Dyslipidaemia in juvenile dermatomyositis: the role of disease activity

K.T. Kozu[1], C.A. Silva[1,2], E. Bonfa[2], A.M. Sallum[1], R.M.R. Pereira[2], V.S. Viana[2], E. Borba[2], L.M. Campos[1]

[1]Paediatric Rheumatology Unit, Children's Institute, and [2]Rheumatology Division, Faculdade de Medicina da Universidade de São Paulo, Brazil.

Abstract

Objective

To evaluate the presence of dyslipidaemia in JDM and its possible risk factors.

Methods

Twenty-five JDM patients were compared to 25 healthy controls according to demographic data, body composition, fasting lipoproteins, glycaemia, insulin, antibodies and muscle enzymes. JDM scores were assessed: CMAS, MMT, DAS, MYOACT and MYTAX.

Results

Abnormal lipid profile was found in nine patients and four controls (36% vs. 16%, p=0.196). JDM patients demonstrated significant higher levels of triglycerides (TG) [80(31-340) vs. 61(19-182) mg/dL, p=0.011] and higher frequency of abnormal levels of high density lipoproteins (HDL) (28% vs. 4%, p=0.04) when compared to controls. JDM patients with dyslipidaemia demonstrated significant lower median of HDL levels [29(0-49) vs. 50(39-72) mg/dL, p=0.0005], higher frequency of low HDL levels (77% vs. 0%, p=0.0001), higher TG levels [128(31-340) vs. 69(46-138) mg/dL, p=0.011], and also a higher frequency of increased levels of TG (44% vs. 0%, p=0.01), and TC (33% vs. 0%, p=0.03) when compared to those without this condition. Positive anti-LPL antibody was detected in just one JDM patient with abnormal lipid profile. JDM with dyslipidaemia had higher ESR (26 vs. 1 4.5mm/1st hour, p=0.006), CRP (2.1 vs. 0.4mg/dL, p=0.01), DAS (6 vs. 2, p=0.008), MYOACT(0.13 vs. 0.01, p=0.012), MYTAX(0.06vs.0,p=0.018), and lower scores of CMAS (47 vs. 52, p=0.024) and MMT (78 vs. 80, p=0.001) compared to JDM without dyslipidaemia. Positive correlations were detected between TG levels and CRP (r=0.697, p=0.001), DAS (r=0.610, p=0.001), MYOACT (r=0.661, p=0.001), MYTAX (r=0.511, p=0.008), and negative correlations with CMAS (r=-0.506, p=0.009) and MMT (r=-0.535, p=0.005). No differences were found between these groups regarding body composition, lipodystrophy, anti-LPL antibodies, and treatment except by higher frequency of cyclosporine current use in patients with dyslipidaemia (33% vs. 0%, p=0.03).

Conclusions

Dyslipidaemia in JDM patients was characterised by increased levels of TG and low levels of HDL. Disease activity and cyclosporine use were the mainly factors associated to these abnormalities.

Keywords

dyslipidaemia, juvenile dermatomyositis, children, autoantibody, cyclosporine, disease activity.

Katia T. Kozu, MD
Clovis A. Silva, MD, PhD
Eloisa Bonfa, MD, PhD
Adriana M. Sallum, MD, PhD
Rosa M.R. Pereira, MD, PhD
Vilma S. Viana, MD, PhD
*Eduardo Borba, MD, PhD**
*Lucia M. Campos, MD, PhD**

**These authors contributed equally to this study.*

Please address correspondence and reprint requests to:
Lucia M. de Arruda Campos, MD, PhD, Rua Tucuman 177, apto 181B, São Paulo, 01455-010 Brazil.
E-mail: lucia@arrudacampos.com

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Introduction

Dyslipidaemia has been infrequently investigated in paediatric populations with autoimmune rheumatic diseases. However, lipid abnormalities in these diseases may occur due to multiple risk factors such as body composition, chronic inflammation, autoantibodies, lipodystrophy, sedentarism and therapy, especially glucocorticoids (1).

