Assessment of Prevalence of Dyslipidemia and to Evaluate the Role of Corticosteroids among Patients with Connective Tissue Disorder: Prospective Clinical Study

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ABSTRACT

Introduction: Atherosclerosis and cardiovascular disease risk is enhanced in various connective tissue diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and antiphospholipid syndrome. A number of alterations in lipid profiles have also been documented which may further enhance risk for CHD in SLE. The main aim of the study was to assess the prevalence of dyslipidemia and to evaluate the role of corticosteroids in patients with connective tissue disorders.

Material and methods: The study is a prospective clinical study in which 30 patients were included into the study. Patients who were newly diagnosed with Connective tissue disorders were taken. A detailed history, clinical examination and investigations such as CRP- ESR, RA and ANA were performed depending on the requirement.

Results: There was significant dyslipidemia found in majority of the cases in connective tissue disorders. It was found that the lipid profile was deranged with increased total cholesterol and triglycerides levels after following up for a period of 3months with the initiation of corticosteroids.

Conclusion: Dyslipidaemia is a contributing risk factor for atherosclerosis in CTD due to chronic inflammation.

Keywords: Dyslipidemia, Corticosteroids, Atherosclerosis, SLE, Lipid Profile

INTRODUCTION

Connective tissue connects, supports, binds, and separates organs and tissues, forming a framework for structural and metabolic purposes. A connective tissue disease is any disease that has the connective tissues of the body as a target of pathology. Connective tissue is any type of biological tissue with an extensive extracellular matrix that supports, binds together, and protects organs. These tissues form a framework, or matrix, for the body, and are composed of two major structural protein molecules which are collagen and elastin.[1] Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs), or both, or a low HDL cholesterol level that contributes to the development of atherosclerosis.

Atherosclerosis and cardiovascular disease risk is enhanced in certain connective tissue diseases such as Systemic lupus erythematosus, Rheumatoid arthritis, Sjogren's syndrome, and mixed connective tissue disorders. The reason for this accelerated process is likely multifactorial. Theoretically, this increased cardiovascular risk in these patients could be caused by various reasons such as an increased prevalence of known risk factors for cardiovascular diseases such as dyslipidemia, diabetes mellitus, hypertension, body mass index, physical fitness and smoking habits, connective tissue disorder itself and the underlying inflammatory process or decreased functional capacity.[2,3]

Systemic lupus erythematosus (SLE) is a chronic, inflammatory disease characterized by a perturbed immune response with the consequent production of autoantibodies. Clinically, it is characterized by a plethora of disease manifestations including nephritis, arthritis, pleuritis, pericarditis and vasculitis. Patients with SLE have a higher risk of CVD than in the general population, and it occurs in younger individuals. Several case control studies indicated that classic coronary heart disease risk factors are associated with the development of atherosclerotic disease in systemic lupus erythematosus, significantly associated with hypercholesterolemia. One more established cause of atherosclerosis in systemic lupus erythematosus is steroid therapy, which is assumed to be a key mediator of coronary heart disease.[4]

Steroids at high doses can cause metabolic abnormalities including central obesity, hypertension, glucose intolerance and alterations in lipid profiles. It has, however been noted that low dose steroids do not adversely affect the lipid profile in systemic lupus erythematosus but at higher doses can cause increased low density lipoprotein cholesterol and triglycerides.[5]

In mixed connective tissue disorders (MCTD) there is presence of anti-U1 RNP antibodies which is characterized by puffy hands combined with Raynaud phenomenon. Atherosclerosis lead to CVD and is accelerated in autoimmune diseases such as SLE, Anti-Phospholipid Syndrome (APS) and MCTD.[6]

Epidemiological studies have shown elevated LDL levels to be one of the strongest predictors of coronary artery disease. To combat this risk, guidelines have been developed, with

