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Original Research Article

Study on Lupus Pattern of Dyslipidemia in Systemic Lupus Erythematosus

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Abstract

This study aimed to find a lupus pattern of dyslipidemia in Systemic Lupus Erythematosus (SLE).Thirty SLE cases and thirty age matched controls are included in this study. Fasting venous blood was collected and base line investigations, lipid profile, apoB and apoA1 estimations were done. Statistical analysis was performed using SPSS package 19. The groups were compared using Student's t test. Analysis of lipid profile across the cases and controls reveals that the mean triglycerides, the mean Low Density Lipoproteins and the mean Very Low Density Lipoproteins were higher among cases with statistical significance and the mean total cholesterol and the mean High Density Lipoproteins seen more in controls with statistically insignificant p value. Apo B values were high and low APOA1 values seen in SLE compared to controls. Higher Apo B/Apo A1 ratio in SLE cases. This ratio implies that the number of small dense LDL particles are the most atherogenic particles that are easily oxidize and promote inflammation and growth of plaques. This elevated lipid profile and apolipoprotein levels in SLE patients throws light on the fact that SLE patients are at increased risk for Coronary Artery Disease.

Keywords: SLE, Lipid profile, Apo B/Apo A1ratio, Coronary Artery Disease.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a systemic autoimmune disease caused by inflammation in which the immune system attacks self tissues all over the body. Mortality in SLE patients follows a bimodal pattern. Patients with active lupus treated with large dose of steroids are died due to high incidence of infections. Patients with inactive lupus on long duration of steroid therapy are died due to rising incidence of coronary artery disease (CAD) [1]. It is expected that CAD dominate more morbidity and mortality trends rising in the days ahead. About 5 million people all over the world are suffering from lupus and predominantly they are young women of child bearing age.

Approximately 66% of deaths in India are attributable to noncommunicable diseases, about 33% of all deaths are due to cardiovascular disease alone and is expected to be the leading cause of mortality and morbidity.

According to a multisite international SLE cohort study by Bernatsy *et al*., [2], American college of Rheumatology, there is increased mortality rate in SLE patients compared with the general population and they suggest that female sex, younger age, shorter SLE duration and black/African American population are associated with CAD risk.

The risk for deaths, primarily caused by lupus activity (such as renal disease), has reduced over time, while the risk for deaths caused by circulatory disease are not reduced.

It was found that thrombosis/embolism, vaculitis and severe coronary atherosclerosis were seen in nine (33.33%), five (18.52%) and one (3.70%) subjects respectively in an autopsy study of 27 SLE patients [3]. It has been estimated that the risk for cardiovascular disease in middle aged women is increased to be as high as 50- fold.

Although atherosclerosis develops early in the course of the disease, the diagnosis is typically at an older age. In the major clinicalstudies on atherosclerosis, older age at disease diagnosis, hypercholesterolemia and hypertension, are the traditional risk factors which are most commonly predictive of cardiovascular events. Dyslipidemia with low high-density lipoprotein (HDL), elevated triglycerides (TG), mild increase in LDL levels and increased lipoprotein(a) [Lp(a)] is characteristic of SLE.

This pattern of lipid levels was described as the'lupus pattern of dyslipoproteinemia'. This pattern and inflammation are important contributors to the increased risk for atherosclerosis in SLE [4]. The increased cardiovascular risk is explained by increased inflammation along with prevalence of classical risk factors.

Lipoproteins are involved in the pathogenesis of atherosclerosis. Epidemiologic studies have established that , there exist an transposed relationship between serum levels of high-density lipoprotein (HDL), apo A1 the main component of HDL and the occurrence of CAD (antiatherogenesis), whereas low density lipoprotein (LDL) has been established as an proatherogenic factor. The qualitative and quantitative changes in lipids are proatherogenic. These modified lipids in the circulation will accelerate the development of CAD.

These findings could help in lifestyle modification and the choice and dosage of specific drugs. The best way to fight the burden of CAD is the preventive approach. The purpose of my study is to analyze the pattern of lipoproteins levels and lipid profile in patients with SLE.

MATERIALS AND METHODS

This study was conducted in the Department of Biochemistry in association with Department of Rheumatology, Kilpauk Medical College Hospital, Chennai. All procedures concerning human subjects or patients were permitted by the Institutional Ethical Committee. Explicit written consent was obtained from the study population.

The study group consisted of 30 SLE patients attending the Rheumatology OP, at Kilpauk Medical College Hospital; Chennai. The diagnosis was based on complete physical and clinical examination of patients followed by appropriate investigations.