In juvenile systemic lupus erythematosus (JSLE), dyslipidaemia is mainly caused by disease activity and corticosteroid use (2-5). Disease activity induces an increase in tryglicerides (TG) and also a decrease in high density lipoprotein (HDL) levels, regardless of therapeutic (4). Corticosteroid use promotes an increase in total cholesterol (TC) and low density lipoprotein (LDL) cholesterol (1, 2). On the other hand, the beneficial effect of antimalarials had been demonstrated, with an increase of HDL levels, apart from corticosteroid use (6). In juvenile idiopathic arthritis (JIA) the lipid profile has been seldom published (7, 8).

Juvenile dermatomyositis (JDM) is a multisystem disease of unknown etiology characterised by non-suppurative inflammation of striated muscles and skin (9, 10). However, disturbances in lipoprotein metabolism have rarely been described in JDM patients, and most of the studies lack a control group (11-13) or have an incomplete assessment (14). To our knowledge, a systematic study of dyslipidaemia in JDM patients, including a concomitant evaluation of JDM scores, laboratory exams, myositis-specific and myositis-associated antibodies, anti-lipoprotein lipase antibody (anti-LPL) and treatment, has not been performed.

Therefore, the aim of this study was to perform a global assessment of lipid profile in JDM patients and healthy controls, and to evaluate demographic and anthropometric data, laboratorial exams, autoantibodies, disease scores and treatment in JDM patients with and without dyslipidaemia.

Patients and methods

JDM patients and controls

From September 2009 to January 2011, 33 JDM patients were regularly followed at the Paediatric Rheumatology Unit of our University Hospital. All of them fulfilled Bohan and Peter criteria for JDM diagnosis that was the main inclusion criteria (15). Exclusion criteria were: diabetes mellitus (fasting glycaemia higher than 126 mg/dL), renal insufficiency (creatinine clearance <70 ml/min/1.73m^2), proteinuria greater than 0.3g/24hours, liver and thyroid dysfunction, neoplasia, infection in last 15 days, hospitalisation in the last month, previous/current smoking and alcohol use, pregnancy, hormonal therapy, and use of hypolipidemic, anticonvulsant and antihypertensive (thiazide diuretics or betablockers) drugs.

Twenty-five consecutive JDM patients were selected for this study since seven had an incomplete evaluation and one was using hormonal contraceptive. The age-matched control group included 25 healthy children and adolescents recruited from the families of the JDM patients (either cousins or siblings) in order to minimise the differences in some of the risk factors such as nutrition, constitutional and genetic factors. This study was approved by the Local Ethics Committee (protocol 0580/09, date of approval 1st/July/2009) and an age-appropriate written informed consent was obtained from all participants and their legal guardians.

Methods

1. Demographic, anthropometric data and body composition

Current age and gender were recorded for all subjects. For JDM patients, age at disease onset, disease duration from first symptoms to time of study and disease duration from first symptoms to time of first therapy were also studied. Anthropometric data included blood pressure, weight in kilogrammes, height in meters, and body mass index (BMI) defined by the formula weight/height^2 (kg/m^2). For measurement of body composition, fat and lean mass and percentual fat were evaluated by dual-energy x-ray absorptiometry (DXA) using the densitometer Hologic QDR 4500 with a paediatric software. A questionnaire of life style/life habits was applied to assess information, such as previous breastfeeding, physical activity per week, smoking

habit, alcohol use, and familial history of coronary disease, hyperlipidemia and autoimmune diseases.

2. Clinical evaluation and treatment

All JDM patients were evaluated by the same paediatric rheumatologist in order to evaluate the following disease scores: Disease Activity Score (DAS) (16), Childhood Myositis Assessment Scale (CMAS) (17), Manual Muscle Testing (MMT) (17), Myositis Disease Activity Assessment Analogue Scale (MYOACT) (18) and Myositis Intention To Treat Activity Index (MYTAX) (18). The records of JDM patients were reviewed to assess the JDM treatment at the time of the study (current and cumulative doses of each drug).

Laboratorial analysis

Biochemical analyses were performed for JDM patients and controls on serum samples obtained after 12-hour overnight fast at study entry.

