml) for CBC, 5 ml into plain tubes and serum samples were separated into 2 aliquots for investigations. Serum total cholesterol, triglycerides, and HDL-c concentration were measured.[11]

The material was supplied by Spinreact (Spain) for total cholesterol and triglycerides and by STANBIO (USA) for HDL-c. LDL-c concentration was calculated.[12]

Statistical analysis: Statistical Package for Social Science (SPSS) version 17was used. Quantitative data were expressed as mean ± SD and qualitative data (SD) were calculated. Comparing the mean ± SD of 2 groups was done using the unpaired t test. Determining the extent that a single observed series of proportions differs from a theoretical or expected distribution was done using the Chi square test. Receiver operator characteristic (ROC) curve was used and sensitivity and specificity for various cut off points were plotted. P was considered non-significant if >0.05, significant if were expressed as number and percentage of the total. The mean and standard deviation.

RESULTS

[Table 1] show that cholesterol level is elevated in active group compared to that in inactive group and healthy controls. This elevation is significant ($P< 0.001$).

[Table 2] shows that CRP level is elevated in active group compared to that in inactive and healthy controls groups. This increase in CRP level in active group is significant ($p<0.001$).

[Table 3] shows that C3 level is decreased in active group compared to that in inactive and healthy controls groups. This decrease in C3 level in active group is significant ($P< 0.001$). Platelet level is decreased in active group compared to inactive and

ISSN (O): 2687-5365; ISSN (P): 2753-6556

healthy controls groups. The decrease level of platelet in active group is significant (P<0.001).

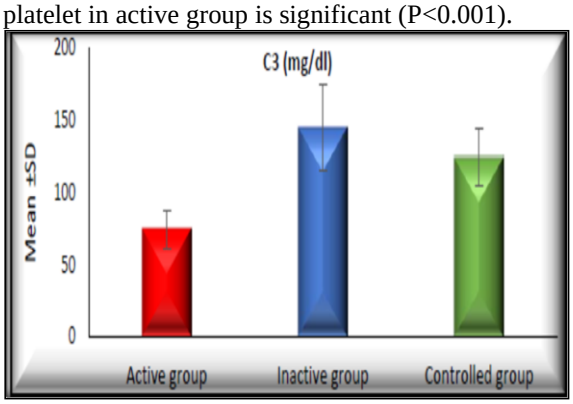

Image 1:

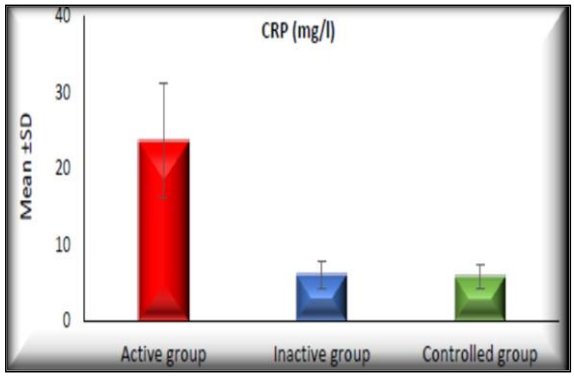

Image 2:

Table 1: Cholesterol level among the studied groups

Groups	Cholesterol (mg/dl)		
	Range	Mean	± SD
Active group	164 - 367	227.776	± 55.833
Inactive group	156 - 342	294.776	± 48.604
Control group	165 - 256	149.100	± 22.613

Table 2: CRP level in the active group compared to that in the inactive and healthy controls groups

Groups	CRP (mg/l)		
	Range	Mean	± SD
Active group	12 - 43	26.333	± 8.622
Inactive group	4 - 10	6.067	± 2.780
Control group	5 - 10	6.800	± 2.508

DISCUSSION

Patients with SLE have higher mortality and morbidity rate compared to the general population. The major causes of death remain to be infection, lupus nephritis (LN), and cardiovascular disease (CVD).[3] There is increased cardiovascular mortality in SLE. Accelerated atherosclerosis leading to coronary artery disease (CAD) and other cardiac manifestations have increasing importance for the management and outcome of SLE. Several traditional and disease-related risk factors, as well as corticosteroids are suggested to be involved in lupus-associated atherosclerosis and its clinical manifestations.[3]

