Original Research Article

Lipid profile in systemic lupus erythematosus: study from a tertiary teaching hospital of Eastern India

Simanchala Dakua[1], Manoranjan Behera[2]*, Jayant Kumar Panda[2], Prabhat Kumar Padhi[2]

[1]Department of Medicine, CHC, G. Udayagiri, Kandhamal, Odisha, India
[2]Department of Medicine, SCB Medical College and Hospital, Cuttack, Odisha, India

*Correspondence:
Dr. Manoranjan Behera,
E-mail: doctor_manoranjan@rediffmail.com

ABSTRACT

Background: Dyslipidemia is an independent modifiable risk factor for coronary artery disease. Patients with systemic lupus erythematosus (SLE) have dyslipidemia and accelerated atherosclerosis; however, there is paucity of published data on the lipid profile in patients with SLE in Eastern India. This study was done to assess the prevalence and abnormality of lipid profile in patients with SLE admitted to a tertiary care teaching hospital in Eastern India.
Methods: This was a hospital based prospective study evaluating SLE patients admitted to a tertiary care institution in Eastern India. 101 patients with SLE admitted consecutively and 100 age and sex matched controls were enrolled for study. Fasting total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured in plasma whereas very low-density lipoprotein cholesterol (VLDL-C) was calculated. Statistical analysis was done using the standard statistical techniques.
Results: Out of 101 patients of SLE, 97 were female and 4 were of male gender. The age of the patients ranged from 15 to 47 years with a mean of 27.17 (±8.4) years. Dyslipidemia was found in 58(57.4%) patients. Hypercholesterolemia was found in 23 (22.7%), hypertriglyceridemia in 55 (54.4%), raised LDL-C in 24 (23.7%) cases. Raised TC, TG, and LDL-C was found in 18 (17.8%), and raised TC, TG, LDL-C and low HDL-C was found in 9 (8.9%) cases. There was significant increase in serum cholesterol, triglyceride and VLDL-C while decrease in HDL-C in SLE patients than controls (p <0.001). Statistically no difference in lipid profile was found in between groups of SLE receiving steroid and without steroid.
Conclusions: Abnormal lipid profiles are very common in patients with SLE, though the patients are very young. Control of dyslipidemia can favourably affect cardiovascular related morbidity and mortality.

Keywords: Dyslipdemia, Premature atherosclerosis, Systemic lupus erythematosus

INTRODUCTION

Premature atherosclerosis is an important cause of coronary artery disease (CAD) in patients of Systemic Lupus Erythematosus (SLE) leading to increased morbidity and late stage mortality.[1] The exact mechanism of this accelerated atherosclerosis remains unclear. SLE disease activity with its immunological events, the presence of anticardiolipin antibodies, and traditional risk factors like dyslipidemia contribute to the development of atherosclerosis.[2,3] Traditional risk factors for CAD were very common in the Hopkin's lupus cohort study, despite the fact that average age of the patient was only 38.3 years.[4] The prevalence of dyslipidemia ranges between 30% and 73% of adult SLE cases.[5-7] Studies reveal that there are two patterns of dyslipidemia observed in

patients of SLE, one is related to active disease process itself where there are elevated triglyceride (TG) and low levels of high density lipoprotein cholesterol (HDL-C) in association with up regulation of tumor necrosis factor-α (TNF-α)/tumor necrosis factor receptor system, while the second is related to high dose steroid therapy and not related to activity of SLE.[8-10] Practically it is difficult to differentiate between two patterns. Dyslipidemia in SLE may be causally related to or influence pathogenic process of lupus.[11] Dyslipidemia is one among the three leading factors for death in patients with SLE, but Hopkin's lupus cohort study has focussed on control of hypertension as preventive strategy for CAD without addressing smoking, obesity and dyslipidemia.[12]

Much earlier study from north-eastern India has also reported the high prevalence of dyslipidemia amongst the SLE patients. [13] Since then there was no prospective study evaluating serum lipid profile in SLE patients of this part of the country. Hence, the present study was undertaken to determine the prevalence and abnormality of lipid profile in patients with SLE.

