Clinical features, treatment and outcomes of Italian children with enthesitis-related arthritis and juvenile psoriatic arthritis: a cross-sectional cohort study

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Abstract

Objective

Limited information is available on the clinical features, treatment modalities and outcomes of the juvenile idiopathic arthritis (JIA) categories of enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA). This study was aimed to describe the characteristics of Italian children with ERA and JPsA and to compare them with those of patients with the other categories of JIA.

Methods

Patients were part of a multinational sample included in a study aimed to investigate the prevalence of disease categories, treatment approaches, and disease status in patients from across different geographical areas (EPOCA Study). All patients underwent a retrospective assessment, based on the review of clinical chart, and a cross-sectional evaluation, which included assessment of physician- and parent-reported outcomes and laboratory tests, and recording of ongoing therapies.

Results

Of the 9081 children with JIA enrolled in the EPOCA Study, 1300 were recruited at 18 paediatric rheumatology centres in Italy. 45 (3.5%) had ERA and 49 (3.8%) had JPsA. Several remarkable differences in demographic features and frequency of articular and extra-articular manifestations, disease damage, impairment in physical function and health-related quality of life, school-related problems, comorbidities, and ongoing treatments were observed between ERA and JPsA and the other JIA categories.

Conclusion

We described the characteristics of Italian children with ERA and JPsA and highlighted their peculiarities and their differences from the other JIA subsets. These data provide useful insights for future revisions of JIA classification and a benchmarking against which the features from other cohorts may be compared.

Key words

juvenile idiopathic arthritis, enthesitis-related arthritis, psoriatic arthritis, spondylarthritis, paediatric rheumatology

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Introduction

Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are part of the seven categories of juvenile idiopathic arthritis (JIA) outlined by the current International League of Associations for Rheumatology (ILAR) classification (1). ERA belongs to the spectrum of spondyloarthritis and is defined as the association of arthritis and enthesitis or as the presence of arthritis or enthesitis with two or more of the following: sacroiliac joint tenderness and/or inflammatory lumbosacral pain; presence of HLA-B27; onset of arthritis in a boy after 6 years of age; family history of HLA-B27-associated disease in a first-degree relative; acute symptomatic anterior uveitis. The diagnosis of JPsA requires the presence of arthritis plus psoriasis or arthritis with two or more of the following: dactylitis; nail pits or onycholysis; family history of psoriasis in a first-degree relative.

As compared to the abundance of studies that have described the clinical features, treatment modalities and outcomes in the categories of oligoarthritis, polyarthritis and systemic arthritis, scarce information is available for ERA and JPsA. As a result, their clinical phenotype, course and impact on child wellbeing are ill-defined, their classification is controversial (2), and the optimal therapeutic approach is still uncertain. One of the reasons that explain the dearth of data is the relative infrequency of these disorders, which are less common than the other forms of JIA in most parts of the world (3). To gain further insights into the characteristics of these conditions, there is, thus, the need to describe the characteristics of additional series of patients.

Taking advantage of a recent multinational, cross-sectional, observational cohort study aimed to investigate the prevalence of disease categories, treatment approaches, and disease status of patients from across different geographical areas (EPOCA Study) (4), the purpose of the present study was to report the features of the sample of children with ERA and JPsA recruited in Italy and to compare them with those of the patients with the other categories of JIA.

Methods

Study design and participants

The study design and the modality of involvement of paediatric rheumatology centres have been described previously (4). Briefly, after agreeing to take part in the study, each participating centre was asked to enroll a total of 100 patients meeting the ILAR criteria for JIA (1) that were seen consecutively over 6 months or, if the centre did not expect to see at least 100 patients within 6 months, to enroll all patients seen consecutively within the first 6 months after study start.

All participating centres obtained approval of the study protocol from their local ethics committee. The parents or guardians of all patients or the patients themselves (if appropriate) provided written informed consent to participate in the study.

