Longitudinal assessment of disease activity and muscle strength in juvenile dermatomyositis: a multicentre registry study

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Abstract

Objective

To define disease activity measures, muscle strength and functional assessments in new-onset juvenile dermatomyositis (JDM) patients, at disease onset and follow up.

Methods

A registry was set up in 18 hospitals, enrolling patients over 3-years (2015-2018). Clinical assessments were performed at baseline, and at 6, 12, 18 and 24 months after diagnosis. Disease Activity Score (DAS20), skin and musculoskeletal DAS sub-scales; Manual Muscle Test (MMT8); Childhood Myositis Assessment Scale (CMAS); Childhood Health Assessment Questionnaire disability index (CHAQ_DI 0-3) and 10 cm Visual Analogue Scale (VAS) for overall well-being scores were compared by Poisson Model and Wald post-test for repeated measures.

Results

Ninety-six cases, being 61 (64%) females, median age 10 years had JDM diagnosis and 12 (13%) onset calcinosis. Mean ±SD scores at diagnosis and 6 months intervals for DAS20 (0-20) were 7.8±5, 6.3 ±4.8, 5±4, 4.9 ±5 and 0.5 ±2.3; with significant difference from baseline ($p<0.01$). Skin DAS subscales were 2.8±3.3, 1.8±2.9, 1,1±2.2, 0.6±1.8, 0.4±1.5. MMT (0-80) 62.6±20.4, 70.2±13.5, 73.3±11, 75.7±7.9 and 74.8±7.8, with significant difference from baseline up to 6 months ($p=0.016$); CMAS (0-53) 29.5±11.4, 33.1±8.3, 34.2±5.8, 34±6 and 33.3±5.4. CHAQ-DI (0-3) 1±0.9, 0.6±0.7, 0.8±0.8, 1±0.8 and 1±0.3; parents VAS 4.1±2.5, 2±2.1; 1.3±2.8, 4.1±3.1, 1.7±2.2. There was no significant difference for CMAS, CHAQ-DI and parents VAS from baseline up to 24-month assessment.

Conclusion

DAS20 scores improved gradually during follow up, MMT8 improved significantly during the first 6 months and CMAS, CHAQ-DI and parents VAS scores had no significant improvement with persistent functional impairment over 2-years.

Key words

disability, juvenile dermatomyositis, muscle strength, myositis

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Introduction

Juvenile dermatomyositis (JDM) is a rare chronic autoimmune disease with heterogeneous clinical features. It affects skin and muscles, with variable presentation of skin rash and muscle weakness. Symmetric proximal muscle weakness in limb girdles and neck flexors is often progressive, with a variable degree of severity, both at onset and during disease course, with fatigue, myalgia, abnormal gait, swallowing dysfunction and limitation for physical functions and daily living activities (1). Early treatment is needed, although some patients remain in active state, even when treated early with high dose prednisolone associated with methotrexate, as first line recommended treatment (2). Disease activity monitoring by quantitative tools has been recommended (3).

We have previously started a multicentre registry, with a retrospective review of cases on follow up, in 7 Paediatric Rheumatology centres (4); it has been extended to the whole country with 18 centres, enrolling new onset JDM cases and collecting prospective data.

The myositis core set of outcome measures was developed for adult and paediatric patients (5, 6) and those measures have been used in clinical trials (2, 7) for defining response to treatment; as well as in research registries and clinical practice, according to experts' recommendation guidelines (3). Therefore, we prospectively explored the global disease activity measures and muscle strength testing and function with quantitative tools, in JDM patients from a national registry.

Methods

A survey of cases with less than 18 years of age, seen within the first 6 months of the diagnosis, was filled out by participating physicians, with demographic and clinical variables at diagnosis, and during follow up at 6, 12, 18 and 24 months after diagnosis. Twenty Paediatric Rheumatology centres agreed to participate and 18 of them enrolled patients. Data capture was carried out in electronic forms. Data storage and analysis were carried out in a single centre. Ethics Committees of all participating centres approved the study protocol, after the approval of the coordinating centre under the number 639104 (2014). Signed informed consent and assent forms were obtained for all patients, parents or legal guardians, prior to performing any study activity.