1. Inflammatory profile and muscle enzymes

Erythrocyte sedimentation rate (ESR) was evaluated using the Westergren method and C-reactive protein (CRP) by nephelometry. Skeletal muscle enzymes included creatine kinase (CK) and aldolase measured by kinetic automated method, and lactate dehydrogenase (LDH), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) by kinetic method. The normal range of laboratory parameters were: ESR<20mm/1st hour, CRP<5mg/L, CK 26-192U/L, aldolase<7.6U/L, LDH 141-237U/L, AST 5-36U/L, and ALT 24-44U/L.

2. Lipid profile

TC and TG were measured enzymatically on a Technicom RA 1000System analyser (Boehringer Mannheim, Argentina and Merck, Alemanha) (19, 20). HDL cholesterol was obtained after precipitation of very low-density lipoprotein (VLDL) cholesterol and LDL cholesterol by phosphotungstic acid and magnesium chloride (21) and serum levels were determined by colorimetric method (Roche Diagnostics). Levels of VLDL were estimated using the formula of triglyceride levels divided by 5 (TG/5), since all samples had a triglyceride level <400mg/dL (22), and LDL cholesterol levels were estimated using the following equation: TC – (HDL+VLDL) (22). Normal values according to national norms for metabolic data for children and adolescents were defined as: TC≤200mg/dL, HDL≥35mg/dL, LDL≤130mg/dL and TG≤150mg/dL (23). Dyslipidaemia was defined when patients and controls presented at least one of these lipid abnormalities.

3. Glycaemic profile

Fluorimetric test was used to determine the fasting insulin rate (normal values <25μU/ml) and the kinetic UV hexokinase Dimenson RxL (DADE) (Behring) to determine the fasting glycaemia (normal range 70-99mg/dl). The relation glucose/insulin was also determined by the division of fasting glycemia and fasting insulin values, and it was considered normal values <7. The homeostasis model assessment-insulin resistance (HOMA -IR) score was calculated by the formula: fasting insulin (μU/ml) x fasting glycaemia (mmol/L) divided by 22.5 (normal values <3.4).

4. Metabolic syndrome definition

Presence of three out of the four following criteria: obesity (BMI >95th percentile for age and gender), abnormal glycaemic profile, hypertension (systolic blood pressure >95th percentile for age and gender) and dyslipidaemia (TG levels >150mg/dL; HDL <35 mg/dL; TC >200 mg/dL) (11).

5. Anti-lipoprotein lipase (LPL) antibodies

Anti-LPL reactivity of IgG isotype was measured in double-enzyme-linked immunosorbent assay (ELISA). Costar polystyrene plates coated overnight with commercially available LPL from bovine milk (5μg/ml; Sigma, St Louis, MO) and then blocked with 15% adult bovine serum in Tris buffered saline (ABS-T) for one hour at room temperature. The test was performed with serum samples diluted 1:100 in ABS-T incubated for one hour at room temperature. Anti-LPL IgG isotype antibodies were determined with alkaline phosphatase-conjugated goat anti-human IgG (Sigma). The reaction was developed with p-nitrophenylphosphate and optical density (OD) was read at 405 nm with a labsystems Multiskan MS (Labsystems, Helsinki, Finland). Positive results were defined as OD values ≥3 standard deviation (SD) above the mean OD values of the 25 healthy control serum samples included in each assay (cut-off value 0.36). To ensure consistency between assays, serial dilutions of known positive serum samples were included in each study (24).

6. Myositis-specific and myositis-associated antibodies

Anti-Jo1, anti-Mi2, anti-PL-7, anti-PL-12, anti-Ku and anti-PM-Scl were measured using a commercial available line blot immunoassay (EUROLINE Myositis profile, EUROIMMUN AG, Lüebeck, Germany). Serum testing (1:10 diluted) was performed according manufacturer's protocol and results were kindly scanned and evaluated with the computer programme EUROLineScan by EUROIMMUN AG.