Clinical assessment

All patients were evaluated according to a standard protocol, which included a retrospective assessment, based on the review of the clinical chart, and a cross-sectional assessment, performed at the study visit. Retrospective assessment included demographic data, ILAR category, history of uveitis, and medications received from disease onset to the date of the visit. Cross-sectional evaluation included a standardised joint examination, a physician's global assessment of disease activity (PhGA) on a 21-numbered circle visual analogue scale (0 = no activity, 10 = maximum activity) and the measurement of articular and extra-articular damage with the Juvenile Arthritis Damage Index (JADI) (5). Briefly, the JADI is composed of two parts: one devoted to the assessment of articular damage (JADI-A), and one devoted to the assessment of extraarticular damage (JADI-E). In the JADI-A, 36 joints or joint groups are assessed for the presence of damage, and the damage observed in each joint is scored on a 3-point scale (where 0 = no damage, 1 = moderate damage, and 2 = severe damage, ankylosis, or prosthesis). The maximum total score is 72. The JADI-E includes 13 items in 5 different organs/systems. Each item is scored as 0 if damage is absent or as 1 if

Table I. Demographic characteristics of the patient sample.

	Systemic arthritis (n=94)	Oligoarthritis (n=614)	Polyarthritis (n=498)	ERA (n=45)	Psoriatic arthritis (n=49)	*p*-value
Females, n (%)	47 (50.0)	463 (75.4)	409 (82.1)	14 (31.1)	33 (67.3)	<0.001
Age at disease onset, years	6.6 [2.2, 10.9]	3.1 [1.9, 6.3]	3.0 [1.7, 6.5]	9.8 [8.5, 12.4]	4.9 [2.0, 10.0]	<0.001
Disease duration at study visit, years	3.6 [1.6, 7.4]	3.4 [1.4, 6.5]	5.2 [2.5, 8.9]	3.4 [1.5, 4.9]	5.4 [2.7, 7.6]	<0.001
Disease duration at first visit, years	0.2 [0.1, 1.0]	0.2 [0.1, 0.6]	0.3 [0.1, 1.1]	0.3 [0.1, 1.0]	0.5 [0.2, 1.3]	<0.001
HLA-B27 positive, n/tested (%)	1/36 (2.8)	24/267 (9.0)	5/214 (2.3)	27/44 (61.4)	0/29 (0.0)	<0.001
ANA positivity*	4/50 (8.0)	412/562 (73.3)	131/188 (69.7)	5/31 (16.1)	19/35 (54.3)	<0.001

Data are the median [1st, 3rd quartile], unless not otherwise indicated.
ERA: enthesitis-related arthritis; ANA: antinuclear antibodies. *ANA status was reported only for patients with at least two ANA determination at least 3 months apart. ANA were considered positive with at least one positive determination with a titre ≥1:160.

Table II. Physician-reported outcomes, distinctive clinical manifestations, laboratory tests, and composite indices at cross-sectional visit.