METHODS

This was a prospective hospital based study conducted in the Post Graduate Department of medicine, SCB Medical College and hospital, Cuttack, Odisha, India. On hundred and one cases of patients of SLE who fulfilled American College of Rheumatology Revised Classification Criteria for SLE (1997) and admitted consecutively to the P.G. Dept. of Medicine, SCB Medical College and hospital, Cuttack between September 2011 to September 2012, of both gender and age group ≥15 were included in the study.[12] Normal age and sex matched individuals were enrolled as control. Persons suffering from diabetes mellitus or hypertension, persons having family history of dyslipidemia, known cases of hypothyroidism and patients suffering from infection or on hypolipidemic drugs, gonadal hormones, alcoholics, smokers were excluded from this study. Institutional ethical committee clearance was duly obtained.

Each patient underwent detailed history taking and complete clinical examination. Details regarding age, sex, urban or rural, socio-economic status, duration of SLE, and treatment history of SLE were recorded for all the patients. SLE was diagnosed according to American College of Rheumatology Revised Classification Criteria for SLE (1997).[12] Baseline laboratory tests done for each patient include complete blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and routine and microscopic urinalysis. Blood glucose level estimation was done by glucose oxidase method using a standard kit supplied by Acutex Biochemical Pvt. Ltd. (Mumbai, India). Lipid profile, liver function test, blood

urea, serum creatinine, and serum electrolytes were done by auto analyzer (TBA 120 FR, TOSHIBA) using specific kits.

Lipid profile was measured after an overnight fasting. Serum cholesterol was estimated using a standard kit (Enzokit) supplied by Ranbaxy Fine Chemicals Ltd. Diagnostic Centre;serum TG was estimated using a standard kit supplied by Chemelex SA, Barcelona;serum low-density lipoprotein cholesterol (LDL-C) was estimated using a standard kit supplied by Agappe Diagnostics Ltd., (Kerala, India); serum HDL-C was estimated using a standard kit supplied by Transasia Biomedicals Ltd. (Daman, India) and the Boehringer Mannheim photometer 5010 (Birkenfeld, Germany).Very low-density lipoprotein cholesterol(VLDL-C) was estimated by dividing the TG by 5. Cholesterol levels were considered to be normal at <200mg/dl, TG at <150 mg/dl, HDL-C >50mg/dl, and LDL-C at < 130 mg/dl.[14] Fasting lipid profiles of controls were also measured.

Antinuclear antibodies (ANA) and anti- double stranded deoxyribonucleic acid antibodies (ds- DNA) were performed by immunofluorescence and complement (C3 and C4) by radial Immunodiffusion method. All statistical analysis was done using SPSS statistical package version 16. Quantitative variables were described as mean +/-SD unless otherwise indicated. Qualitative variables were described by percentage. Comparison between two groups was done by unpaired chi-square test. For all statistical tests, p value <0.05 was considered significant.

RESULTS

Present study is a hospital based study and reflects the prevalence of dyslipidemia in SLE patients in the in-patient setting.

A total of 101 patients with SLE and 100 age and sex matched controls were included in the present study. Table 1 shows the baseline characteristics of the patients. The age of the patients ranged from 15 to 47 years with a mean of 27.17 (±8.4) years.

Maximum number of patients belonged to age group of 16-40 years (93.08%). The age of control group ranged from 16 to 46 years with a mean of 27.64 (±8.6) years. Females constituted 96% and 89% of case and control population respectively. Out of 101 SLE patients, 58 (57.4%) had dyslipidemia. Hypercholesterolemia was found in 23 (22.7%), hypertriglyceridemia in 55 (54.4%), raised LDL-C in 24 (23.7%) cases. Raised total cholesterol (TC), TG, and LDL-C was found in 18 (17.8%) cases, and raised TC, TG, LDL-C and low HDL-C was found in 9 (8.9%) cases.