Disease Activity Score (DAS20) (8); Manual Muscle Strength for 8 muscle groups (MMT8) (9); the Childhood Myositis Assessment Score (CMAS) (10) version with 0-53 possible scores (11) were completed by assistant physicians in each one of the participating centres. Further descriptive analysis of the DAS 20 subscales for cutaneous manifestations, rash and vasculopathy, the Skin-DAS (0-11) and the musculoskeletal subscale MSK-DAS (0-9) was carried out (12).

The Childhood Health Assessment Questionnaire Disability Index (CHAQ-DI 0-3) and its associated scale for overall well-being reported by parents, in a 0-10 cm Visual Analogue Scale (VAS) were filled out by parents (13-15).

All the tools' scoring training was provided for all participants with handouts on how the tests were performed. Investigations included: serum muscle enzymes, full-blood count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), renal function, magnetic resonance imaging (MRI), electromyogram (EMG), muscle biopsy, soft tissue calcinosis imaging, and autoantibodies; all indicated according to availability during each assessment. Medications were prescribed according to physicians' decision with international recommendation guidelines (3), and medication use recorded at the time of baseline enrolment and during follow up, being reported as cumulative use from diagnosis up to the latest appointment.

DAS20 is a composite score of 20 items of global disease activity including: skin signs, vasculopathy signs and muscle strength testing that is completed by the physician. Manual Muscle Test (MMT8) is a valid measure of muscle strength, that captures moderate to severe muscle weakness. The version of 0–10 scale in 8 muscle groups (MMT8) with possible scores of 0-80 was used. It was performed by the patients under command with opposed resistance of a

trained observer, asking for movements against gravity and resistance. It has limited validity for patients younger than 5 years old (9).

The Childhood Myositis Assessment Scale (CMAS) was developed for quantitative measuring of muscle strength and endurance of myositis patients older than 4 years of age. It is a patient-friendly exercise testing, comprising 14 domains and manoeuvres, testing proximal muscle strength, endurance and functional performance guided by a trained observer. The CMAS domains are: 1- head elevation/neck flexors; 2- leg raise (touch object); 3- straight leg lift duration; 4- move from supine to prone; 5- sit ups; 6- move from supine to sit; 7- arm raise /straight; 8- arm raise duration; 9- floor sit; 10- floor rise; 11- chair sit; 12- chair rise; 13- stool step and 14- pick up. All the items are ordinal variables ranked by standardised performance. The developers' video-guided instructions testing patients with variable degree of muscle weakness were provided for training. There are different published versions of CMAS with maximum possible scores of 51, 52 and 53; we used the 53-scored version (11).

The Childhood Health Assessment Questionnaire is a 30-items 0-3 scale in 8 domains of daily living activities and capacity, that is reported by parents grading difficulty for performing the task, due to the disease. It is accompanied by a Visual Analog Scale of overall well-being and another for pain. It was developed for arthritis functional assessment (13). CHAQ-DI and parents' perception of overall well-being has been recently recommended in composite measures for defining JDM improvement concepts (14). The cross-cultural adapted version was applied and self-reported by parents, independently of age (15).

The JDM registry working group was established in 2014. After the feasibility survey and protocol training, multicentric ethics approval in all the centres, the enrolment started in 2015 and closed in 2017. A follow up protocol was applied over 2-years and the period of data capture was from 2015-2020. Interim analysis checking for data consistency and counting missing values was conducted, after the last enrolled patient performed the last appointment. Only valid data was used for analysis.

Demographic and clinical variables were reported by frequency of valid reports. DAS20, MMT8, CMAS, CHAQ-DI and VAS scores at diagnosis, as well as 6, 12, 18 and 24 months follow up were reported by descriptive statistics. They are presented in a descriptive table with mean and standard deviation (mean ±SD), median, minimum and maximum values. The longitudinal scores were compared by Poisson model and Wald test for repeated measures, with significance set at 5% or $p<0.05$.