7. Other autoantibodies

Anti-Sm, anti-Ro, anti-La and anti-U1 RNP autoantibodies were tested using ELISA (Inova Diagnostics, Inc., CA, USA, cut-off value >20U). Anti-double-stranded DNA antibodies (anti-dsDNA) were tested by indirect immunefluorescence in *Crithidia Luciliae* (kit EUROIMMUNE Medizinische Labordiagnostika AG, Lübeck, Germany, cut-off value >1/10).

Statistical analysis

Data were presented in median (range) or mean ± SD for continuous variables according to abnormal or normal distribution, respectively. Data were presented in number (percentages) for categorical variables. For continuous variables data were compared using Mann-Whitney test to evaluate differences between JDM patients and controls, and patients with and without dyslipidaemia according to demographic, anthropometric and laboratorial parameters. For categorical variables, differences were assessed by Fisher exact test. In JDM patients Pearson's correlation coefficient was used to identify the variables correlated to dyslipidaemia. *p*-values less than 0.05 were considered significant.

Results

JDM vs. controls

Demographic, anthropometrical, body

Table I. Demographic, anthropometric, body composition and laboratorial data in juvenile dermatomyositis (JDM) patients and controls.

Variables	JDM Patients n=25	Controls n=25	*p*-value
Demographic data			
Current age, months	138 ± 45	134 ± 31	0.703
Gender, female	14 (56)	13 (52)	0.500
Anthropometric data			
BMI, kg/m^2	19.1 (12.7-30)	17.1 (14.4-27.5)	0.503
Systolic pressure, mmHg	90 (80-118)	90 (80-110)	0.099
Diastolic pressure, mmHg	60 (50-85)	60 (45-70)	0.211
Body composition			
Percentage fat	27.5 (10.9-45.4)	22.5 (10.2-42.3)	0.230
Fat mass, kg	10.7 (2.9-27.1)	6.7 (2.8-30.5)	0.274
Lean mass, kg	24.8 ± 6.4	25.4 ± 7.6	0.599
Lipid profile			
Dyslipidaemia	9 (36)	4 (16)	0.196
Total cholesterol, mg/dL	151 (102-227)	151 (121-207)	0.941
>200mg/dL	3 (12)	1 (4)	0.600
HDL, mg/dL	44 (0-72)	50 (30-65)	0.117
<35 mg/dL	7 (28)	1 (4)	0.040
LDL, mg/dL	87 (56-148)	91 (54-140)	0.675
>130 mg/dL	1 (4)	2 (8)	1.000
VLDL, mg/dL	16 (6-68)	13 (4-36)	0.020
Tyigliceride, mg/dL	80 (31-340)	61 (19-182)	0.011
>150 mg/dL	4 (16)	1 (4)	0.340
Glycaemic profile			
Fasting glycaemia, mg/dL	80 (63-95)	86 (76-102)	0.009
Fasting insulinaemia, µU/ml	8 (3-45)	3.9 (2-63)	0.010
Glucose/insulin rate	8.8 (1.5-32)	19.7 (1.6-39)	0.004
HOMA-IR	1.31 (0.22-8.6)	0.78 (0.35-14.2)	0.062
Metabolic syndrome	2 (8)	0	1.000
Positive anti-LPL antibody	1 (4)	0	1.000

Values expressed in mean ± SD, median (range) and n (%); BMI (body mass index), HDL (high density lipoprotein), LDL (low density lipoprotein, VLDL (very low density lipoprotein), HOMA-IR (homeostasis model assessment insulin resistance), anti-LPL (anti-lipoprotein lipase).

composition and laboratorial data in JDM patients and controls are shown in Table I. No significant differences were detected regarding current mean age and frequency of female gender between groups ($p>0.05$). The median BMI, lean and fat mass, percentual fat, systolic and diastolic blood pressures were also alike in both groups (Table I). No differences were observed regarding lifestyle/life habits either. Family history of autoimmune diseases was not found in these JDM patients and controls. The presence of familial hyperlipidemia was observed in one (4%) JDM patient and none of controls.