Traditional risk factors, such as altered lipid levels, aging and smoking, do not fully explain this increased risk of CVD, and strongly suggesting that autoimmunity contributes to accelerated atherosclerosis.[3]

Altered immune system function is recognized as the primary contributor to both the initiation and progression of atherosclerosis. Many mechanisms of autoimmunity, including changes in cytokine levels and innate immune responses, autoantibodies, dysfunctional lipids, and oxidative stress, could heighten atherosclerotic risk. In addition, multiple SLE therapeutics seems to affect the development and progression of atherosclerosis both positively and negatively.[13]

The aim of this study was to evaluate the plasma lipid (cholesterol, HDL, LDL, and triglyceride) and its relation to systemic lupus erythematosus activity. The present study revealed elevated levels of serum TG, LDL and TC in active group compared to that revealed in the inactive group or healthy control. This elevation was statistically highly significant (P < 0.001). Also, the study revealed decreased serum HDL level in the active group compared to that the in inactive group or healthy controls. The degree of decreased HDL level is significant (P < 0.001). The findings in the current study are ongoing with general consensus of the so called ―Lupus pattern‖ of dyslipoproteinemia which defined by elevated levels of TC, LDL and TG, and lower HDL levels.[14] Lupus pattern is reported to be associated with atherosclerotic risks.[15]

The findings in active lupus group in this study are supported by several previous studies.[16-19] and one study,[7] demonstrated that increased expression of TGs and low levels of HDL (lupus dyslipidemia) were associated with disease activity in SLE and suggested their use as markers of disease activity. Dyslipoproteinemia in lupus patients are attributed to various etiologies. Autoimmunity and inflammation are among players.[9] It seems reasonable to accept that inflammatory conditions of the disease itself would induce specific alterations in the lipid profile. It is known that TNF-Alfa which presents in a high concentration in SLE patients; promote a significant increase in circulating TG due to increase hepatic synthesis of VLDL. In addition; TNF has the ability to inhibit LPL.[16]

The production of a large variety of autoantibodies is a prominent pathogenic feature of SLE and it had

ISSN (O): 2687-5365; ISSN (P): 2753-6556

been proved that it lead to autoimmune Hyperlipidemia. The binding of autoantibodies to LPL impair its enzymatic activity, and titters of anti-LPL antibody correlate with TG levels, disease activity, and markers of inflammation.[9] Chronic activation or damage to endothelium in SLE may trigger the inflammatory cascade and thereby promote atherogenesis. Several forms of endothelial insult are being recognized in SLE, including hypercholesterolemia, hyperhomocysteinemia, and mechanical stress from hypertension, increased oxidative stress and immunologic injury as a result of immune complex deposition.[20] In contrast to the findings of the current study; some other studies,[21,22] reported relatively low LDL, low HDL, high VLDL, and high TG levels. They attributed these finding to impaired LPL activity which degrades VLDL, with subsequent conversion to LDL. Also Das reported high levels of VLDL and TG and low level of HDL in inactive lupus patients and decrease in LDL during active disease, the so called ―active lupus pattern‖, suggesting a defect in VLDL metabolism.[23] Determinations of serum anti-ds DNA titter and complement levels (C3, C4) are the most common and useful tests for assessment of disease activity and predicting flare in SLE. The current work demonstrated a significant increase in anti-dsDNA antibodies levels in active SLE patients in comparison to patients in remission. Anti-dsDNA and anti-Sm antibodies are highly specific for idiopathic SLE. Combination of anti-dsDNA, serum complements C3 and C4, ESR and CRP supported by relevant tissue histology, probably provides the most useful information on disease activity, particularly in patients with lupus nephritis. However, results of any laboratory test should always be interpreted with reference to the clinical presentation.[24] The present study show that there was a statistically significant difference between active and inactive SLE patients regarding anti-ds DNA levels, which agrees with (AbdElsamad et al., 2000).[25]

However some authors observed that raised anti-dsDNA titter is of no significance and may be found raised in quiescent diseases.[23]

In the present study there was a statistically significant difference between the active group and inactive group with SLE as regarding serum complement (C3) level (p concluded that C3 provides the best assessment of disease activity in patients with SLE.[23] On other hand some authors observed that C3 level was low in active stage of SLE especially during clinical exacerbation but its concentration was often normal in mild to moderate active stage.[24]