Table I. Demographic of 96 new onset JDM patients from 18 registry centres.

Age (years) at diagnosis: median (mean±SD), (min-max)	10; (10.8±4.2); (4-18)
Gender: female: male (n) (%)	61 (63.5%): 35 (36.5%)
Time from the first symptom up to diagnosis (months) median, (mean±SD), (min-max)	3; (4 ±4); 0-12
Frequency of cases by geographic region n (%)	
North	8 (8.3%)
no. of hospitals	1
Northeast	22 (22.9%)
no. of hospitals	4
Southeast	50 (52.1%)
no. of hospitals	9
South	8 (8.3%)
no. of hospitals	2
Central-West	8 (8.3%)
no. of hospitals	2

Results

The survey was based on clinical presentation at JDM onset. Diagnoses were established in 96 cases from 18 referral hospitals, 60 towns (zip code), in five different geographic regions of the country, North (1 hospital), Northeast (4 hospitals), Southeast (9 hospitals), South (2 hospitals) and Central West (2 hospitals). The current country population is 211 million people, being 54.5 million under 18 years living in a geographic area of 8.5 million km^2 extension, in a tropical and subtropical environment and a gradient of sun exposure from moderate to high. This is a representative sample from different environment and resources in public hospitals with the same health care insurance. Demographic data is presented on Table I. Of 96 enrolled cases, 61 (63.5%) were females, 35 (36.5%) males, with median age 10 years, mean ±SD 10.8±4.2, range from 4-18 years and only 5 patients were under 5-years of age. Mean disease duration from the first symptoms to diagnosis (mean ±SD) 4±4; median 3 months, range 0.5 -12 months. Cases were identified by experts in referral hospitals from the public hospital's network within the National Health System (SUS) as complex care centres in Paediatric Rheumatology clinics (16). Treatment decision was under attending physician discretion in each of the centres, and availability of exams and medication was variable among the centres.

A variable number of records of signs, symptoms and tests for each patient, during each of the appointments for the longitudinal assessment, was systematically analysed. Physicians' diagnoses were based on signs of proximal muscle weakness, typical skin rash, elevated muscle enzymes, myopathic EMG, abnormal MRI and muscle biopsy. Overall, ascertainment diagnoses were based on the variables deemed important by participants to select and enrol. The main signs and symptoms frequency reported are described on Table II. Muscle weakness was present in 88 of 90 reports (98%), typical skin rash in 82 of 90 reports (97%). Interestingly, onset facial oedema was observed in 47%, body oedema in 27%, and calcinosis in 13% of the reports. These are considered signs and predictors of more severe disease course. Only 20% of the cases underwent muscle biopsy for diagnosis work up. Classification by Bohan and Peter criteria (17) resulted in 61.8% of the cases with equal or more 4 criteria, 34.8% with 3, and 3.4% with only 2 of the criteria (Table II).

Table II. Frequency of reported clinical features for the diagnosis work up in new onset JDM patients.

Variable	no. of reports	Frequency n (%)	Feature description
Typical skin rash	92	89 (97%)	Rash, heliotrope, nailfold erythema
Gottron sign	92	86 (93%)	
Skin ulceration	92	28 (30%)	
Facial oedema	92	43 (47%)	
Body oedema	90	24 (27%)	
Calcinosis	91	12 (13%)	Superficial (10), deep (3), nodular (4), widespread (1)
Proximal muscle weakness	90	88 (98%)	
Arthritis	92	34 (37%)	
Dyspnoea	92	18 (20%)	
Dysphagia	92	37 (40%)	
Nasal speech	92	25 (27%)	
Constitutional signs and symptoms			
Weight loss	91	34 (37%)	
Myalgia	90	78 (87%)	
Fatigue	91	80 (88%)	
Fever	92	47 (51%)	
Alopecia	92	29 (32%)	
Headaches	88	15 (16%)	
Irritability	92	39 (41%)	
Arthralgia	90	55 (61%)	
Stiffness	91	34 (37%)	
Chest pain	89	5 (6%)	
Abdominal pain	91	22 (24%)	
Diarrhoea	92	5 (5%)	
Haematuria	92	3 (3%)	
Muscle wasting	90	24 (27%)	
Other	83	23 (28%)	Paraesthesia, myocarditis, vasculitis, livedo reticularis, joint contractures cracked lips, Raynaud's phenomenon
Diagnosis			
Muscle biopsy	96	19 (20%)	
Skin biopsy	96	18 (20%)	
Bohan & Peter (n of criteria)	96		
5		18 (20.2%)	
4		37 (41.6%)	
3		31 (34.8%)	
2		3 (3.4%)	

