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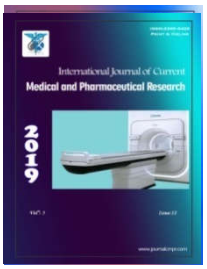

Research Article

LIPID PROFILE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS IN ACTIVE AND INACTIVE STATE OF DISEASE

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ABSTRACT

Background: Dyslipidemia is a feature of Juvenile idiopathic arthritis (JIA) and may act as a fertile soil for future cardiovascular morbidity due to pro-atherogenic lipid profile that may run in parallel with inflammation. Controlling the inflammation with adequate treatment may normalize the lipid profile to less atherogenic.
Objectives: To assess and compare the lipid profile in active and inactive state of disease and to determine the relationship of lipid profile with disease duration.
Methodology: In this prospective observational study, 55 newly diagnosed cases of JIA fulfilling the inclusion criteria were included by purposive sampling method. A detailed questionnaire was completed for each participant taken into account of the socio-demographic, clinical and laboratory parameters including fasting lipid profile and other base line investigations. Thirty-two children were in inactive disease state after treatment by attending paediatric rheumatologist. Clinical and laboratory parameters were again recorded for comparing the lipid profile of children in active and inactive disease state.
Results: Low level of High density lipoprotein (HDL) and abnormal high level of Triglyceride (TG) were present in 70.9% and 45.5% of JIA children. While lipid profile was compared, HDL cholesterol and TG levels were significantly improved during inactive state (p-value <0.05). Though not significant, increase trend of total cholesterol was present when the disease became inactive.
Conclusion: Dyslipidemia was present in JIA patients that included decrease HDL cholesterol levels and high TG levels. This pro-atherogenic lipid profile became normal when the disease became inactive.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children and one of the most common chronic illnesses of the childhood.[1] Juvenile idiopathic arthritis is defined by the International League of Associations for Rheumatology (ILAR) as arthritis of unknown etiology beginning before the sixteenth birthday and persisting for at least six weeks with other known conditions excluded.[2]

Dyslipidemia is a feature of certain rheumatic diseases, mainly systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) in adults.[3] Dyslipidemia has also been reported to occur in children with rheumatic diseases, mainly those with juvenile rheumatoid arthritis[4,5] and SLE.[6]An altered lipid profile can occur in chronic inflammatory states that may lead to atherosclerosis.[7] Despite the diversity of the clinical manifestations of the different JIA subsets, most patients have evidence of chronic inflammation and therefore are probably at risk for early atherosclerosis.[8]Children with JIA are seen to have lipid metabolism dysfunction.[9] The mechanism of altered lipid profile in JIA is not well established. There are several hypotheses regarding alteration in lipid metabolism in adult RA patients. The chronic inflammation process, immobilization, systemic complications of chronic diseases, several inflammatory mediators, and drugs may affect lipid metabolism.[10] Abnormal lipid levels in active JIA may be related to the inflammatory state of the diseases.[11] Several studies have tried to examine the mechanisms of correlation between inflammation and lipid profiles in JIA patients, but a definitive understanding of this correlation has not yet been established. Cytokines induced activation of the reticuloendothelial system is potentially critical to such changes.[12] The observed variability in lipid profiles relates to the variable disease subtypes and the levels of disease activity, which may have impact on the composition of lipid fractions in the blood.[13]The ultimate goal of treatment in children with JIA is remission, i.e. complete suppression of disease activity. When the active disease process is stopped, the inflammatory

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process is also stopped with normalization of lipid profile. The objective of the study was to assess and compare the lipid profile in active and inactive state of disease and to determine the relationship of lipid profile with disease duration at baseline.

MATERIALS AND METHODS

This prospective observational study was carried out in the department of Paediatrics (Indoor and Paediatric Rheumatology follow up clinic), Bangabandhu Sheikh Mujib Medical University from November 2017 to January 2019. This study was conducted with prior approval of the Institutional Review Board of BSMMU, Dhaka, Bangladesh.

Fifty five newly diagnosed cases of different subtypes of JIA fulfilling ILAR classification criteria were included in this study. Children who were known to be suffering from diabetes mellitus, hypertension, renal disease, infection, thyroid or hepatic dysfunction, children getting hormones, lipid-lowering agents, diuretics, and prednisolone which could interfere with lipid metabolism and overweight and obese children were not included in this study. A predesigned structured questionnaire was completed for each patient by interviewing them or their parents.

