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Original Research Article

Changes in biomarkers of lipid in juvenile idiopathic arthritis and its association with various disease parameters: a 6-month follow-up study

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ABSTRACT

Background: The objectives of our study were to determine the changes in lipid profile (total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C)) in juvenile idiopathic arthritis (JIA) and assess its association with epidemiological and clinical profile of JIA patients.
Methods: This observational study was performed with 46 patients at presentation followed by 38 cases at 3 months and 18 cases at 6 months of follow up. Their demographic profile and clinical parameters including juvenile disease activity score (JADAS 27) were compared with the biomarkers of lipid profile.
Results: The mean (SD) age was 105.85 (20.23) months at first visit with mean (SD) disease duration being 15 (6.4) months. Twenty-six participants had oligoarthritic (56.5%), while the rest had polyarthritis (43.4%). Most of the patients had borderline raised TG and LDL-C (cases with raised TG n=14 (30.4%), 12 (31.5%), 5 (27.7%) at 1st visit, 3 months, and 6 months respectively and LDL-C n=12 (26%), 10 (26.3%), 6 (33.3%) at 1stvisit, 3 months, and 6 months respectively). HDL-C level was low in 36 (78.2%) cases at first visit, 28 cases (73.6%) at 3 months and 12 cases (66.6%) at 6 months respectively. Lipid profile was significantly affected by gender difference, duration of disease and drug therapy ($p<0.05$). Significant association have been found between JADAS score and TGL level with p value 0.03.
Conclusions: Children with JIA definitely suffer from dyslipidemia. Among the biomarkers of lipid profile, low level of HDL-C is one of the most important highlights of our study. Further studies can help to strengthen the findings and formulate necessary interventions at an early stage.

Keywords: Lipid profile, Juvenile idiopathic arthritis, Juvenile disease activity score 27

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the commonest cause of chronic arthritis in children worldwide.[1] It is associated with prolonged and variable periods inflammation of joints with raised cytokines such as interleukin-1 and 6 (IL1 and IL6), and tumor necrosis factor-alpha (TNF-α). These inflammatory markers are known to have a role in pathogenesis and progression of dyslipidemia.[1-4] Prolonged dyslipidaemia is a known precursor of atherosclerosis which is a chronic inflammatory condition affecting the arteries. Among all the biomarkers of lipid profile, low level of plasma high-density lipoprotein cholesterol (HDL-C) has been associated with acute coronary events as it plays an important role in reducing the formation of atherosclerotic lesions by removing excess cholesterol from cells and preventing endothelial damage.[5] Multiple studies have shown that HDL-C is usually decreased early along with increase in triglyceride (TG) and low density lipoprotein cholesterol (LDL-C)

levels in rheumatic patients in comparison to their healthy cohort.[6,7] So it is important to find out the degree of dyslipidaemia associated with JIA and its variations with disease activity, duration, subtypes and drugs as it can have serious consequences in future such as ischemic heart disease and stroke.

Although there are publications highlighting this association in rheumatoid arthritis in adults, there are very few in children, especially from this part of the country, where there may be variations in disease phenotypes. Moreover, in a resource limited setting like ours, the general level of disease control may not be optimum as compared to advanced settings. So, it is necessary that we have specific information regarding lipid profile in children of JIA from our population before planning or contemplating any intervention strategies. Hence, we conducted this study with an aim to delineate if JIA is associated with dyslipidaemia and whether the lipid profile correlates with JIA phenotypes, clinical parameters disease activity scores and drug therapy.

Objectives

Objectives of the study were to determine the changes in lipid profile (total cholesterol (TC), TG, HDL-C, and LDL-C) in children suffering from JIA and assess its association with patient characteristics, disease severity, duration, disease activity score, JIA subcategory and medications used.