Elevated muscle enzymes were considered if at least one of the tested enzymes were above the upper limit of reference values, and for diagnosis purpose recorded as normal or abnormal. The results were normalised to the same units for all the centres before analysis. Elevated CK was found in 60 of 88 reports (68%), LDH in 65 of 81 (80%), AST in 68 of 88 (77%), ALT in 50 of 85 (59%) and aldolase in 46 of 56 (82%). Descriptive reference values of serum muscle enzymes are presented on Table III.

The immunologic biomarkers, such as ANA and other non-specific autoantibodies were reported. Positive ANA with titres higher than 1:80 were found in 43 (56%) of 77 tested. Other autoantibodies were detected in 22 (67%) of 33 tested. Overall, the autoantibodies found were anti-Sm, anti-ENA-RNP. anti-Ro, anti-La, Coombs test, anti-Jo1, Mi2 and anticardiolipin. Myositis-specific autoantibodies were only sporadically reported, with anti-synthetase being the only reported test (Table III).

MRI and muscle ultrasound were performed in 28% and 8.3% of the cases with reports of muscle and subcutaneous oedema in 81% and 87%, respectively. Swallow imaging and gastrointestinal motility imaging tests were performed in 32.2% of the cases, of those 35% had reports of either nasopharyngeal reflux, gastrointestinal dysmotility or tracheoesophageal aspiration.

Cumulative drug treatment and physical therapy received by JDM patients during follow up are shown on Table IV, and the majority received first line high dose prednisolone or prednisone associated with methotrexate and intravenous immunoglobulin (IVIG). Rehabilitation with physical therapy, either dry-land or hydrotherapy, were reported in only 29% and 16%, respectively.

Disease activity status scored by DAS20 mean ± SD at diagnosis were 7.8±5, 6m 6.3±4.8, 12m 5±4, 18m 4.9±5 and 24m 0.5±2.3; all had a significant difference from diagnosis up to 24 months ($p<0.01$). There was a wide scoring variation and a significant improvement over the 2-years follow up. Values were compared by Poisson model and the significant difference for all the visits compared to baseline ($p<0.01$) was indicated by Wald post-test analysis (Table V). Descriptive values for the DAS-20 subscales were in keeping with the global Disease Activity Score (DAS20). The Skin DAS subscales (0-11) from the baseline up to 2-years mean (SD) were 2.8±3.3, 1.8±2.9, 1.1±2.2, 0.6±1.8 and 0.4±1.5, respectively at diagnosis, 6, 12, 18 and 24 months. Like the Skin-DAS subscale, the MSK-DAS (0-9) mean±SD scores were 1.6±2.6, 0.8±1.8, 0.4±1.3, 0.2±0.8 and 0.2±0.9 respectively at diagnosis, 6, 12, 18 and 24 months.

MMT (0-80 possible range) mean ± SD scores at diagnosis were 62.6±20.4, 6m 70.2±13.5, 12m 73.3±11, 18m 75.7±7.9 and 24m 74.8±7.8. There was a significant difference from the time of diagnosis up to 6 months follow up ($p=0.016$). CMAS scores (0-53 possible range) mean ±SD were low at diagnosis 29.5±11.4, and the values after 6m 33.1±8.3, 12m 34.2±5.8, 18m 34±6 and 24m 33.3±5.4 had only mild improvement with no significant difference from the baseline up to the last visit, and the persistent low values indicated persistent muscle weakness ($p=0.06$) (Table V).