SLE was diagnosed according to the American College of Rheumatology criteria. (i.e.4/11 criteria to be classified as SLE) [5].

Controls

30 healthy subjects were included in the study as controls.

Exclusion Criteria

1. Patients with nephrotic syndrome.
2. Patients with hypothyroidism.

Both these conditions associated with hyperlipidemia.

For the study, 5 ml of 12 hours Fasting Venous Blood was collected under sterile conditions from the ante cubital vein .Serum was separated after centrifugation at 3000 rpm for 10 minutes and alliquoted, into 3 eppendorfs and stored at -20°C and were not thawed until the batch was analyzed for extended Lipid profile and routine chemistry examinations.

All biochemical analyses were performed using semi-automated (MERCK) clinical chemistry analyzer.

Estimation of Serum triglyceride

Method: Enzymatic colorimetric method: GPO – PAP method
Kit used: ERBA

Estimation of serum total cholesterol

Method: CHOD - PAP method
Kit used: ERBA

Estimation of HDL cholesterol and LDL cholesterol

Method: Direct enzymatic colorimetric
Kit used: Spinreact

Estimation of apolipoprotein B and apolipoprotein A1

Method: Turbidimetry
Kit Used: Spinreact

Quality control

All biochemical analyses were done using RANDOX calibrator (lot no 2351-562UE) and Controls (lot no 768UN level 2) for checking internal quality. The CVs of all the analytes performed were within the prescribed limits in accordance with CLIA.

RESULTS AND DISCUSSION

Table-1: Age and BMI between Cases and Control

Variable	Group	N	Mean	Std.Deviation	P-Value
Age	Case	30	32.83	12.44	0.906
	Control	30	32.46	11.66	
BMI	Case	30	23.20	5.76	0.173
	Control	30	25.10	4.84	

The mean age of cases is 32.83 years and controls is 32.46 years, p = 0.906.
The mean BMI of cases is 23.20 and controls is 25.10, p = 0.173

Table-2: Lipid Profile of Cases and Control

Variable	Group	N	Mean	Std.Deviation	P-Value
Total Cholesterol	Case	30	193.1	53.32	0.745
	Control	30	189.6	24.41	
Triglyceride	Case	30	158.06	90.50	0.0002
	Control	30	103.93	27.98	
HDL	Case	30	49.71	9.12	0.23
	Control	30	52.16	6.67	
LDL	Case	30	145.6	49.0	0.0003
	Control	30	109.6	16.47	
VLDL	Case	30	31.61	18.10	0.002
	Control	30	20.78	5.59	

The mean total cholesterol value of cases is 193.1mg/dl and controls is 189.6mg/dl, p=0.745.
The mean triglycerides value of cases is 158.06 mg/dl and controls is 103.93mg/dl, p= 0.002.
The mean HDL value of cases is 49.71mg/dl and controls is 52.16 mg/dl, p=0.23.
The mean LDL value of cases is 145.6 mg/dl and controls is 109.6 mg/dl, p= 0.003.
The mean VLDL value of cases is 31.61mg/dl and controls is 20.78 mg/dl, p= 0.002.

Table-3: Represents Mean Values of Apolipoprotein Levels In Cases and Controls

Variables	Group	N	Mean	SD	p-Value
APO B	Case	30	95.92	16.30	0.017
	Control	30	87.61	13.41	
APO A1	Case	30	120.58	22.16	0.26
	Control	30	125.39	7.90	
APO B/APOA1	Case	30	0.85	0.83	0.004
	Control	30	0.76	0.121	

The mean value of APO B in cases is 95.92 mg/dl and controls is 87.61mg/dl, p= 0.017.
The mean value of APO A1in cases is 120.58mg/dl and controls is 125.39 mg/dl, p=0.26.
The mean value of APO B/ APO A1 ratio in cases is 0.83 and controls is 0.76, p=0.004.

DISCUSSION

The mean age of SLE patients is 32.83yrs. This shows the population most affected by lupus is women of childbearing age between 3rd and 4th decades of life [5]. (lupus foundation 2011) and study population is age matched (p value is not significant).

On comparing the triglycerides level between cases and controls there is statistically significant difference with p value (0.002).This observation is supported by Seok Hai Kaang *et al*., that steroids will increase lipolysis and thereby increasing nonesterified fatty acids and triglycerides in SLE patients [6].

Serum total cholesterol levels show no statistical difference between the cases and the controls.This observation is supported by a study by Staphanie J Morris *et al*., that hydroxy chloroquine decrease scholesterol level by inhibiting hydrolysis of cholesteryl esters through an increase in lysosomal pH and inactivates acid proteases and it stimulates the capacity of LDL receptor [7].