METHODS

Study setting and participant selection

This is a single-centre, longitudinal, observational study which was performed at a tertiary care hospital of Kolkata, India from January to December 2021. Children in the age group of 1 month till 12 years who fulfilled the International League of Association for Rheumatology (ILAR) classification criteria for JIA were initially screened to include in the project. We adopted a purposive technique of sampling for case recruitment and subdivided them as per their disease activity status. The sample size calculation was done based on the previous record of such patients attending the hospital in the last year. Grossly malnourished children, both wasted and obese, critically ill, those with known comorbidities, known thyroid disease, history of intake of lipid lowering agents and known family history of dyslipidaemia were excluded. Children with systemic JIA were also excluded because the disease activity stratification criteria used here were not validated in systemic-onset JIA. Necessary permissions for the study were obtained from institutional ethics committee NO/NMC/10115. Proper counselling was done and written informed consent was obtained from each participant or their guardian maintaining appropriate confidentiality as applicable.

Data collection

The epidemiological and clinical background information of each participant was entered in a predesigned pretested proforma. The subjects were divided two subtypes of JIA -oligoarthritic and polyarthritis, depending upon the number of joints involved in them, ≤4 and ≥5, respectively. The disease activity in each case was measured by juvenile arthritis disease activity score 27 (JADAS27).[8] The following joints were included for assessing disease activity: cervical spine, elbows, wrists, metacarpophalangeal joints (from first to third), proximal interphalangeal joints, hips, knees, and ankles. JADAS27 score was calculated and the patients were categorized as inactive disease, low disease activity, moderate disease activity, and high disease activity with scores ≤1, 1.1-2, 2.1-4.2, and >4.2 in oligoarthritic and ≤1, 1.1-3.8, 3.9-8.5, and >8.5 in polyarthritis, respectively.[8]

Clinical and laboratory data were filled up on inclusion at presentation and at 3 months and 6 months of follow up in a predesigned and pretested proforma. The criteria for clinical remission were state of inactive disease as per JADAS 27 for a minimum of six consecutive months.

Lipid profile estimation method

We collected the venous blood of the enrolled children after at least 12 hours of fasting in the early morning in a coagulant free venipuncture tube with asepsis and adequate precautions. Samples were centrifuged and TC, TG and HDL-C were measured by enzymatic assay (ERBA-Mannheim XL system packs) and LDL-C was derived by Friedewald's equation: LDL=total cholesterol - HDL - triglycerides/5. The lipid level of JIA cases was evaluated based on the values mentioned in report of expert panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents published by National Heart, Lung, and Blood Institute.[9]

Statistical analysis

Microsoft excel 2016 software was used to collect and store information. Mean and standard deviations (SDs) for the numerical variables and counts and percentages for the categorical variables were computed. Statistical analysis was performed with the help of statistical package for the social sciences (SPSS) version 25.0. The student’s t-test was used to compare means between two groups. One-way analysis of variance (ANOVA) followed by post hoc Tukey’s B test was performed when the means of two or more continuous variables were compared. Chi square test was employed to find the association between two categorical variables. A p value of <0.05 was considered statistically significant.

RESULTS

Out of a total of 53 patients initially assessed for eligibility, 7 were excluded as they met one or more exclusion criteria

as mentioned above. So, the final sample size (n) for data compilation and analysis was 46 at presentation. Due to participant attrition, 38 and 18 children could be studied at 3 months and 6 months respectively. The attrition rate was high at the end of 6 months because of the lockdown imposed to combat global COVID pandemic. Figure 1 is a flow chart of study showing patient recruitment at presentation, at 3 months and 6 months. The demographic, clinical and other background characteristics of the participants at presentation, at 3-month and 6-month follow up is enumerated in Table 1.

At initial presentation, the mean (SD) age in months of the participants was 105.85 (20.23) with a range of 64-141 months, and the entire cohort comprised of 22 males (47.83%) and 24 females (52.17%) children. Most of the patients were from Kolkata city and outskirts, 15 were from districts as the institution serves as a tertiary care referral centre. However, the attrition rate of patients from far off places was proportionately more at 3 and 6 months of follow up, probably because of lockdown and lack of conveyance to travel. The mean (SD) duration of the disease among the subjects in months was observed as 15(6.4) with a range of 7-36 months. Twenty-six participants had oligoarthritic (56.5%), while the rest had polyarthritis (43.4%). Overall, most of the patients received nonsteroidal anti-inflammatory drug (NSAID) and methotrexate (MTX), some required steroids in addition. Steroids were given only to a few patients as bridging therapy as prednisolone at 2 mg/kg for a maximum of 4-6 weeks followed by gradual tapering. None received parenteral, intraarticular or intraocular steroids. Also, none received biologics in this series.