The CHAQ- DI scores (0-3 possible range) mean ± SD at diagnosis were 1±0.9, after 6m 0.6±0.7, 12m 0.8±0.8, 18m 0.2±0.8 and 24m 0.2±0.9 and there was no significant difference from the baseline up to the last visit.

Table III. Frequency of investigations for diagnosis in new onset JDM patients.

Variable (normal range)	no. of tests	Mean ± SD	Median (min-max)	Descriptive
CK (55-170 U/L)	88	1,835 ± 3,821	237 (6 -17,842)	
LDH (120-246 U/L)	81	933 ± 798	693 (2-5,394)	
AST (17-59 U/L)	88	204 ± 622	67 (1- 5,694)	
ALT (<50 U/L)	85	118 ± 208	48 (2-1472)	
GGT(15-73 U/L)	63	57 ± 107	23 (0-575)	
Aldolase (1.2-8.8 IU/ml)	58	18 ± 26	14 (0,2-147)	
CRP (<1 mg/dL)	72	5 ± 8.3	3 (0-55)	
ESR (mm/h)	85	32 ± 24	25 (1-120)	
Hb (mg/dL)	90	12 ± 1.3	12 (9-15)	
WBC (4,350-13,650/mm^3)	89	8,297 ± 4,151	7,422 (3,200-27,000)	
C3 (88-165 mg/dL)	48	108 ± 35	112 (13-177)	
C4 (14-44 mg/dL)	49	26 ± 19	29 (0-121)	
	no. of tests	Frequency		
Positive RF	67	1 (1.5%)		
Positive ANA (>1:80 titre)	77	43 (56%)		
Positive autoantibodies	33	22 (67%)		Sm, ENA-RNP, Ro, La, Coombs, Jo1, Mi2, anticardiolipin
Echocardiogram	42	8 (19%)		Pericardial effusion, valvar reflux, pulmonary hypertension
MRI	27	22 (81 %)		Muscle and subcutaneous oedema
Muscle ultrasound	8	7 (87%)		
CT scan	17	2 (11.2%)		
Swallowing image	31	11 (35%)		Nasopharyngeal reflux, GI motility dysfunction, tracheoesophageal aspiration

CK: creatin phosphokinase; LDH: lactic dehydrogenase; AST: aspartate aminotransferase; ALT: alanine aminotransferase; CRP: protein C-reactive; ESR: erythrocyte sedimentation rate; Hb: haemoglobin; WBC: white blood cell count; C3: complement factor 3; C4: complement factor 4; RF: rheumatoid factor; ANA: antinuclear antibodies; MRI: magnetic resonance imaging; CT: computerised tomography.

Table IV. Treatment received by JDM patients at diagnosis and during follow up.

Treatment	no. of records	no. of patients treated (%)
Methylprednisolone pulse	90	46 (51%)
High dose oral prednisone	90	81 (90%)
Methotrexate (oral or subcutaneous)	90	72 (80%)
Cyclosporine A	91	3 (3%)
Azathioprine	90	3 (3%)
Cyclophosphamide	90	4 (4%)
Intravenous immunoglobulin	91	15 (16%)
Hydroxychloroquine	91	40 (44%)
Plasmapheresis	90	1 (1%)
Rituximab	90	1 (1%)
Bisphosphonates	90	6 (7%)
Ibuprofen	89	9 (10%)
Naproxen	90	2 (2%)
Folic acid	90	59 (66%)
Omeprazole	90	27 (30%)
Calcium	90	51 (57%)
Vitamin D	90	55 (61%)
Physical therapy		
Dry land	91	26 (29%)
Hydrotherapy	91	15 (16%)

The parents VAS for rating child overall well-being (0–10 possible range) mean ± SD at diagnosis were 4.1±2.5, 6m 2±2.1, 12m 1.3±2.8, 18m 4.1±3.1 and 24m 1.7±2.2; and there was also no significant difference from the baseline up to the last visit (Table V).