The present study showed a statistically significant decrease in level of serum complement (C4) in patients with SLE activity. Level of C4 concentration was lower in the active groups than in the inactive group of SLE. Similar results were reported by.[25]

Plasma levels of C3 and C4 were significantly decreased on comparing SLE patients to healthy normal subjects. Significant decrease in their levels was also found on comparing active SLE patients with patients in remission. Inspite of many years of study of the SLE, the pathology or disease process in systemic lupus erythematosus remains unclear. Various laboratory tests were used for detection of the activity of the disease as ESR, plasma complements concentrations, and formation of autoantibodies.[25]

The present study showed significant decrease in RBC, WBC and platelet counts in patients with active SLE compared to patients in remission, as well as, to the healthy controls. Decreased RBC count could be explained by impaired renal function with decreased erythropoietin formation, and also due to poor general condition, cachexia and anorexia, in addition to bone marrow suppression by aggressive cytotoxic therapy Leucopoenia in SLE patients occurs as part of drug toxicity-induced modularly hyperplasia. Also, it may be due to disease activity, bone marrow failure, peripheral destruction and sepsis.

The most common mechanism of thrombocytopenia in SLE patients is believed to be increased RBCs, platelets clearance mediated by anti-platelet auto-antibodies.[25]

ESR was significantly higher on comparing active SLE patients to patients in remission and healthy controls, and was significantly higher on comparing patients in remission to controls. This could be attributed to reduction of their synthesis and, also, their consumption in immune complex formation. These results indicated that complement dysfunction may be an important factor in the pathophysiology of SLE.[25]

CONCLUSION

Dyslipidemia in SLE includes elevated levels of total cholesterol, TG, and LDL and decreased level of HDL. Elevation of TC, TG, LDL and decrease HDL are considered an independent risk factor for CVD share in premature atherosclerosis in these patients. Some SLE complication and disease activity contributes to dyslipidemia and hence cardiovascular risk associated with SLE.

REFERENCES

1. Lupus. 1997;6(6):533-9 - PubMed.
2. J Clin Invest. 1995 Dec;96(6):2758-67 - PubMed
3. Arthritis Rheum. 2012 Jan;64(1):285-96 - PubMed
4. J Lipid Res. 1997 Nov;38(11):2173-92 - PubMed
5. Lupus. 2011 Jan;20(1):5-13 - PubMed
6. J Biol Regul Homeost Agents. 2011 Jul-Sep;25(3):397-403 - PubMed
7. Nat Rev Immunol. 2006 May;6(5):358-70 - PubMed
8. Lupus. 2006;15(2):80-6 - PubMed
9. Semin Arthritis Rheum. 2016 Apr;45(5):604-10 - PubMed
10. Endocrinol Metab Clin North Am. 1998 Sep;27(3):503-19 - PubMed
11. Rheumatology (Oxford). 2007 Oct;46(10):1560-5 - PubMed

ISSN (O): 2687-5365; ISSN (P): 2753-6556

12. Arthritis Care Res (Hoboken). 2011 Jun;63(6):875-83 - PubMed
13. Ann Rheum Dis. 2011 Feb;70(2):245-8 - PubMed
14. Arthritis Rheum. 2004 Nov;50(11):3610-5 - PubMed
15. Lupus. 2000;9(6):413-6 - PubMed
16. J Card Fail. 2017 Feb;23 (2):113-120 - PubMed
17. Arthritis Rheum. 2006 Jun;54(6):1928-39 - PubMed
18. Blood. 2001 Apr 15;97(8):2381-9 - PubMed
19. Am J Med. 1994 Mar;96(3):254-9 - PubMed
20. Autoimmun Rev. 2013 Aug;12(10):1004-15 - PubMed
21. Nat Rev Rheumatol. 2011 May 31;7(7):399-408 - PubMed
22. BMC Med Genet. 2011 Jan 11;12:7 - PubMed
23. Arthritis Rheum. 1988 Jul;31(7):859-63 - PubMed
24. Med Clin North Am. 1994 Jan;78(1):143-61 - PubMed
25. Lupus. 2014 Sep;23(10):1014-22 - PubMed

ISSN (O): 2687-5365; ISSN (P): 2753-6556