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LDL as the primary focus for lipid lowering therapy. Lipid levels should be monitored and managed in patients with connective tissue disorders to minimize the long-term risk of cardiovascular disease. More research is needed to quantify the relationship between systemic inflammation and lipoprotein levels and to determine the impact of specific lipoprotein particles, e.g. low-density lipoprotein, HDL on long-term risk.[7]

Control of inflammation may have an effect on modifying cardiovascular risk. Dyslipidaemia in Rheumatoid Arthritis is also similar to the profile noticed in Systemic Lupus Erythematosus with reduced HDL and LDL with elevated VLDL and Triglycerides. Traditional risk factors are more prevalent in some of these patient groups compared with the general population, however these factors do not fully explain that enhanced risk. Mortality compared to general population is also increased in such patients. Corticosteroids are commonly used in patients with connective tissue disorders. It is known from literature that glucocorticoids induce hypercholesterolemia which acts as a risk factor for cardiovascular diseases.[8]

Corticosteroids are still a mainstay of treatment in most autoimmune rheumatic conditions. The use of corticosteroids in systemic sclerosis is controversial as steroids inhibit proteases that increase connective tissue turnover, thus counteracting fibrosis. The effect of corticosteroids administration (long term) on lipid profiles is also uncertain. Very few studies have been done till date that have conducted studies in patients with connective tissue disorders, indicating either an increase or no effect of total cholesterol levels during long term glucocorticoids administration.

MATERIAL AND METHODS

The present study was a prospective study which was conducted at Vydehi Institute of Medical Sciences and Hospital, Bangalore. The study was performed from January 2015 to June 2016 for a period of about one year. Voluntary written informed consent was taken from the subjects before starting the study. It involved about 30 patients under age group of 18 to 50 years, both males and females admitted under Department of General Medicine with connective tissue disorder. Patients who were newly detected with connective tissue disorders were included in the study. Patients who were already on lipid lowering drugs and the patients who have other diseases which causes rise in lipid levels like Diabetes mellitus, Hypertension, Lipid storage disorders, Thyroid dysfunction and any Renal disorders were excluded from the study. Patients were followed after 3months.

After obtaining a detailed history, a complete general physical and systemic examination was done and the patients were directed to take relevant investigations. All the investigations such as ESR-CRP, RA factor, lipid profile, ANA were performed under the direct supervision. Lipid profile was repeated after 3 months. The complete data was recorded in a specially designed case recording form. The data collected was transferred into a Master Chart which is subjected to statistical analysis. All the patients included in the study were explained about the procedure in detail and were issued with Patient Information Sheet.

STATISTICAL ANALYSIS

Prevalence of dyslipidemia was calculated using descriptive statistics and the effect of corticosteroids in connective tissue disorders was analysed with inferential statistics using paired‘t’ test. The statistical analysis was performed by STATA 11.2 (College Station TX USA). Shapiro-Wilk test has been used to check normality and student’s paired t-test has been used to find the significance difference between the lipid profiles 1 day before initiating steroids and after 3 months and those was expressed as mean and standard deviation. The study variables included, age, gender, duration of symptoms and diagnosed disease at the time of admission, ANA, RA, duration of symptoms, ESR-CRP and final results were reported. Continuous variables were expressed as mean and standard deviation and categorical variables were expressed as frequency and percentage. Disease at the time of admission has been compared with final results after giving steroids at 3 months.

RESULTS

In the present study, maximum number of connective tissue disorders occurred in the age group of 25 – 40 years followed by in the age group of 40-55 years and least was found in <25 years (Graph-1). In this study, the prevalence of connective tissue disorders was found to be more among females (80%) than in males (20%) [Graph-2]. The majority

	Number of Cases	Percentage
2+positive	6	20%
3+strongly positive	14	47%
Negative	16	33%
Total	30	100%

Table-1: Shows percentage of ANA in CTD

	Number of Cases	Percentage
Positive	10	33%
Negative	20	67%
Total	30	100%

Table-2: Shows percentage of RA in CTD

	Duration of symptoms (years)	ESR	CRP
Mean	1.06	67.8	1.07
SD	1.35	32.13	0.91
Min-Max	2 Months – 7 years	15-130	0.2 – 3.40