In our study, 6 cases (13%) at first visit, 8 (21%) at 3 months, 4 (22.2%) at 6months had TC more than 160 mg/dl, which poses a risk for coronary artery disease (CAD).[9] None of the patients had elevated cholesterol more than 200 mg/dl. The majority of the patients had borderline raised TG and LDL-C presentation, at 3 months and 6 months of visit (TGn=14 (30.4%), 12 (31.5%), 5 (27.7%) at 1st visit, 3 months, and 6 months respectively and LDL-C n=12 (26%), 10 (26.3%), 6 (33.3%) at 1st visit, 3 months, and 6 months respectively).[9] HDL-C level was low in 36 (78.2%) cases at first visit followed by 28 cases (73.6%) at 3months and 12 cases (66.6%) at 6 months respectively.[9]

The clinical and laboratory parameters including JADAS 27, haemoglobin (Hb), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), total leucocyte count (TLC), platelet and lipid profile (TC, LDL-C, HDL-C, and TG) of the patients are discussed with values of their mean and standard deviation in Table 2 where it was seen that the mean (SD) JADAS27 values were higher at presentation and at 6 months visit [3.05 (2.94) and 3.64 (3.36)] respectively.[8] It is also found that mean (SD) HDL-C was low at first, 3 months and 6 months visit [35.97 (5.2), 37.4 (5.4), and 37.35 (5.3) respectively].[9]

The effect of epidemiological and clinical parameters on lipid profile of JIA patients at 1st visit have been clearly depicted in Table 3. It shows that girls had higher lipid levels in comparison to boys of which values of TC and LDL-C have been found to be correlated significantly (p values 0.002 and 0.001 respectively) with gender difference. There was no significant variation in lipid levels between the subcategories of JIA as assessed by independent student t test. It was further seen that with the increase in duration, TC, TG, and LDL-C were found to rise and HDL-C level decreased, of which rise in cholesterol and LDL is statistically significant as analysed by ANOVA test (p values 0.02 and 0.01 respectively). Significant association have been found between JADAS score and TGL level with p value 0.03 while in others no notable change was found at first visit.

No significant changes were found in inflammatory markers (ESR, CRP, PLT, and WBC) with change in lipid profile in the included cases at first visit as well as in subsequent follow up.

Table 4 clearly shows that there is an effect of change in JADAS 27 on lipid profile as analysed by one-way ANOVA test. The TC, TG and LDL-C have been found to rise significantly with increase in JADAS 27 (p values<0.05) in follow up visits at 3 months and 6 months. HDL -C levels were low though not significant (p value 0.08 and 0.40 at 3 months and 6 months respectively).

Further analysis showed that combined use of NSAID and MTX changed the lipid levels with significant effect on TC and LDL-C as calculated by independent student t test with p values (95% CI) of 0.02 (43.4, 3.8), 0.01 (35.39, 5.41) at 3 months and 0.02 (38.9, 3.61), 0.04 (32.68, 0.32) at 6 months respectively as shown in Table 5. Only 3 patients at 3 months and one patient at 6 months received steroid along with other drugs as a bridging therapy but as the number is too small it cannot be used in analysis.

Table 1: Patient profile characteristics at presentation, 3 months and 6 months of follow-up.

Clinical profile	At presentation n=46 (%)	At 3 months follow-up n=38 (%)	At 6 months follow-up n=18 (%)
Gender			
Male	22 (47.8)	20 (52.6)	11 (61.1)
Female	24 (52.17)	18 (47.3)	7 (38.8)
Residence			
Kolkata and outskirts	31 (67.3)	28 (73.6)	15 (66.6)

Continued.