JDM patients demonstrated significant higher levels of VLDL and TG compared to controls [16 (6–68) *vs*. 13 (4–36) mg/dL, $p=0.02$; and 80 (31–340) *vs*. 61 (19–182) mg/dL, $p=0.011$ respectively]. The apparent lower HDL levels observed in JDM did not reach statistical significance [44 (0–72) *vs*. 50 (30–65) mg/dL, $p=0.117$) but this group demonstrated a higher frequency of low HDL levels (28% *vs*. 4%, $p=0.04$). Abnormal lipid profile was detected in 9 JDM patients and 4 controls (36% *vs*. 16%, $p=0.196$). In JDM, dyslipidaemia were characterised by low HDL levels in seven patients (28%), high TG in four (16%), high TC in three (12%), and high LDL in one (4%) (Table I).

JDM patients presented significantly higher levels of fasting insulin [8 (3–45) *vs*. 3.9 (2–63) µU/ml, $p=0.01$], and lower levels of fasting glycaemia [80 (63-95) *vs*. 86 (76–102) mg/dL, $p=0.009$] and glucose/insulin rate [8.8 (1.5–32) *vs*. 19.7 (1.6–39), $p=0.004$] compared to controls. None of JDM patients or controls fulfilled diabetes mellitus criteria (Table I).

JDM patients with and without dyslipidaemia

Demographic, anthropometric, body composition, laboratorial and disease scores in JDM patients with and without dyslipidaemia are shown in Table II. No significant differences were observed between JDM patients with dyslipidaemia compared to those without this lipid abnormality according to demographic data, except for a shorter period of disease duration from 1st symptoms to time of first therapy in the JDM patients with *versus* without dyslipidaemia [1 (0-6) *vs*. 4 (0-12) months, $p=0.045$]. No differences were found between the groups regarding anthropometric data and body composition (Table II), neither lifestyle/life habits.

JDM patients with dyslipidaemia demonstrated significant lower median of HDL levels compared to those without this condition [29 (0–49) *vs*. 50 (39–72) mg/dL, $p=0.0005$] and also had significant higher VLDL [34 (6–68) *vs*. 14 (9–28) mg/dL, $p=0.011$] and TG levels [128 (31–340) *vs*. 69 (46–138) mg/dL, $p=0.011$] (Table II). JDM with dyslipidaemia demonstrated a higher frequency of low HDL levels (77% *vs*. 0%, $p=0.0001$), and also a higher frequency of increased levels of TG (44% *vs*. 0%, $p=0.01$), and TC (33% *vs*. 0%, $p=0.03$) (Table II).

JDM patients with and without dyslipidaemia had comparable levels of fasting insulin, fasting glycaemia and glucose/insulin rate (Table II). Lipodystrophy, metabolic syndrome and anti-LPL antibodies were only detected in patients with abnormal lipid profile (increase LDL in one, low HDL in two, and high TC and TG in one, respectively), although no differences were observed when compared to patients without dyslipidaemia. Myositis-specific and myositis-associated antibodies were negative in all JDM patients, except by anti-Ku antibody, but its frequency was alike between both groups ($p=1.0$) (Table II). Only one JDM patient had moderate titers for anti-U1 RNP antibodies (54 U) and all other autoantibodies (anti-Sm, anti-Ro, anti-La and anti-dsDNA antibodies) were also negative in patients and controls.

JDM with dyslipidaemia had significantly higher levels of ESR [26 (20–50) *vs*. 14.5 (2–54) mm/1st hour, *p*=0.006], CRP [2.1 (0.5-26) *vs*. 0.4 (0.1–8.1) mg/dL, *p*=0.01] and AST [32 (24–82) *vs*. 24.5 (13–122) U/L, *p*=0.044] compared to those without dyslipidaemia. Moreover, the median of CMAS [47 (17–52) *vs*. 52 (47–52), *p*=0.024] and MMT [78 (38–80) *vs*. 80, *p*=0.001] were significantly lower in JDM patients with dyslipidaemia *versus* without. In contrast, the median of DAS, MYOACT and MYTAX scores were significantly higher in the former group [6 (0–18) *vs*. 2 (0–8), *p*=0.008; 0.13 (0–0.3) *vs*. 0.01(0–0.08), *p*=0.012; 0.06 (0–0.28) *vs*. 0 (0–0.16), *p*=0.018; respectively] (Table II). Muscle DAS was significantly higher in JDM with *versus* without dyslipidaemia [3 (0-9) *vs*. 1 (0–5), *p*=0.044].