Table-3: Shows ESR-CRP in CTD

Disease	Number of Cases	Percentage
Dyslipidemia	24	80%
Normal	6	20%
Total	30	100%

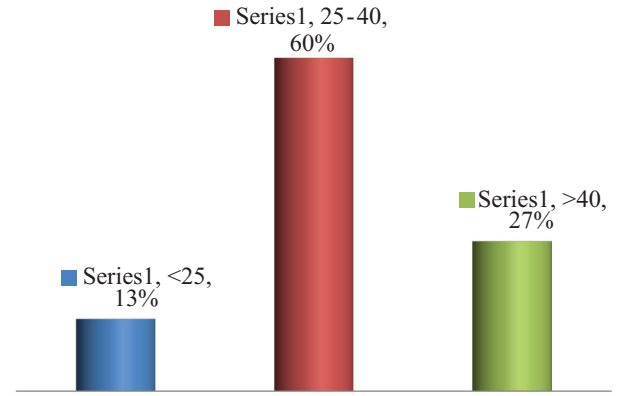
Table-4: Shows prevalence of dyslipidemia

	1 day before Initiating steroids	3 months after steroids	Mean Difference	p-value
	Mean ± SD	Mean ± SD		
Total Cholesterol	205.17 ± 63.23	204.52 ± 61.20	0.64	0.909
LDL	74.77 ± 37.56	72.19 ± 29.24	2.58	0.428
Triglycerides	181.30 ± 67.23	174.09 ± 66.0	7.21	0.324
HDL	32.86 ± 11.49	32.24 ± 9.97	0.62	0.477
VLDL	28.27 ± 12.92	30.27 ± 13.65	1.99	<0.001

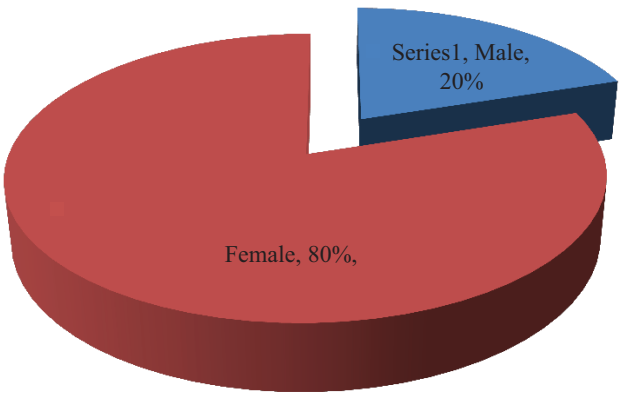
Table-5: Shows mean difference before and after giving corticosteroids

	Deranged	Improved	Normal	Total
MCTD	3 (75%)	1 (25%)	0	4
RA	5 (50%)	3 (30%)	2 (20%)	10
SLE	1 (17%)	2 (33%)	3 (50%)	6
Scleroderma	5 (63%)	2 (25%)	1 (12%)	8
Sjogren's	2 (100%)	0	0	2
Total	16	8	6	30

Table-6: Shows the effects of corticosteroids after 3 months of treatment



Graph-1: Shows age distribution in CTD



Graph-2: Shows gender distribution in CTD

of the cases were diagnosed at the time of admission in this study and were patients of RA (33%), Scleroderma (27%), SLE (20%), and MCTD (13%) followed by Sjogren's syndrome (7%).

As shown in Table-1, out of 20 patients, ANA was found to be positive among 6 patients, 14 patients were found to be strongly positive and in 16 patients it was found to be negative. Among 33% patients RA was found to be positive and in 67% patients it was found to be negative (Table-2). Mean duration of symptoms was found to be 1.06 years which was studied for ESR-CRP (Table-3) in this study. The duration of symptoms were found to be less than 1 year in 83% of cases, followed by 1 to 2 years in 10% of cases which were diagnosed at the time of admission. The prevalence of dyslipidemia was found to be 80% i.e. out of 30 patients, 24 developed dyslipidemia and 6 patients were normal (Table-4).