Clinical profile	At presentation n=46 (%)	At 3 months follow-up n=38 (%)	At 6 months follow-up n=18 (%)
More than 100 km	15 (32.6)	10 (26.3)	3 (16.6)
JIA category			
Oligoarticular	26 (56.5)	25 (65.7)	10 (55.5)
Polyarticular	20 (43.4)	13 (34.2)	8 (44.4)
Juvenile disease activity score (JADAS 27)			
Low	19 (41.3)	16 (42.10)	6 (33.3)
Moderate	15 (32.6)	15 (39.47)	10 (55.5)
High	12 (26.0)	7 (19.4)	2 (11.1)
***Modalities of treatment**			
NSAID only	25 (54.3)	15 (39.4)	5 (27.7)
NSAID+MTX	11 (23.9)	20 (52.6)	12 (66.6)
NSAID+MTX+steroids	10 (21.7)	3 (7.8)	1 (5.5)

*NSAID-nonsteroidal-anti-inflammatory drugs, MTX-methotrexate

Table 2: Clinical and laboratory parameters at presentation, and at 3 and 6 months of follow-up.

Follow up	Age (months)	JADAS 27*	Hb (gm/dl)	ESR (mm/1 hour)	CRP (mg/dl)	TLC (1000/mm^3)	Platelet (lac/mm^3)	TC (mg/dl)	LDL-C (mg/dl)	HDL-C (mg/dl)	TG (mg/dl)
At presentation (n=46)	105.85 (20.23)	3.05 (2.94)	11.14 (1.24)	31.52 (6.8)	4.19 (2.4)	8840.6 (1171.4)	3.42 (0.93)	127.58 (24.97)	77.9 (20.4)	35.97 (5.2)	68.38 (9.7)
At 3 months (n=38)	108 (18.6)	2.51 (1.91)	11.10 (1.14)	31.67 (6.8)	5.15 (7.9)	8865 (1724.7)	3.42 (0.80)	132.48 (22.6)	81.25 (17.8)	37.4 (5.4)	69.68 (8.9)
At 6 months (n=18)	118 (12.3)	3.64 (3.36)	11.01 (1.00)	31.97 (8.2)	3.75 (2.3)	8841.6 (1461.8)	3.40 (0.65)	134.77 (28.0)	83.08 (23.2)	37.35 (5.3)	71.7 (10.1)

*JADAS 27-Juvenile arthritis disease activity score, Hb-hemoglobin, ESR-erythrocyte sedimentation rate, CRP-C-reactive protein, TLC-total leucocyte count, TC-total cholesterol, LDL-C-low density lipoprotein cholesterol, HDL-C-high density lipoprotein cholesterol, TG-triglyceride, all results are calculated in mean±SD

Table 3: Association of epidemiological and clinical profile with lipid parameters at presentation.

Clinical profile	Sample size (n)	*Serum TC (mg/dl)	P value	*Serum TG (mg/dl)	P value	*Serum LDL-C (mg/dl)	P value	*Serum HDL-C (mg/dl)	P value
Gender									
Male	22 (47.8)	121.50 (18.14)	0.002	66.80 (7.92)	0.071	72.19 (15.30)	0.001	35.94 (4.85)	0.065
Female	24 (52.17)	136.70 (29)		70.75 (11.80)		86.45 (26.33)		36 (5.95)	
JIA category									
Polyarticular	26 (56.5)	119.636 (18.9569)	0.524	65.636 (98.4329)	0.516	71.21 (16.069)		35.24 (4.84)	0.654
Oligoarticular	20 (43.4)	120.769 (20.1583)		66.769 (6.8939)		72.46 (17.91)		35.00 (5.275)	
Duration of disease (months)									
Less than 12	18	126 (23)	0.026	68 (9.1)	0.152	77 (20)	0.011	39 (5.5)	0.868
12-60	18	128 (24)		68 (9.8)		78 (20)		36 (5.3)	
More than 60	10	129 (24)		68 (10)		79 (21)		36 (5.3)	
Disease activity *(JADAS 27)									
Low	19 (30.4)	127 (23)	0.071	67 (9.1)	0.037	77 (20)	0.098	36 (5.2)	0.670
Moderate	15 (32.6)	127 (24)		68 (9.8)		78 (21)		36 (5.3)	
High	12 (26.0)	127 (24)		68 (10)		77 (21)		36 (5.4)	

*JADAS 27-Juvenile arthritis disease activity score, TC-total cholesterol, LDL-C-low density lipoprotein cholesterol, HDL-C-high density lipoprotein cholesterol, TG-triglyceride, all results are calculated in mean±SD

Table 4: Comparison of JADAS 27 score with lipid profile at 3 months and 6 months of visit.