Positive significant correlations were detected between TG levels and CRP (r=0.697, *p*=0.001), DAS (r=0.610, *p*=0.001), MYOACT (r=0.661, *p*=0.001) and MYTAX (r=0.511, *p*=0.008). Negative correlations were seen between TG and CMAS (r=-0.506, *p*=0.009) and MMT (r=-0.535, *p*=0.005). Furthermore, positive correlations were found between LDL and MYOACT (r=0.534, *p*=0.006) and LDL and DAS (r=0.425, *p*=0.034), and negative correlation between LDL and CMAS (r=-0.480, *p*=0.024) (Table III).

The frequency of current cyclosporine use was significantly higher in JDM patients with dyslipidaemia compared to those without this alteration (33% *vs*. 0%, *p*=0.03). No differences were observed in the frequency of current use, current dose and cumulative dose of prednisone, methotrexate and hydroxichloroquine in both groups (Table IV).

Discussion

Our study clearly demonstrated that active JDM patients under cyclosporine therapy had dyslipidaemia characterised by low HDL and high TG levels. The anti-LPL antibodies seem not to contribute to the dyslipidaemia in this idio-pathic inflammatory myopathy.

The advantage of the present study was to perform a global evaluation of metabolic profile, including insulin resist-

Table II. Demographic, anthropometric, body composition and laboratorial data and disease scores in juvenile dermatomyositis (JDM) patients with and without dyslipidaemia.

Variables	JDM with dyslipidaemia n=9	JDM without dyslipidaemia n=16	*p*-value
Demographic data			
Current age, months	132 (66-200)	135 (86-221)	0.755
Age at onset, months	60 (24-120)	64 (31-132)	0.834
Disease duration from 1st symptoms to time of study, months	39 (6-138)	60 (23-134)	0.386
Disease duration from 1st symptoms to time of first therapy, months	1 (0-6)	4 (0-12)	0.045
Gender, female	5 (55)	9 (56)	1.000
Anthropometric data			
BMI, kg/m^2	20.4 (16.7-28.3)	18.3 (12.7-30)	0.315
Body composition			
Percentage fat	26.9 (10.9-42)	26.7 (11-45)	0.668
Fat mass, kg	9.6 (2.9-27.1)	9.8 (3.4-27.1)	0.834
Lean mass, kg	26.7 (20-35)	25.8 (15.4-44.5)	0.540
Lipid profile			
Total cholesterol, mg/dL	179 (102-227)	144 (115-189)	0.308
>200mg/dL	3 (33)	0	0.030
HDL, mg/dL	29 (0-49)	50 (39-72)	0.0005
<35 mg/dL	7 (77)	0	0.0001
LDL, mg/dL	110 (70-148)	81 (56-123)	0.089
>130 mg/dL	1 (11)	0	0.360
VLDL, mg/dL	34 (6-68)	14 (9-28)	0.011
Trygliceride, mg/dL	128 (31-340)	69 (46-138)	0.011
>150 mg/dL	4 (44)	0	0.010
Glycaemic profile			
Fasting glycaemia, mg/dL	80 (70-86)	80.5 (63-95)	0.392
Fasting insulinaemia, µU/ml	10.4 (2.5-69)	7.2 (2.8-19.4)	0.119
Glucose/insulin rate	7.4 (1.4-28)	12.3 (4-32)	0.084
HOMA-IR	1.3 (0.22-8.6)	1.29 (0.5-3.4)	0.865
Lipodystrophy	1 (11)	0	1.000
Metabolic syndrome	2 (22)	0	0.090
Anti-LPL antibody	1 (11)	0	0.750
Anti-Ku antibody	1 (11)	3 (19)	1.000
Muscle enzymes			
AST, U/L	32 (24-82)	24.5 (13-122)	0.044
ALT, U/L	36 (26-79)	33 (22-123)	0.495
CK, U/L	80 (38-478)	112 (33-224)	0.887
DHL, U/L	220 (162-562)	180 (107-1234)	0.155
Aldolase, U/L	5.7 (4.6-14.6)	5.8 (3.4-7.7)	0.649
Inflammatory profile			
ESR, mm/1st hour	26 (20-50)	14.5 (2-54)	0.006
CRP, mg/dL	2.1 (0.5-26)	0.4 (0.1-8.1)	0.010
JDM scores			
CMAS, 0-52	47 (17-52)	52 (47-52)	0.024
MMT, 0-80	78 (38-80)	80 (80)	0.001
DAS, 0-20	6 (0-18)	2 (0-8)	0.008
Skin DAS, 0-9	2 (0-9)	1 (0-8)	0.137
Muscle DAS, 0-11	3 (0-9)	1 (0-5)	0.044
MYOACT, 0-1	0.13 (0-0.3)	0.01 (0-0.08)	0.012
MITAX, 0-1	0.06 (0-0.28)	0 (0-0.16)	0.018