In the current study, the mean difference between before and after giving corticosteroids was found to be deranged in VLDL which statistically significantly with a p value of 0.001. Out of all, abnormal parameter found before starting treatment was found to be total cholesterol and triglyceride (Table-5). It was found that the effect of corticosteroids after 3 months of treatment was found to be improved in 8 cases i.e. in 3 cases of R.A, 2 cases of Scleroderma, 2 case of SLE followed by 1 case of MCTD and the derangement was found in 16 patients (Table-6).

DISCUSSION

It was found in the present study that the incidence of CTD varied from minimum age of 19 years to maximum age of 55 years and the maximum cases were found between 25 to 40 years (60%) followed by in the age group of 40 to 55 years (27%) whereas in the study conducted by M.Gaubitz et al found that connective tissue disorders were common in the age group of 15 to 40 years.[9] According to Mc Carty DJ et al stated that SLEs peak incidence occurs between 15 to 40 years, which is in concordance with the results of our study with the incidence of SLE being 18 to 45 years. In a study conducted by Drosos et al he stated that Sjogren's syndrome occurs at all ages and about 3% of people were found to be affected at an age of above 50 years.[10,11]

In this study, the prevalence of CTD was reported to be more among female population (80%) when compared to male population (20%). In a similar study done by Lahita RG et al stated that CTD s are more common in females than in males, prevalence ranges from as high as 10 to 15 females for each male in SLE. It was estimated that 4 females for every male in RA was recorded. Sjogren's syndrome affects females and males in a ratio of 9:1. Scleroderma affects males to females in a ratio of 5:14.[12]

A study done by Awal, Bruce et al found that traditional risk factors like dyslipidemia is more prevalent in CTD, when compared to general population. As compared to our study 80% of the patients had dyslipidemia, when diagnosed with CTD which is a traditional risk factor for cardiovascular disease. Also, the inflammatory disease process itself can induce alterations in lipid profile, which can be considered a

risk factor for cardiovascular disease, reduction in LDL, and increase in VLDL and Triglycerides and reduction in HDL cholesterol.[6]

It was found that there is hypercholesterolemia and hypertriglyceridemia in patients with CTDs. In this study, it was found that out of 10 patients who were diagnosed to have RA, 8 patients had dyslipidemia with increase in LDL and Triglycerides being elevated. A study investigated that HDL and LDL levels were reduced and increased levels of VLDL and Triglycerides was found which is similar to the study done by Kiranmayi and Suchitra found that there were elevated levels of isolated Triglycerides.[13]

Hyperlipidaemia is one of the three leading risk factors for death in SLE. In our study cholesterol and triglycerides were elevated and HDL and VLDL were normal. It was found that 6 out of 30 patients who were diagnosed with SLE, 3 patients developed dyslipidemia, accounting to 50%. In a similar study done by Kakati and Doley evaluated 30 patients out of which 19 SLE patients developed dyslipidemia (63%). Abnormal lipid profile is very common in patients of SLE even in younger age groups. The findings of our study revealed that out of 6 patients, 3 patients of age group 25 to 40 had dyslipidemia, youngest being 26 years.[14]

A study performed by Lodde et al, investigated serum lipid levels in Sjogren's and found that there was significant reduction in HDL and increased level in total cholesterol. In comparison to our study, 2 out of 30 patients had an increase in Total Cholesterol and Triglycerides. Till date there are no studies done which confirmed an increased cardiovascular risk in Sjogren's. Unlike other CTDs, primary cardiovascular involvement is rare in this condition. Studies examining clinical coronary heart disease and the presence of cardiovascular disease risk factors in Sjogren's syndrome are limited.[15]

In the present study, total cholesterol and triglycerides worsened after steroid therapy, there are no corresponding studies to show changes in lipid profile. In our study, 7 patients had dyslipidemia, Total Cholesterol, Triglycerides, VLDL, and in about 5 patients lipid levels were found to be deranged. In our study, around 80% patient of connective tissue disease had dyslipidemia. So, dyslipidemia is one of the major risk factor in on-going process of cardiovascular risk factor.