Clinical profile and duration (months)	Sample size n (%)	*Serum TC (mg/dl) Mean (SD*)	P value	*Serum TG (mg/dl) Mean (SD)	P value	*Serum LDL-C Mean (SD)	P value	*Serum HDL-C (mg/dl) Mean (SD)	P value
Disease activity at 3 months *(JADAS-27)									
Low	16 (42.10)	130.7 (26.26)	0.03	68.9 (10.73)	0.33	81.25 (17.88)	0.02	38.11 (7.79)	0.48
Moderate	15 (39.47)	132.09 (23.19)		70 (9.15)		80.92 (18.37)		37.25 (5.28)	
High	7 (19.4)	134.12 (22.05)		70.28 (9.06)		82.05 (17.03)		38.02 (5.13)	
Disease activity at 6 months (JADAS-27)									
Low	6 (33.3)	134.06 (27.76)	0.02	71.59 (10.22)	0.002	82.53 (23.04)	0.03	37.22 (5.31)	0.08
Moderate	10 (55.5)	134.46 (28.27)		71.68 (11.08		82.58 (23.23)		37.55 (5.15)	
High	2 (11.1)	135.56 (29.61)		72.60 (11.47)		83.04 (24.25)		38 (5.01)	

*JADAS 27-Juvenile arthritis disease activity score, TC-total cholesterol, LDL-C-low density lipoprotein cholesterol, HDL-C-high density lipoprotein cholesterol, TG-triglyceride, SD-standard deviation

Table 5: Association of treatment modalities with lipid profile at 3 months and 6 months following initiation of therapy.

Treatment modalities and duration (months)*	Sample size n (%)	*Serum TC (mg/dl) Mean (SD)*	P value (95% CI)*	*Serum TG (mg/dl) Mean (SD)	P value (95% CI)	*Serum LDL-C Mean (SD)	P value (95% CI)	*Serum HDL-C (mg/dl) Mean (SD)	P value (95% CI)
At 3 months									
NSAIDS	15 (39.4)	119.51 (12.07)	0.02 (43.4, 3.8)	65.89 (5.37)	0.22 (13.71, 3.74)	70.59 (8.77)	0.01 (35.39, 5.41)	35.73 (4.50)	0.33 (9.8, 3.76)
NSAIDS+ MTX	20 (52.6)	143.12 (23.53)		70.85 (10.37)		91 (17.81)		38.75 (8.04)	
At 6 months									
NSAIDS	5 (27.7)	118.36 (15.60)	0.02 (38.9, 3.61)	66.63 (5.89)	0.22 (10.58, 2.86)	70.24 (14.13)	0.04 (32.68, 0.32)	34.77 (4.36)	0.07 (8.33, 0.39)
NSAIDS+ MTX	12 (66.6)	139.62 (20.73)		70.50 (7.91)		86.75 (19.02)		38.75 (5.09)	

*NSAID-nonsteroidal-anti-inflammatory drugs, MTX-methotrexate, TC-total cholesterol, LDL-C-low density lipoprotein cholesterol, HDL-C-high density lipoprotein cholesterol, TG-triglyceride, SD-standard deviation, CI-confidence interval