	Systemic arthritis (n=94)	Oligoarthritis (n=614)	Polyarthritis (n=498)	ERA (n=45)	Psoriatic arthritis (n=49)	*p*-value
Patients with swollen joint count ≥1	27 (28.7)	209 (34.0)	198 (39.8)	10 (22.2)	19 (38.8)	0.039
Patients with tender joints count ≥1	29 (30.9)	151 (24.6)	151 (30.3)	12 (26.7)	12 (24.5)	0.252
Patients with limited joint count ≥1	35 (37.2)	213 (34.7)	226 (45.4)	14 (31.1)	22 (44.9)	0.004
Patients with active joint count ≥1	34 (36.2)	227 (37.0)	216 (43.4)	13 (28.9)	19 (38.8)	0.121
Patients with PhGA >0	48 (51.1)	281 (45.8)	263 (52.8)	20 (44.4)	24 (49.0)	0.199
Patients with sacroiliac joint involvement	2 (2.1)	7 (1.1)	8 (1.6)	2 (4.4)	0 (0.0)	0.366
Patients with active uveitis	0 (0.0)	36 (5.9)	30 (6.0)	0 (0.0)	1 (2.0)	<0.001
Patients with dactylitis	3 (3.2)	12 (2.0)	14 (2.8)	1 (2.2)	6 (12.2)	0.001
Patients with enthesitis	0 (0.0)	6 (1.0)	6 (1.2)	9 (20.0)	1 (2.0)	<0.001
Median [1st, 3rd quartile] ESR, mm/h	10.0 [5.5, 21.0]	10.0 [6.0, 18.8]	12.0 [7.0, 22.0]	9.0 [4.0, 12.0]	11.0 [7.0, 18.0]	0.062
Median [1st, 3rd quartile] JADAS10	2.0 [0.0, 9.8]	2.0 [0.0, 6.0]	3.0 [0.0, 8.7]	2.0 [0.0, 10.0]	1.5 [0.0, 5.0]	0.039
Patients with JADI-A ≥1	17 (18.1)	52 (8.5)	96 (19.3)	6 (13.3)	11 (22.4)	<0.001
Patients with JADI-E ≥1	18 (19.1)	71 (11.6)	54 (10.8)	3 (6.7)	6 (12.2)	0.163

Data are the number (%), unless otherwise indicated.
ERA: enthesitis-related arthritis; PhGA: physician's global assessment of overall disease activity; ESR: erythrocyte sedimentation rate; JADAS10: Juvenile Arthritis Disease Activity Score 10; JADI-A: Juvenile Arthritis Damage Index-Articular; JADI-E: Juvenile Arthritis Damage Index-Extra-articular

damage is present. Due to the relevant impact of ocular damage on the child's health, in each eye a score of 2 is given in case the patient has had ocular surgery, and a score of 3 is given in case the patient has developed legal blindness. The maximum total score is 17.

The level of disease activity was measured by means of the Juvenile Arthritis Disease Activity Score 10 (JADAS10) (6). Briefly, the JADAS10 is composed of the following four variables: (1) PhGA; (2) parent global assessment of child's wellbeing; (3) 10-joint reduced active joint count; and (4) ESR. The JADAS10 is calculated as the sum of the scores of its individual components, which yields a global score of 0–40.

The presence of sacroiliitis at cross-sectional visit was assessed clinically as the presence of pain on pressure on the right or left sacroiliac joint and was reported by each investigator in the rheumatological examination form.

Before the cross-sectional visit, a parent or guardian completed a parent proxy-report Italian version of a multidimensional questionnaire, which included assessments of the child's physical function, overall wellbeing, pain intensity, health-related quality of life, and morning stiffness. For this study, the questionnaire was translated and cross-culturally validated into 54 languages of 52 countries, as described elsewhere (7). Data were collected in an SQL database (Microsoft SQL server) placed in a dedicated secure web server powered by the Paediatric Rheumatology International Trials Organization (PRINTO).

Statistical analysis

We reported descriptive statistics as medians with interquartile range (IQR) for continuous variables and absolute frequencies and percentages for categorical variables. We compared categorical variables with the χ^2 test. R statistics v. 3.5.0 was used for all statistical analyses.

Results

Of the 9081 children with JIA enrolled in the EPOCA study (4), 1300 were recruited at 18 paediatric rheumatology centres in Italy. Of these patients, 45 (3.5%) had ERA and 49 (3.8%) had JPsA. The comparison of the main features of these patients with those of patients with the other ILAR categories of systemic arthritis (n=94), polyarthritis (n=498), and oligoarthritis (n=614) is presented in Tables I to VI.

The demographic characteristics are shown in Table I. As compared to the other JIA categories, the ERA sample included a lower proportion of girls and had an older age at disease onset. For JPsA, these figures fall-between those of systemic arthritis and oligo-polyarthritis. As expected, the percentage of HLA-B27-positive patients was much higher in patients with ERA. JPsA patients had positive antinuclear antibodies with at least one determination in more than half of subjects.