History, clinical examination findings and relevant investigations were included in the questionnaire. After diagnosis of JIA, fasting lipid profile was assessed after ten (10) hours overnight fast and consumption of normal diet for previous 2 days (without fat restriction). Two (2) ml blood was drawn from each patient from the antecubital vein under aseptic precaution by a disposable syringe. Lipid profiles were assessed including total cholesterol (TC), high density lipoprotein cholesterol (HDL), triglycerides (TG) and low-density lipoprotein cholesterol (LDL). Baseline fasting lipid profiles were measured during active disease state in all cases. After enrollment all the JIA patients were treated by the pediatric rheumatologists according to standard protocol with the aim to bring them into inactive disease state. Diseases activity was evaluated by WALLACE criteria.[14] Active disease state took about 3 to 12 months to become inactive. So, follow up was done to all the patients at 3 months/ 6 months/ 9 months/12 months. Among all the cases enrolled, thirty-two patients (58%) went in to inactive disease state. Whenever these patients were found in inactive state of disease, blood samples were again taken for measurement of fasting lipid profile. All the parameters of the 32 patients were compared between active and inactive diseases state. The rest 23 patients were excluded from comparative analysis.

Statistical Analysis

The entered data were checked, verified and analyzed by SPSS (statistical program for social science) software version 22. Numeric data were expressed as mean ± standard deviation. Paired student't' test was applied to compare means of two dependent groups. Pearson's co-efficient was used to investigate the correlation between the two variables. A P-value less than 0.05 were considered as significant.

RESULTS

Among 55 cases mean age of the patients was 9.3 years and highest number of (47.3%) cases was older than 10 years. 60% cases were male and 40% were female. Diagnosis was done within 6 months in 60% cases and in 29.1% cases disease duration at diagnosis was more than 1 year. While lipid profile was measured at baseline at active state, it was found that mean TG level was 120.16 ± 51.52 mg/dl, total cholesterol was 152.36 ± 30.96 mg/dl, HDL level was 33.05 ± 10.31 mg/dl, and LDL level was 95.26 ± 29.50 mg/dl (Table-I). When the lipid profile was adjusted for normal age range according to the Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents'2011[15], low level of HDL cholesterol (70.9%) and abnormally high TG level (45.5%) which were proatherogenic, was present in most of the cases in active state of disease (Table-II). Difference of HDL cholesterol and TG during active and inactive state of disease was highly significant (P<0.05). There was also decreased trend of LDL and increased trend of total cholesterol level during inactive state though not significant (Table-III). In this study, no significant correlation between lipid profile at baseline and disease duration was found (figure- I).

Table I Fasting Lipid Profiles of the Study Subject at Baseline (n-55)

Parameters	Mean ± SD
TG (mg/dl)	120.16±51.52
Cholesterol (mg/dl)	152.36±30.96
HDL (mg/dl)	33.05±10.31
LDL (mg/dl)	95.26±29.50

Data expressed as Mean ± SD.

Table II Fasting Lipid Profile Categories Among JIA Patients at Baseline (n-55)

Parameters	Acceptable n(%)	Borderline n(%)	Abnormal n(%)
TG	12 (21.8)	18 (32.7)	25 (45.5)
Cholesterol	42 (76.4)	10 (18.2)	3 (5.5)
HDL	6 (10.9)	10 (18.2)	39 (70.9)
LDL	41 (74.5)	8 (14.5)	6 (10.9)

Table III Comparison of Fasting Lipid Profile between Active and Inactive State of Disease (n-32)

Parameters	Active state (Mean± SD)	Inactive state (Mean± SD)	p-value
TG	113.06 ± 38.56	95.09 ± 39.21	0.017
Cholesterol	149.87 ± 26.26	156.37 ± 31.51	0.261^{ns}
HDL	34.53 ± 10.30	48.84 ± 16.35	0.000
LDL	92.74 ± 25.33	87.91 ± 22.74	0.239^{ns}