There is no statistically significant difference between the HDL values of cases and the controls. The minimal difference between cases and control may be due to statin therapy to SLE patients which is supported by Philips Barker *et al*., study which explains the possible reasons as upregulation of hepatic ATP binding Cassette (ABC) transporter A1 gene expression by statins [8].

LDL levels in Cases and Controls differs significantly with p value 0.003. The increase in LDL cholesterol level can be explained by study that steroids can inhibit receptor uptake and the internalization and degradation of LDL particles leading to elevated level of LDL and cholesterol in cases as explained by Talin Sarkissian *et al.*, in lipid profile study in paediatric Systemic Lupus Erythematosus [9].

VLDL level between cases and controls is statistically significant with p value 0.002. This observation is supported by a study by Awal Al Husain *et al*., that SLE cases had lupus pattern of dyslipidemia with raised triglycerides due to steroid therapy and the chronic inflammation associated with alterations in the metabolism of lipoproteins compared with controls [10].

There is statistically significant difference in apoB levels between cases and controls with p value 0.017. This is supported by Tracy E. Toms *et al*., that reduced activity of enzyme lipoprotein lipase (LPL) governed by inflammatory mediators and antibodies directed against LPL ntibodies causes accumulation of triglyceride rich particles [11]. Apo B value indicates the total number of potentially atherogenic lipoproteins

in LDL, IDL and VLDL. ApoB containing particles enhance the risk of thrombosis by inhibiting the fibrinolysis and stimulates cytokine production and inflammation. The interaction of positively charged ApoB to negatively charged proteoglycans leads to the retention of ApoB linked proteins in the vessel wall and susceptible to modification by oxidation, enzymatic cleavage and aggregation [12].

Apo A1 values of cases and controls have no statistical difference. This observation is supported by J. Delgado Alves *et al*., that the antioxidant mechanism of HDL is due mainly to the presence of paraoxonase enzyme which is stabilized by apoA1. Hence the antioxidant mechanism of HDL is lesser in SLE patients, so the oxidation of LDL and its consequent uptake by monocytes in the formation of foam cells will not be prevented enhancing the atherogenic risk [13].

There is statistical difference in apoB/apoA1 ratio between cases and controls with p value 0.004. This observation is supported in a study by V. Lilleyby *et al*., that the steroid use in childhood onset SLE contributes to proatherogenic lipid profile. ApoB/ApoA1 ratio determines cholesterol balance between potentially atherogenic lipoprotein particles (ApoB) in relation to all antiatherogenic particles (ApoA1) and is a better marker than lipids, reflecting the balance between the arterial deposition of cholesterol and the reverse cholesterol transport to the liver [14].

Furthermore ApoB has been found to be an independent predictor of endothelial vasodilatory function, increased carotid intima media thickness and arterial stiffness. This elevated lipid profile in SLE patients as compared to controls throws light on the fact that SLE patients are at increased risk for Coronary Artery Disease. This could have been better substantiated by measuring Carotid intima media thickness measured by B-mode ultrasound as a surrogate measure of atherosclerosis.

This study proves the association that SLE patients are at increased risk for CAD as evidenced by their lipid profile and apolipoprotein levels.

Conclusion

This study strongly supports the increased proatherogenic risk factors in systemic lupus erythematosus compared with age matched controls. SLE patients should be regarded as a population at high risk for the development of CVD similar to patients with Diabetes in whom identification and stringent treatment of CVD risk factors is recommended. CVD risk and its complications in SLE patients can be prevented by monitoring regularly the lipid level modification according to National Cholesterol Education Programme (NCEP) Adult Treatment Plan (ATP III) guidelines, viewing SLE as a CHD equivalent condition by

- Therapeutic life style changes (dietary modification, weight reduction, increase in moderate physical activity).
- Review the steroid dose.
- Drug therapy (statins to reduce total and LDL cholesterol, fibrates and niacin to reduce triglycerides and to improve HDL cholesterol level).

Thus benefiting the SLE patients to lead a better quality life.

Scope for future study

Clearly, more research into the cellular and inflammatory components at different stages of Coronary Artery Disease and Systemic Lupus Erythematosus is needed to identify therapeutic targets, inflammatory biomarkers, and imaging modalities suitable for improved identification of patients and monitoring therapies.

Ethical approval: All procedures performed in this studies involving human participants were in accordance with the ethical standards of Institution.

Source of support: Nil

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