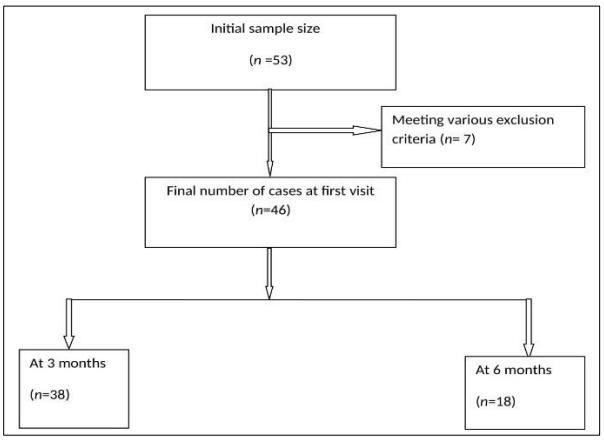

Figure 1: The study showing patient recruited at presentation, at 3 months and 6 months to be 46, 38 and 18 respectively after exclusion of 7 cases at the first visit out of 53 cases initially examined for enrolment.

DISCUSSION

The American Heart Association had already stated in their guidelines (2006) that hyperinflammation for prolong period itself is a risk factor for cardiovascular diseases.[10] Chronic arthritis in children, particularly JIA being most common among them, is associated with cytokinemia which has been found to damage blood vessel wall.[4] Together with this, whether the dyslipidaemia aggravates the condition and lead to increased possibility of cardiovascular accidents in chronic childhood arthritis in near future needs to be studied further. Hence, awareness of the fact that alteration in lipid profile can cause atherosclerotic changes of the arteries whose known clinical consequences are ischemic heart disease, stroke and circulatory disorders of peripheral arteries, emphasizes the need for identifying, monitoring and controlling the risk factors associated with it in children suffering from chronic arthritis. it would be prudent to know the association of lipid biomarkers with disease

activity in JIA and its association with drug therapy, duration and other clinical parameters. Although there are some studies highlighting this association in world literature, there are very few from this part of our country. Table 6 highlights the comparison between major findings on this aspect in previous publications and our study in a nutshell.[11-16]

Our research work is one of the few in literature which assessed the clinical symptoms and the effect of alterations in complete blood counts, acute phase reactants and first line drugs on lipid profile in JIA patients.

This study shows that dyslipidaemia affected majority of JIA patients, with TG and LDL-C levels being borderline raised and low level of HDL-C persisted at first visit and subsequent follow up as well as a significant association have been found with disease activity score and duration. Similar findings were found in the study done by Rodrigues et al in 2021 on changes in biomarkers of lipid metabolism in JIA and their association with inflammatory markers.[15] Also, in the study by Urban et al involving 25 children with JIA, they showed that HDL-C level was low along with raised homocysteine levels in children with JIA.[17]

One of the highlights of the present study, which has not been pointed out in any of previous publications is lipid levels, particularly TC and TG, are higher in girls compared to boys. It may be coincidental or may be due to hormonal effect. No significant difference in lipid levels could be delineated between the JIA subtypes, oligoarticular and polyarticular variety, like previous publications.

In a study conducted by Goncalves et al in 28 cases of polyarticular JIA, majority of them had low HDL-C concentration and elevated LDL-C while few of them had raised TG and TC as well.[12] So, also they could not delineate any association between lipid biomarkers and disease activity, the duration of the disease or the treatment given. A similar study was done by Skare et al published in 2013 on adults, where lipid parameters of 54 JIA patients were compared with 54 healthy adults.[7] They found that TC and LDL-C levels were significantly high and HDL-C level was low in children with chronic arthritis than their healthy peer groups, more commonly in older children, though the levels of lipid profile did not correlate with RA and ANA levels significantly.

Table 6: Literature review and comparison of findings of different studies with our study.