CONCLUSION

Atherosclerosis and CVD risk factors are enhanced in CTD. Dyslipidaemia is one of the risk factor for atherosclerosis in CTD due to chronic inflammation. Corticosteroids are commonly used in patients with CTD. As this study has a small sample size, results are indeterminate and this type of study requires larger group and a longer follow up.

REFERENCES

1. Nick Calvino. Connective tissue: Vascular and haematological (blood) support. Journal of Chiropractic medicine 2003; 2:25-36.
2. Francis J. Alenghat. The prevalence of atherosclerosis in those with inflammatory connective tissue disease by race, age and traditional risk factors. Scientific reports. Nature 2016; 6:1-9.
3. Ewa Hatadyj, Agnieszka Paradowska-Gorycka, Anna Felis-Giemza, Marzena Olesinska. Immunity and early atherosclerosis in the course of systemic lupus erythematosus, mixed connective tissue disease and antiphospholipid syndrome. Reumatologia 2016; 54:187-195.
4. Maureen McMahon, Bevra H Hahn, Brian J Skaggs. Systemic lupus erythematosus and cardiovascular disease: prediction and potential for therapeutic intervention. Expert Rev Clin Immunol 2011;7:227-241.
5. Mayada Ali Abdalla, Soha Mostafa El Desouky, Amira Sayed Ahmed. Clinical significance of lipid profile in systemic lupus erythematosus patients: Relation to disease activity and therapeutic potential of drugs. The Egyptian Rheumatologist 2017; 39:93-98.
6. Awal Al Husain, Ian N. Bruce. Risk factors for coronary heart disease in connective tissue diseases. Ther Adv Musculoskel Dis 2010; 2:145-153.
7. Brian A. Ference, Henry N. Ginsberg, Ian Graham, Kausik K. Ray et al. Low density lipoproteins cause atherosclerotic cardiovascular disease. Evidence from genetic, epidemiologic and clinical studies. European Heart Journal 2017; 38:2459-2472.
8. Simanchala Dakua, Manoranjan Behera, Jayant Kumar Panda, Prabhat Kumar Padhi. Lipid profile in systemic lupus erythematosus: study from a tertiary teaching hospital of Eastern India. Int J Res Med Sci. 2017; 5:4749-4753.
9. Gaubitz M. Epidemiology of connective tissue disorders. Rheumatology 2006; 47:234-235.
10. McCarty DJ, Manzi S, Medsger TA Jr et al. Incidence of systemic lupus erythematosus. Race and gender differences. Arthritis Rheum 1995; 38:1260-70.
11. Drosos AA, Andaonopoulos AP, Costopoulos JS et al. Prevalence of primary Sjogren's syndrome in an elderly population. Br J Rheumatol 1988; 27:123-127.
12. Lahita RG. The connective tissue diseases and the overall influence of gender. Int J Fertil Menopausal Stud. 1996; 41:156-165.
13. Kiranmayi S;Suchitra. Evaluation od dyslipidemia in patients with rheumatoid arthritis in South Indian population. Ind J Reumatol 2012; 12:123-200.
14. Kakati S, Doley B, Devee A, Dihingia P, Shram PK. Serum lipid profiles with systemic lupus erythematosus. J Indian Rheumatol Assos 2003; 11:5-7.
15. Lodde BM;Shanker V;Kok MR;Leakan RA et.al. Serum Lipid levels in Sjogren's syndrome. Rheumatology 2006; 45:481-484.

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