Discussion

Epidemiologic research registries are important data source about rare chronic diseases, especially for JDM (18). Data from collaborative multicentric research and biologic samples repositories have been used to better define practice, biomarkers and standard of care. There are ethnic and environmental disparities reflecting variable morbidity and mortality; race and income are critical for JDM outcome, therefore comparison of different populations in distinct settings is needed (19, 20). The minimum data set recommended for JDM registries were recently published, aiming at harmonising internationally, the data collection for clinical practice and research purposes (21).

We herein reported a comprehensive clinical profile of JDM cases at presentation and the diagnosis work up, during routine practice. Onset calcinosis was reported in 13% of the cases, a lower proportion compared to earlier reports on the same population (4, 22) and other series reported on different populations (23-27). In contrast, the CARRA registry in North America reported lower rates of calcinosis with 3.4% (28, 29). Calcinosis is the main JDM morbidity, related to chronic persistent disease activity and damage. New and increased calcinosis deposition in subcutaneous and muscle tissues indicates active disease and a severe disease course (1, 4, 22, 30).

We reviewed immunologic parameters such as ANA that was the most accessible test. Other autoantibodies were reported, but myositis associated antibody tests and biologic sample storage were very limited in our practices.

JDM disease activity and muscle strength were assessed based on paediatric core set measures (5). DAS20, its subscales for cutaneous and vasculopathy assessment (Skin-DAS) and the musculoskeletal (MSK-DAS)

Table V. Disease activity scores by DAS20, Skin-DAS and MSK-DAS subscales; muscle strength by MMT-8 and CMAS; CHAQ-DI and Parents VAS for overall well-being in JDM patients, at diagnosis and during follow up.

Measures	Diagnosis	6 months	12 months	18 months	24 months	*p* value
DAS-20 (0-20) no. of tests (mean ±SD)	56 (7.8±5)	41 (6.3±4.8) *	30 (5 ±4)*	15 (4.9 ±5)*	12 (4.9 ±5.2)*	<0.01
median	7	5	4	2	2	
minimum	1	1	1	1	1	
maximum	20	19	15	13	13	
Skin-DAS (0-11) (mean ±SD)	(2.8 ±3.3)	(1.8 ±2.9)	(1.1 ±2.2)	(0.6 ±1.8)	(0.4 ±1.5)	
median	1	0	0	0	0	
minimum	0	0	0	0	0	
maximum	11	11	9	10	9	
MSK-DAS (0-9) (mean ±SD)	(1.6 ±2.6)	(0.8 ±1.8)	(0.4 ±1.3)	(0.2 ±0.8)	(0.2±0.9)	
median	0	0	0	0	0	
minimum	0	0	0	0	0	
maximum	9	7	7	5	5	
MMT-8 (0-80) no. of tests (mean ±SD)	55 (62.6 ±20.4)	50 (70.2 ±13.5)*	40 (73.3 ±11)*	25 v	17 (74.8±7.8)*	0.016
median	72	75	78.5	80	79	
minimum	8	16	28	49	53	
maximum	80	80	80	80	80	
CMAS (0-53) no. of tests (mean ±SD)	60 (29.5±11.4)	48 (33.1±8.3)	41 (34.2±5.8)	23 (34 ±6)	15 (33.3 ±5.4)	NS
median	34	34	35	37	35	
minimum	5	8	11	20	28	
maximum	43	32	42	39	39	
CHAQ-DI (0-3) no. of tests (mean ±SD)	43 (1 ±0.9)	37 (0.6 ±0.7)	21 (0.8±0.8)	9 v	7 (1 ±0.3)	NS
median	0.75	0.25	1	0.75	1	
minimum	0	0	0	0	0.37	
maximum	3	3	3	3	2	
VAS-Parents (0-10 cm) no. of tests (mean ±SD)	37 (4.1±2.5)	37 (2 ±2.1)	15 (1.3 ±2.8)	7 (4.1 ±3.1)	7 (1.7±2.2)	NS
median	4	2	2.5	4	0	
minimum	1	0	2	0.1	0	
maximum	9	7	9	9	5	