Table 1: Baseline characteristics.

Characteristics	Patients	Controls
Total no.	101	100
Male (%)	O4 (3.96%)	11 (11%)
Female (%)	97 (96.04%)	89 (89%)
Age (±SD) in years	27.17(±8.4)	27.64 (±8.6)
Average BMI (kg/m^2)	20.41±2.28	20±1.75
Familial hyperlipidemia	Nil	Nil
ESR (mm Ist hour)	46.19±34.38	14.03±9.38
CRP (mg/L)	08.92±7.1	1.58±1.06
FBG (mg/dL)	88.14±12.54	82.97±8.54
(Abbreviations: BMI, body mass index; ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; FBG, fasting blood glucose)		

Table 2: Comparison of lipid profile between SLE patients and control.

Lipid profile (mg/dl)	SLE mean±SD (ranges)	Control mean±SD (ranges)	P value
Cholesterol	179.6±43.48 (97-296)	154.8±21.16(121-206)	<0.0001
Triglyceride	174.1±60.54(89-310)	132.2±25.54 (87-198)	<0.0001
HDL-C	40.82±7.27(25-62)	47.12±5.72(38-59)	<0.0001
LDL-C	110.0±38.55(40-213)	81.61±23.88 (34-137)	<0.0001
VLDL-C	28.74±5.02(20-42)	26.07±4.65 (15-40)	0.0001
Abbreviations: HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.			

Table 3: Relationship between lipid profile and use of steroid in SLE.

Lipid profile (mg/dl)	Use of steroid		P value
	Not on steroid therapy mean+SD (ranges)	On steroid therapy mean+SD (ranges)	
Cholesterol	177±45.25 (97-296)	183.9±40.59(110-282)	0.22
Triglyceride	172.8±60.0 (89-310)	177.8±60.85(97-299)	0.79
HDL-C	40.70±7.42 (28-62)	41.03±7.13 (25-56)	0.62
LDL-C	107.7±19.59 (43-213)	113.8±37.69 (40-200)	0.29
VLDL-C	28.52±5.0 (20-42)	29.11±5.2 (20-40)	0.57
Abbreviations: HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; VLDL-C, very low-density lipoprotein cholesterol.			

Table 2 shows the lipid profile of both SLE patients, controls and their significance. The mean cholesterol, TG, and LDL-C were significantly higher in SLE group thal control cohort (p <0.0001). The mean VLDL-C in SLE patients was also significantly higher than controls (p<0.001). The mean HDL-C was lower in patients of SLE than controls which was also statistically significant (p <0.0001). Study of relationship between lipid profile and use of steroid in patients of SLE revealed no statistical significance when compared with those without steroid (Table 3).

DISCUSSION

SLE is a multisystem autoimmune disease that predominately affects premenopausal females, with a peak age of onset between 20-30 years. The condition can manifest with a broad spectrum clinical signs and symptoms, ranging from relatively minor symptoms such as arthralgia to life-threatening organ involvement.[12] In our series, the mean age of the patients was 27.17±(8.4) years, which signifies that the patients were very young. SLE confers a massive cardio vascular disease (CVD) risk, which is far greater than described in other autoimmune diseases.[3,7] The dyslipidemia seen in conjunction with SLE is more typical of that described in the general population in relation to CVD, with elevations in TG, LDL-C and TC and a fall in HDL-C levels. Dyslipidemia was found in 57.4% cases in our series which is at par with the observations by Kakati et al. from northeastern India (63.3%).[13] Present study revealed higher prevalence of hypertriglyceridemia (54.4%) and lower prevalence of hypercholesterolemia (22.7%) as compared to observations by Abdalla MA et al. from Egypt who reported the prevalence as 33.3% and 47.9 respectively.[15] This could be due to smaller sample size of Egyptian study, genetic, ethnic, environmental and dietary factors.[15] Mean fasting serum cholesterol, TG and