Values expressed median (range) and n (%), BMI: (body mass index); HDL: (high density lipoprotein); LDL: (low density lipoprotein; VLDL: (very low density lipoprotein); HOMA-IR: (homeostasis model assessment insulin resistance); anti-LPL: (anti-lipoprotein lipase); AST: (aspartato aminotransferase); ALT: (alanine aminotransferase; CK: (creatine kinase); LDH: (lactate dehydrogenase); ESR: (erythrocyte sedimentation rate); CRP: (C-reactive protein); CMAS: (Childhood Myositis Assessment Scale); MMT: (Manual Muscle Testing); DAS: (Disease Activity Score); MYOACT: (Myositis Disease Activity Assessment Analogue Scale); MYTAX: (Myositis Intention To Treat Activity Index).

Table III. Correlations between tryglicerides (TG) and low density lipoprotein (LDL) and juvenile dematomyositis scores.

Variables	R Spearman	*p*-value
TG x CMAS	-0.506	0.009
TG x MMT	-0.535	0.005
TG x DAS	0.610	0.001
TG x MYOACT	0.661	0.001
TG x MYTAX	0.511	0.008
LDL x CMAS	-0.480	0.024
LDL x DAS	0.425	0.034
LDL x MYOACT	0.534	0.006

CMAS: (Childhood Myositis Assessment Scale); MMT: (Manual Muscle Testing); DAS: (Disease Activity Score); MYOACT: (Myositis Disease Activity Assessment Analogue Scale); MYTAX: (Myositis Intention To Treat Activity Index).

Table IV. Treatment in patients with juvenile dermatoyositis (JDM) according to lipid profile.

Drugs	JDM patients with dyslipidaemia n=9	JDM patients without dyslipidaemia n=16	*p*-value
Prednisone			
Current use	7 (78)	6 (37)	0.090
Current dose, mg/kg/day	0.67 (0.12-1)	0.49 (0.24-0.9)	0.620
Cumulative dose, g/kg	14 (3.9-51)	16.2 (4.9-31.9)	0.970
Antimalarial			
Current use	3 (33)	5 (31)	1.000
Current dose, mg/kg/day	4.6 (4-7.2)	5 (3-5.7)	1.000
Methotrexate			
Current use	6 (67)	5 (31)	0.100
Current dose, mg/kg/week	0.84 (0.5-1)	0.41 (0.3-1)	0.400
Cumulative dose, g/kg	1.9 (0.4-16.9)	2.9 (0.3-5.8)	0.910
Cyclosporine			
Current use	3 (33)	0	0.030
Current dose, mg/kg/day	4.2 (3.6-5)	0	0.080
Cumulative dose, g/kg	17.4 (11.4-23.5)	18 (14.4-19.8)	0.700

Values expressed in median (range) and n (%).

ance indexes and life style/life habits in a population of JDM patients and matched controls. In addition, we systematically studied several JDM activity scores blinded to metabolic assessment which was performed in parallel with the determination of anti-LPL and myositis auto-antibodies.