Table III. Parent-reported outcomes.

	Systemic arthritis (n=94)	Oligoarthritis (n=614)	Polyarthritis (n=498)	ERA (n=45)	Psoriatic arthritis (n=49)	*p*-value
Patients with well-being VAS >0	49 (52.1)	309 (50.7)	291 (58.4)	27 (60.0)	28 (57.1)	0.106
Patients with physical function score >0	31 (33.7)	249 (40.8)	240 (48.5)	16 (35.6)	28 (58.3)	0.003
Patients with HRQL total score > 1 ds	37 (40.7)	149 (25.6)	162 (34.0)	15 (33.3)	16 (34.0)	0.007
Patients with HRQL PhS >1 ds	35 (37.6)	217 (36.0)	206 (41.8)	19 (42.2)	16 (32.7)	0.311
Patients with HRQL PsS >1 ds	24 (26.1)	87 (14.9)	111 (23.2)	10 (22.2)	12 (25.5)	0.003
Patients with pain VAS >0	43 (46.2)	278 (45.4)	265 (53.3)	23 (51.1)	27 (56.2)	0.084
Patients with morning stiffness >15min	15 (16.1)	68 (11.2)	70 (14.2)	8 (17.8)	6 (12.2)	0.39
Parents satisfied with illness outcome	76 (81.7)	472 (77.6)	375 (75.8)	36 (80.0)	40 (81.6)	0.653

Data are the number (%)
ERA: enthesitis-related arthritis; VAS: visual analogue scale; HRQL: health-related quality of life; PhS: physical; PsS: psychosocial.
>1 ds = greater than 1 standard deviation from the mean of healthy controls.

Table IV. Parents' assessment of school problems related to JIA. Only children attending school are included.

	Systemic arthritis (n=94)	Oligoarthritis (n=614)	Polyarthritis (n=498)	ERA (n=45)	Psoriatic arthritis (n=49)	*p*-value
No problems	47 (61.0)	412 (77.7)	337 (73.6)	33 (76.7)	32 (76.2)	0.031
Frequent absences	14 (18.2)	48 (9.1)	71 (15.5)	2 (4.7)	4 (9.5)	0.005
Difficulty in remaining seated for a long time	6 (7.8)	32 (6.0)	33 (7.2)	5 (11.6)	6 (14.3)	0.234
Difficulty in relationships with teachers	3 (3.9)	6 (1.1)	10 (2.2)	2 (4.7)	1 (2.4)	0.26
Decrease in performance	10 13.0)	15 (2.8)	26 (5.7)	2 (4.7)	3 (7.1)	0.002
Other school problems	6 (7.8)	31 (5.8)	27 (5.9)	2 (4.7)	1 (2.4)	0.815

Data are the number (%)
JIA: juvenile idiopathic arthritis; ERA: enthesitis-related arthritis.

Table V. Frequency of comorbidities.

	Systemic arthritis (n=94)	Oligoarthritis (n=614)	Polyarthritis (n=498)	ERA (n=45)	ERA x(n=49)	*p*-value
Patients with comorbidities	10 (10.8)	51 (8.4)	47 (9.7)	2* (4.4)	34 (69.4)	<0.001
Patients with obesity	2 (2.1)	1 (0.2)	0 (0.0)	0 (0.0)	1 (2.0)	0.002
Patients with asthma	0 (0.0)	0 (0.0)	1 (0.2)	0 (0.0)	0 (0.0)	0.807
Patients with psoriasis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	31 (63.3)	<0.001
Patients with inflammatory bowel disease	1 (1.1)	1 (0.2)	1 (0.2)	0 (0.0)	1 (2.0)	0.121
Patients with coeliac disease	1 (1.1)	5 (0.8)	14 (2.8)	0 (0.0)	2 (4.1)	0.055
Patients with diabetes mellitus	0 (0.0)	6 (1.0)	0 (0.0)	0 (0.0)	1 (2.0)	0.102
Patients with thyroiditis	1 (1.1)	9 (1.5)	7 (1.4)	0 (0.0)	2 (4.1)	0.538

Data are the number (%). *Co-morbid conditions in ERA patients were IgA deficiency and epilepsy.
JIA: juvenile idiopathic arthritis; ERA: enthesitis-related arthritis.