LDL-C levels were significantly higher in SLE patients when compared to control group (p<0.000l) but HDL-C was significantly lower than controls (p<0.000l). The mean serum VLDL-C was also significantly higher in SLE patients (p<0.001) (Table 1). This pattern of dyslipidemia was also observed by Borba F et al and Kakati S et al, whereas as per observations of Sabio JM et al TG was slightly increased in the patients group, TC and LDL-C levels were significantly reduced in patients compared to controls (P <0.001).[13,16,17] The reason attributed to this was intake of statins by SLE patients. SLE is a classic model of chronic immunocomplex mediated inflammatory disease. The possible role of inflammation in modulating Lipoprotein Lipase (LPL) enzyme is emphasized by the recent description of a significant down-regulation of LPL activity induced by TNF-α, IL-1 and IFN-γ.[18] It is well known that the acute phase response promotes an altered hepatic synthesis of a wide array of proteins involved in lipoprotein metabolism, in coagulation and in the complement system.[19] Therefore, it seems reasonable to accept that inflammatory conditions of this disease itself would induce specific alterations in the lipid profile. An enhanced production of these cytokines (IL6) is characteristic of SLE, particularly during active disease, and it supports their role in lupus dyslipoproteinemia.[20] It was recently described that levels of circulating TNF-α are raised in SLE and it correlates with active disease and triglyceride levels.[21] The recent description is that SLE and other autoimmune diseases produce a lot of autoantibodies which form complexes with the enzymes like lipoprotein lipase (anti-LPL) or with apolipoprotein and retards their process of catabolism, which produces varieties of dyslipidemia.[22,23] and is possibly a cause for autoimmune hyperlipidemia.[24] Borba F et al. coined the term "Lupus pattern" of dyslipoproteinemia for elevated levels of VLDL-C and TG, and lower HDL-C levels. During active disease there was decrease in LDL-C, is termed as "active lupus pattern" suggesting a defect in VLDL catabolism.[16,25] Table 2 highlights lipid profile in patients on steroid. It is evident that though the lipid profile was high among SLE patients taking steroid it was not statistically significant when compared to cohorts without steroid. This observation has also been made by Chung CP et al., who found no significant alteration in lipid profile with use of steroid.[26] Steroids form the main stay of treatment in SLE and it alters lipid values significantly. Chronic corticosteroid use in SLE is associated with increased total plasma cholesterol and its fractions, and also TG, which is presumed to be mediated by increased plasma insulin levels, increased lipid production by the liver and impaired lipid catabolism.[27,28] This effect could be identified after a short period of 1-2 months of this therapy and is also dose related.[9,29]

Though, low prednisone dose does not significantly alter the lipid profile, in fact, Petri M et al. showed that for each 10 mg increase in prednisone, there is a 7.5 mg/dl corresponding increase in serum cholesterol.[9] Our finding of lack of significant difference in lipid profile between patients on steroid therapy vis-a-vis patients without steroid, could be explained by the fact that these patients were on hydroxychloroquine therapy (6.5 mg/kg/day) which has been observed to lower lipid levels possibly by negating insulin resistance effect induced by steroid. Most recent study by Abdalla MA et al. from Egypt have reported no significant difference in the lipid profile among patients of SLE who did not received prednisone, those who received 10mg/day and those who received >10mg/day.[15] Kakati S et al. have reported nephropathy and administration of steroid are potential risk factors for the development of dyslipidemia.[13]

CONCLUSION

It is very difficult to interpret the results of lipid profile in patients of SLE as there are multiple confounding factors such as lifestyle, genetic, environmental, medications and comorbidities that can develop during the course of the disease. We found that abnormal lipid profiles are very common in patients with SLE, though the patients are very young. Early diagnosis and judicious use of statins could be an important adjunct therapy to prevent poor cardiovascular related morbidity and mortality, and this need to be objectively proved by randomised control study.

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