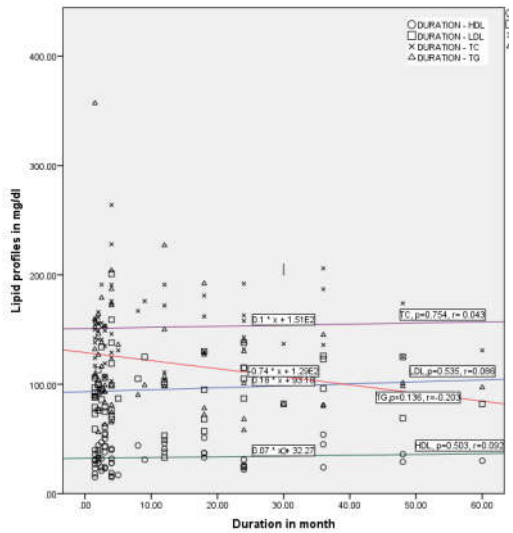

Figure I Scatter Diagram showing the correlation between Duration of disease and Lipid profiles at baseline (n=55).

DISCUSSION

Dyslipidemia is a feature of certain rheumatic diseases in adults. There are also several studies depicting dyslipidemia in child with JIA. In this study mean age of the patients (9.3 years) were similar to the study done by Bakkaloglu et al. where the mean age was 9.5 years.[5] Another Bangladeshi study done by Laila et al. found that mean age of JIA patients was 10.8 which was almost similar to the present study and picturized the age of onset in our context.[16]

In this study male-female ratio was 1.5:1. Similar result with male predominance was found in another study done by Rahman et al. in Bangladesh where male-female ratio was 2:1.[17]

According to the normal lipid profile adjusted for age range[15], low level of HDL cholesterol and high TG level was present in 70.9% and 45.5% of the cases in active state of disease. This result was similar with previous study done by Maragoni et al. where they found that, HDL cholesterol was low in active disease state in most of the JIA patient (57%).[11]

In our study abnormal HDL cholesterol level became normal during inactive state of disease after effective treatment (p-value <0.001). Reduced HDL level during active disease may be explained by inflammation and physical inactivity. A study done by Shen et al. showed similar results.[12] But the study by De Sanctis et al. found no significant change in HDL cholesterol level during the study period.[18] We also found higher TG level in active disease state that became near normal during inactive state of disease ($p < 0.05$). Increased level of TG during active state could be explained by cytokines induced increase in very low density lipoprotein (VLDL) production and a decrease in the clearance of TG rich lipoproteins. Several studies found similar results.[18,19] But no significant change of TG level was found in study done by Shen et al.[12] Regarding LDL levels our study match with the study done by Shen et al. with no significant change during inactive state of disease.[12] Few studies depict significant increase of total cholesterol during inactive state[12,19], but study done by DeSanctis et al. found significant lower level of TC during transition to inactive disease.[18] Though not significant, our study revealed increase trend of total cholesterol level when the disease became inactive. Minimal increase of total cholesterol during inactive disease could be explained by increased appetite and increased HDL particle as a consequence of elevated HDL cholesterol in inactive state of disease. In this study, no significant correlation between lipid profile at baseline and disease duration at onset was found (figure-I). Study done by Bohr et al. also found similar result.[20] Recently several studies have established the link between dyslipidemia and increased risk of cardiovascular morbidity and mortality among rheumatoid arthritis patients.[21] Children with JIA are also prone to cardiovascular complications manifested by subclinical atherosclerosis.[20]

Atherosclerosis is a multifactorial process and one of the modifiable risk factor is dyslipidemia.[22] Our study perhaps also revealed atherogenic lipid profile evidenced by significant low level of HDL cholesterol and high level of TG at active state of disease. But after effective treatment most of the indictors normalized and became less atherogenic, thus hypothetically reduced cardiovascular morbidity. But the long-term outcome needs to be evaluated by future longitudinal study.

Therefore, these results strongly revealed that the higher inflammatory state in JIA patients is associated with the increase risk of dyslipidemia. But effective anti-rheumatic therapy can improve, at least partially, the abnormal lipid profiles and its consequences in patients with JIA.

CONCLUSION

The study found that dyslipidemia is present in most of the cases of children with JIA. Serum HDL cholesterol was reduced and TG was increased significantly at active state of disease. Lipid profile became normal when the disease was inactive after effective treatment.

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