(*) difference from the baseline values at diagnosis and follow up compared by Poisson model and Wald test for repeated measures.
DAS-20 Disease Activity Score 20 items, Skin-DAS (0-11) Disease Activity Score for skin involvement and vasculopathy, MSK-DAS (0-9) Disease Activity Score for musculoskeletal activity and muscle weakness. CHAQ-DI Childhood Health Assessment Questionnaire-Disability Index (0-3 score).
VAS-Parents Visual Analogue Scale for overall wellbeing measured by 0-10 cm scale.

subscale; MMT and CMAS were carried out in longitudinal assessment of patients treated mainly with prednisone and methotrexate. The core sets were established by consensus among adult and paediatric experts in different ways (5, 6), with the purpose of evaluating primary end points in clinical trials (2, 7). It has been used in research registries and we selected some of the measures of the paediatric JDM core set, those with feasibility during daily practice and observed by the attending physician.

DAS20 scale scoring was conducted after physicians training, the tests were performed along physical examination during routine clinical visits. Progressive improvement in disease activity scores was observed, with a significant difference over the follow up. DAS20 comprises combined scores for skin rash, muscle function and the vasculopathy. Dysphagia and dysphonia, as clinical indicators of muscle function, compromise are included among disease activity parameters. We addressed also the skin and musculoskeletal independent subscales, and it presented also wide variability with progressive improvement of disease activity status in both domains.

Disease activity scores must be feasible, valid and interpretable (31, 32) and we addressed a global disease activity tool (DAS20). We had limitations for scoring disease activity by expert clinical judgment with the physician's global assessments VAS (33) in the present study. Although it has been validated in different settings, most participants of the study not only had difficulties with the tool, but it was also considered subjective, difficult to standardise and interpretate. Additionally, we also addressed another functional scale the CHAQ-DI that was developed for arthritis and adapted for JDM. Complex composite scores have been criticised for the burden of applying multiple tests, also mentioned in other studies, and recently simplified versions of those measures have been studied and proposed to lessen the burden of the number of items and tests (34, 35).

MMT tests, capturing moderate to severe muscle weakness, showed improved scores during the first 6 months of disease onset, compared to only mild improvement of CMAS over two-years, that indicated both persistent functional impairment and muscle weakness. The MMT baseline values, and 6 months follow up were comparable to those of patients selected for clinical trials (2, 7) and registries (28, 29). Muscle strength tests and tools were reported with dif-

ferent approach in different time-points in clinical trials or during daily practice, thus limiting the comparison, as recently published in a systematic review (36). MMT and CMAS are different constructs, both assessing muscle strength and CMAS also testing endurance and functionality.

Two patient-reported outcome measures were described, CHAQ-DI and parents VAS, but the self-reported questionnaires filled out by parents with the cross-cultural adapted version (14) was indeed limited in our population.

Insights about the test's feasibility, performance and interpretation of scores to estimate disease extension, severity and possibly tailoring treatment were the main challenges. Low adherence to follow up protocol and the high rates of drop out, especially for the last visits at 18 and 24 months, that were observed for all instrumental assessments either DAS20, MMT, CMAS, CHAQ-DI or parents VAS, were the main limitation for conclusion about JDM outcome, during the second year of follow up. The study was conducted in a standard of care approach in low resource setting within the national health system public hospitals. Long distance travelling or appointments out of the protocol window might be the causes related to low follow up adherence. It is possible that patients with persistent disease activity or limitations could have had longer follow up duration. But this could not be explored further in the current protocol. There were different responses in muscle strength testing comparing MMT8 and CMAS, possibly reflecting the functional component, with MMT8 capturing moderate to severe muscle weakness. CMAS results were in keeping with the functional assessment by CHAQ-DI and parents' perception of overall well-being scored by VAS.

Despite those limitations, this is an inception cohort with a comprehensive diagnosis approach and longitudinal standardised measures of disease activity, muscle strength and functional assessment in a representative sample of the country population and environment. Testing DAS20, MMT, CMAS, CHAQ and parents' VAS scores during routine practice in resource-limited setting indicated its feasibility to guide response to treatment, that might be useful for intervention studies in future.

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