Table II reports physician-reported outcomes, distinctive clinical manifestations, ESR value, and composite scores. Patients with ERA had a lower frequency of swollen joints and of joints with limited range of motion, whereas the proportion of tender and active joints was comparable across categories. There was no difference in the percentage of patients with a PhGA > 0 and in the median ESR value, whereas patients with JPsA had a lower JADAS10 value. As expected, at cross-sectional visit, patients with ERA had more frequently enthesitis and, to a lesser-than-expected extent, signs of sacroiliac joint involvement; however, a history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain was reported for 30% of children with ERA among classification criteria. Dactylitis was recorded more commonly in JPsA. No patient with ERA and only one patient with JPsA had active uveitis at cross-sectional visit. Patients with JPsA had the highest prevalence of articular damage, whereas those with ERA had the lowest frequency of extra-articular damage, although the frequency was not statistically significant.

There were some remarkable disparities in parent-reported outcomes across categories (Table III), with patients with ERA having a lower frequency of impairment in physical function than those with oligo-polyarthritis and JPsA, but not systemic arthritis. JPsA patients had the highest frequency of impairment in physical function. Patients with JPsA had a frequency of impairment in the psychosocial domain of HRQL comparable to that of patients with systemic arthritis and higher than that of patients with oligoarthritis.

The most relevant disparity in school-related issues regarded the tendency of patients with ERA and JPsA to experience more frequently difficulty in remaining

Table VI. Treatments at cross-sectional visit.

	Systemic arthritis (n=94)	Oligoarthritis (n=614)	Polyarthritis (n=498)	ERA (n=45)	Psoriatic arthritis (n=49)	*p*-value
No therapy	26 (27.7)	267 (43.5)	90 (18.1)	10 (22.2)	16 (32.7)	<0.001
NSAIDs	12 (12.8)	65 (10.6)	50 (10.0)	13 (28.9)	3 (6.1)	0.002
Systemic corticosteroids	18 (19.1)	10 (1.6)	26 (5.2)	1 (2.2)	2 (4.1)	<0.001
Intraarticular corticosteroids injections	0 (0.0)	6 (1.0)	3 (0.6)	0 (0.0)	0 (0.0)	0.718
Methotrexate	34 (36.2)	259 (42.2)	298 (59.8)	18 (40.0)	21 (42.9)	<0.001
Salazopyrin	0 (0.0)	1 (0.2)	4 (0.8)	10 (22.2)	0 (0.0)	<0.001
Other synthetic DMARDs	4 (4.3)	6 (1.0)	6 (1.2)	0 (0.0)	0 (0.0)	0.073
Biologic DMARDs	39 (41.5)	74 (12.1)	174 (34.9)	15 (33.3)	17 (34.7)	<0.001
TNF inhibitors	13 (13.8)	73 (11.9)	160 (32.1)	15 (33.3)	16 (32.7)	<0.001
Anti-IL-1 drugs	17 (18.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
Anti-IL-6 drugs	9 (9.6)	1 (0.2)	5 (1.0)	0 (0.0)	0 (0.0)	<0.001

Data are the number (%)
ERA: enthesitis-related arthritis; NSAIDs: non-steroidal anti-inflammatory drugs; DMARDs: disease-modifying anti-rheumatic drugs; TNF: tumour necrosis factor; IL: interleukin.

seated for a long time than patients with the other categories (Table IV).

Patients with JPsA had a remarkably higher prevalence of comorbidities (Table V), which were represented by overt psoriasis in nearly all cases. The prevalence of inflammatory bowel disease was not increased in patients with ERA.