According to its design, the present study identified abnormal HDL and TG levels which were associated with active disease. These findings are in accordance with a previous study that identified hypertriglyceridaemia and low HDL as the main lipid abnormalities in JDM (11). Although this previous study identified alterations in the lipid profile, it lack of a systematic control group (11).

The relation of these lipid abnormalities with JDM activity was previous suggested by Huemer *et al*. (13), however specific scores were not evaluated. Moreover, correlations between lipid profiles and JDM disease scores were determined in a small number of JDM patients in the study of Coyle *et al*. (11). Recently, Eimer *et al*. (25) evaluated adults with history of JDM and compared them to two matched controls. In this study, dyslipidaemia was associated with disease activity, especially using muscle DAS, as also observed herein.

The present study clearly demonstrated a positive correlation between dyslipidaemia and the degree of disease activity, as identified in most of scores usually performed in JDM. This finding is similar to that observed in JSLE, which also presented the same lipid abnormalities face to disease activity (2, 4). JDM scores are more reliable in terms of disease activity assessment than acute phase reactants or muscles enzymes. In fact, although dyslipidemic patients demonstrated increased ESR, CRP and AST values compared to patients with normal lipid profile, their medians were within normal values (26). The disease duration from first symptoms to time of first therapy was shorter in JDM patient with dyslipidaemia suggesting that chronic inflammation before treatment possibly did not contribute to future lipid abnormalities.

The presence of anti-LPL antibodies, not previously investigated in JDM, would be a possible explanation for lipoprotein abnormalities in this disease. Indeed, these antibodies were close related to disease activity and abnormal triglycerides metabolism in SLE, leading to an increase in VLDL and TG levels (24). Our study demonstrated that their presence was not associated to the dyslipidaemia identified herein. In fact, these autoantibodies seem to be rarely observed in our JDM population, even in our active disease patients. In contrast to JSLE disease, JDM is not characterised by the generation of multiple autoantibodies (27), as demonstrated by the low positivity of all myositis-specific and myositis-associated antibodies detected in the studied population.

Of note, the lipid alterations observed in the present study were not related to insulin resistance, expressed by high levels of fasting insulin and lower glucose/insulin rate that had been previously described in JDM patients (13, 14). Interestingly, this metabolic condition is a predictor for the development of lipodystrophy (13), especially in patients with long disease duration (12). In our JDM population, in spite of 32% of insulin resistance, only one patient with eight years of follow-up had lipodystrophy with increased LDL levels. Interestingly, glucose indices have been correlated with chronic inflammation measured by pro-inflammatory cytokine (IL-2 and IL-12) in JDM patients (11), but this was not observed in our JDM patients with dyslipidemia. In addition, cyclosporine was associated with dyslipidaemia in our JDM patients. Indeed, lipid abnormalities were observed after two months of cyclosporine monotherapy and it was reversible after

its discontinuation (28). The effect of this drug in lipoprotein metabolism is well-documented in kidney transplantation (29, 30). Althougth glucocorticoids are well known to induce increased insulin levels and lipoprotein abnormalities (31), these effects did not account on for our findings since similar current prednisone dose were observed in both JDM groups. In the same manner, the beneficial effect of antimalarials on lipid profile previously reported in SLE patients (6) was not observed in our study. The transversal design of the present study brought us some limitations, since at the moment of patients' evaluation most of them were inactive or presented only mild disease activity. The follow up of these patients with periods of active and inactive disease possibly enable us to demonstrate association between dyslipidaemia and insulin resistance and/or other therapeutic agents. As a preventive measurement of long term consequences of dyslipidaemia, a 12-week supervised exercise programme may benefit JDM patients, minimising chronic low-grade systemic inflammation and should be introduced as part of their treatment, as recent demonstrated by our group (32). Despite the increasing number of randomised studies evaluating the efficacy and safety of statins in children with familial hypercholesterolemia (33) and in children and adolescents with JSLE (34), any study evaluated these drugs in inflammatory myopathies.

In conclusion, dyslipidaemia in JDM was associated with active disease, suggesting that adequate disease control and individualised lipid-lowering strategies may reduce the risk of premature atherosclerosis in this idiopathic inflammatory myopathy.

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