Author/year/place/JIA subtype	Participant number/age range /gender (female-male)	Major conclusions*
Bakkaloglu et al /1996/Ankara, Turkey/all JIA types[11]	37/2.5-16 years/18-19	Significant difference in all lipid parameters between active and inactive disease and also with that of controls
Goncalves et al/2011/Sao Paulo, Brazil/pJIA[12]	28/14-26 years/21-7	Decreased HDL-C most common followed by LDL-C. Male patients more affected than female patients
Guha et al/2016-19/Kolkata, India/all JIA subtypes[13]	42/2-16 years/19-23	TC and HDL deranged but significant differences between cases and controls were seen only with HDL levels
Bohr et al/2016/Copenhagen, Denmark/all JIA subtypes[14]	210/7-21 years/149-61	HDL-C decreased with increase in inflammatory marker myelo related protein complex (MRP) 8/14, CRP, JADAS 27
Rodrigues et al/2021/Sao Paulo, Brazil/pJIA, sJIA[15]	62/5-19 years/46-16	Altered lipid levels in 83.3% patients of JIA. Low HDL-C most frequent association/higher LDL-C in systemic JIA than polyarticular JIA
Nasef et al/2021/Ismailia, Egypt/all JIA types[16]	100/7-15 years/78-22	HDL-C most frequently deranged/active disease is a significant risk factor for abnormal TG/No association with ESR or CRP levels
Present study/2022/Kolkata, India/pJIA and oJIA	46/1-12 years/22-24	HDL-C level decreased, TC, TG and LDL-C values significantly changed with increase in duration and disease activity. No association found with ESR and CRP. Girls had higher values of TC and TG in comparison to boys but no significant difference found between the subtypes of JIA.

*JIA-Juvenile idiopathic arthritis, JADAS 27-juvenile arthritis disease activity score, TC-total cholesterol, LDL-C-low density lipoprotein cholesterol, HDL-C-high density lipoprotein cholesterol, TG-triglyceride, ESR-erythrocyte sedimentation rate, CRP-C-reactive protein

In contrast, in our study where we got 6 cases (13%) at first visit, 8 (21%) at 3 months, 4 (22.2%) at 6 months with TC more than 160 mg/dl, a risk factor for coronary artery disease (CAD).[9] Many of the patients had borderline raised TG and LDL-C at first visit, at 3 months and 6 months of visit along with low HDL-C level in 36 (78.2%) cases at first visit followed by 28 cases (73.6%) at 3 months and 12 cases (66.6%) at 6 months respectively. A significant

association have been found between rise in TC, LDL-C, sometimes TG, with JADAS 27, drugs and disease duration. Although, no such statistically significant effect was found on HDL.

Among all the parameters of lipid profile, low HDL-C level in children forms a major concern as it has a definite adverse effect on cardiovascular health as suggested by study of Assman G et al.[18] Studies by Bakkaloglu et al and Tselepis et al also corroborated the findings of our study as they also showed that deranged lipid profile has positive correlation with disease activity in JIA patients increasing chances of endothelial dysfunction and atherosclerosis.[11,19]

Further, it has been shown in TEAR trial by Millan et al that drug like MTX or others, used alone or in combination could affect the lipoprotein levels in children suffering from JIA, further aggravating the dyslipidaemia and predisposing them to cardiovascular complications.[20] Similarly in our study also we used Methotrexate as the main DMARD along with NSAID and found statistically significant association with changes in lipid parameters in the follow up.

Although this study does reveal some important aspects of blood lipid parameters in children with JIA, it does have its' share of limitations. Firstly, children above 12 years of age could not be included because as per government policy, the children above that age do not attend Pediatrics department. Analysing the lipid profile in larger number of peri adolescent children could have thrown some light if pubertal changes have any bearing on lipid parameters. Secondly, due to lack of resources, we could not estimate the levels of proinflammatory cytokines like IL1, IL6 and TNF alpha, which could have revealed if lipid levels are influenced by biochemical inflammatory status of JIA patients. And finally, the study participants were too few, there were higher attrition rate especially at 6 months because of COVID pandemic and follow up period too short to give firm recommendations regarding modalities of intervention strategies to be adopted to tackle the long-term effects of lipid abnormalities.

CONCLUSION

There are definite and discernable lipid profile abnormalities in children with JIA with possible long-term implications. Among the biomarkers of lipid profile, low level of HDL-C is one of the most important highlights of our study which is a known risk factor for cardiovascular disease and are associated with increased coronary events in future. Hence this can be taken as a pilot study to plan and undertake larger multicentric studies of longer duration of follow up to generate a more robust data set to be able to recommend viable guidelines regarding monitoring of lipid abnormalities and the possible need for intervention.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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