A consistent proportion of patients with all categories was receiving no therapy at the time of the cross-sectional visit (Table VI). Among patients who were on medications, non-steroidal anti-inflammatory drugs (NSAIDs) were administered most commonly to those with ERA, methotrexate was prescribed to ERA and JPsA with a frequency comparable to that of oligoarthritis, but lower than that of polyarthritis, whereas sulphasalazine was taken almost exclusively by ERA patients. The proportion of ERA and JPsA patients who were receiving biologic disease-modifying anti-rheumatic drugs (DMARDs) was comparable to that of patients with poly-arthritis. Among patients with ERA and JPsA, one third was being treated with TNF inhibitors, and none with anti-IL-1 or anti-IL-6 drugs.

Discussion

We provide herein a thorough overview of the features of Italian children with the JIA categories of ERA and JPsA and their comparison with those of the other JIA subsets. Because the study population was composed of patients enrolled at the majority of paediatric rheumatology centres in the country, our results are likely generalisable to patients with ERA and JPsA being followed in Italy. A careful method of sampling was applied to minimise a bias in patient selection and to ensure the representativeness of the series included at each participating centre. The reliability of the results was also ensured by the use of a standardised and uniform protocol of clinical assessment and data collection.

We found that ERA was the sole form of JIA that was more prevalent in boys than in girls. Furthermore, its median age at onset was higher than that of the other disease categories. These findings are in keeping with those seen in other series (8-10) and confirm that ERA has a male predilection and tends to develop most commonly in the later school age or adolescence. The prevalence of 3.5% among all forms of JIA seen in our study is in the lower range of the 3–11% reported in other studies (11). It is well known, however, that the relative frequency of ERA is much higher (up to 30%) in some countries of Southeast Asia, especially India (3, 4).

As compared to patients with the other JIA categories, those with ERA had less frequently swollen and limited joints. This finding could be related to the tendency of patients with this condition to present with involvement of few large joints (12). However, the frequency of joint tenderness was similar to that seen in patients with oligoarthritis, which suggests that pain is distinctly more common than the other joint symptoms in patients with ERA. That the overall disease burden was not lesser than that of patients with oligoarthritis is suggested by the comparable frequency of PhGA greater than zero. The prevalence of articular damage was slightly higher in ERA than in oligoarthritis, whereas the frequency of extra-articular damage tended to be lower in the ERA group, perhaps owing, at least in part, to the minor impact of comorbidities, particularly uveitis. Indeed, ocular involvement in ERA is marked by an acute, symptomatic, relapsing iridocyclitis, which if properly recognised and treated does not cause ocular damage (8-10). The higher prevalence of enthesitis and HLA-B27 positivity in patients with ERA was expected as these features are distinctive of this JIA category and are part of its classification criteria. The lower-than-expected frequency of signs of sacroiliac involvement suggests that most children with ERA enrolled in the study had a predominantly peripheral disease. However, the presence of or a history of sacroiliac joint tenderness and/or inflammatory lumbosacral pain was reported for 30% of children with ERA as a classification criteria.

Parent/patient-reported outcomes revealed that the burden of ERA on child's health was substantial, as shown by the frequency of physical wellbeing impairment, pain and morning stiffness comparable to that of the polyarthritis sample. Impairment in psychosocial wellbeing was more pronounced than that of oligoarthritis, but comparable to that of the other subgroups. The marked impact of parent/patient-reported pain and morning stiffness among patients with ERA was expected as these symptoms are

typically prominent in spondylarthritis (13). Such complaints may have been largely responsible for the reported difficulty remaining seated for a long time in a sizeable proportion of ERA patients. At cross-sectional visit, patients with ERA were receiving more commonly NSAIDs than did patients with the other JIA categories. The high proportion of ERA patients who were prescribed sulfasalazine is not surprising as this medication is outlined as the preferred synthetic DMARD for the treatment of peripheral disease activity (13) and is approved for use in juvenile spondylarthritis (14, 15). The frequency of administration of biologics was comparable to that of polyarthritis and PsA, but higher than that of oligoarthritis. That the most commonly prescribed biologic DMARDs were the TNF inhibitors reflects the current wider experience with the use of these medications in spondyloarthropathies.

Considerable controversy exists around the concept and classification of psoriatic arthritis in children (16-20). It is well established that JPsA is a heterogeneous condition (16, 21, 22) that accounts for 3–10% of all JIA cases (11, 23). The ILAR definition of JPsA is similar to that proposed by the previous Vancouver criteria (24), except for the use of some exclusions, which include the presence of ERA/spondylarthritis features. If JPsA is defined according to Vancouver criteria (that is, without the ILAR exclusion criteria), then two distinct subgroups can be recognised. One subgroup consists of children with the characteristics of ERA, who bear close similarities with spondylarthritis, as is the case in adult psoriatic arthritis. The other subgroup consists of children who display the features of early-onset antinuclear antibody (ANA)-positive oligoarthritis. It has been argued that if the ILAR definition is used to diagnose JPsA, patients with a form of psoriatic arthritis similar to that observed in adults are often excluded because of the presence of ERA/spondylarthritis features (25). These patients would be placed into the category of undifferentiated arthritis.

Our sample of JPsA included a larger proportion of females, which accounted for around two thirds of the whole population. This finding is in line with the previous observation that most Italian children with JPsA manifest the features of early-onset ANA-positive JIA, which is characterised by marked female predilection (26, 27). That the majority of our JPsA patients belonged to this subgroup, rather than to that of ERA/spondylarthritis, is also highlighted by their median age at disease onset much lower than that of the ERA cohort. The presence of a relatively low proportion of patients with ERA/spondylarthritis features in the JPsA is also suggested by the absence of HLA-B27-positive patients, the very low frequency of enthesitis, and the uncommon administration of sulphasalazine. The higher frequency of dactylitis was expected, as this feature is one of the ILAR criteria for JPsA.

The frequency of joint swelling, tenderness and active arthritis in JPsA patients was comparable to that of the oligoarthritis sample, whereas the prevalence of limited range of motion was higher and similar to that seen in the polyarthritis subset. This finding suggests that the risk of development of joint changes may be greater in JPsA than in oligoarthritis. This notion was corroborated by the higher frequency of articular damage and functional impairment. That the impact of JPsA on child's health may be superior to that of oligoarthritis is also highlighted by the higher frequency of impaired HRQL in the psychosocial domain. In addition, children with JPsA tended to have a higher frequency of parent wellbeing and pain VAS greater than zero and of difficulty in remaining seated for a long time at school than those with oligoarthritis. Thus, although the vast majority of Italian children with JPsA possess the features of the early-onset ANA-positive phenotype of JIA, their disease course and burden may be worse than that of children with oligoarthritis. The greater severity of JPsA is also suggested by the more frequent prescription of biologic DMARDs.

Our results should be interpreted in the light of some potential limitations. Although the whole JIA sample is large, the size of ERA and JPsA subsets is relatively small. We cannot exclude that a study specifically devoted to these JIA categories could lead to enroll larger patient populations. The cross-sectional design of the study did not allow the comparison of long-term outcomes across JIA subsets. We did not collect information on the family history of HLA-B27-related diseases and psoriasis and we did not ask the study investigators to record isolated gastrointestinal symptoms that could anticipate or overlap with an inflammatory bowel disease. The presence of symptoms indicative of axial involvement, especially back pain, was not looked for specifically in patients with ERA. Finally, several important assessments of disease state, such as imaging studies and biomarker determination, were not included in the study protocol.

In conclusion, our study adds to the available information on ERA and JPsA by describing the characteristics of Italian children with these JIA categories and highlighting their peculiarities and their differences from the other JIA subsets. These data provide useful insights for establishing the right place of these conditions in JIA classification and a benchmarking against which the features from other cohorts may be compared.

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