

Association between duration of symptoms and severity of disease at first presentation to paediatric rheumatology: results from the Childhood Arthritis Prospective Study

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Objectives. To study the association between disease severity at first presentation to paediatric rheumatology (PRh) and length of time since symptom onset in children recruited to the Childhood Arthritis Prospective Study.

Methods. Children ≤ 16 yrs with inflammatory arthritis persisting ≥ 2 weeks were recruited from five UK hospitals. Data including demographics, disease features, Childhood Health Assessment Questionnaire (CHAQ), physician and parent global assessment and blood tests were collected at the first appointment with PRh (baseline). The association between symptom duration (defined as time from first reported symptom onset to presentation at PRh) and baseline disease characteristics was evaluated using non-parametric descriptive statistics and multivariable logistic regression analyses.

Results. Five hundred and seven children (65% female) were included: median age at onset was 6.8 yrs. Two hundred and thirty-three had oligoarthritis, 68 had RF-negative polyarthritis, 27 had systemic onset arthritis and 29 had arthritis that was not JIA. The median symptom duration was 4.6 months. Median symptom duration was shortest for children presenting with systemic arthritis (1.6 months) and longest for those with PsA (8.6 months). Children with a longer duration of symptoms were older and had higher median active joint counts but lower median ESR. Symptom duration did not correlate with CHAQ score at presentation.

Conclusions. Children who have systemic arthritis had the shortest delay to PRh presumably because they are profoundly unwell. Children with joint pain/stiffness but normal ESR had longer delays suggesting that if blood tests do not indicate inflammation, the diagnosis of JIA may be overlooked.

KEY WORDS: Inflammatory arthritis, Juvenile idiopathic arthritis, Presenting symptoms, Symptom duration, Outcome, Paediatric rheumatology.

Introduction

Each year $\sim 10/100\,000$ children develop inflammatory arthritis [1] with many subsequently being diagnosed as juvenile idiopathic arthritis (JIA). Many children continue to have some disability and limitation of their activities of daily living and $\sim 50\text{--}70\%$ are estimated to have active disease into adulthood [2].

In adults with RA, guidelines from both ACR [3] and the British Society for Rheumatology [4] emphasize the need for early diagnosis and treatment to reduce subsequent functional disability. Early disease-modifying drug intervention slows the progression of structural joint damage and improves long-term outcomes as well as overall quality of life [5]. The inherent problem is the long lag time between onset of disease and referral to rheumatologist for treatment with the length of time required to make the diagnosis being the major contributor to this delay. Arthritis in children is a different condition from adult inflammatory arthritis and one cannot directly extrapolate data from adult disease to that of JIA. However, it is recognized that arthritis in children should also be treated early and aggressively to prevent significant structural damage and that clinicians should

not assume that JIA is a self-limiting condition that will remit as the child grows [2].

Prompt diagnosis and referral to experienced care, ideally a paediatric rheumatology (PRh) multidisciplinary team, are essential and the UK Arthritis and Musculoskeletal Alliance (ARMA) recommend in their 'Standards of Care for People with Inflammatory Arthritis' (<http://www.arma.uk.net/pdfs/ia.pdf>) that children with inflammatory arthritis should be assessed by a specialist in rheumatology within 4 weeks of GP referral. However, there remain few data on the factors associated with delay to PRh care and the effects of this delay on both short- and long-term outcomes. The aim of this initial study was to assess whether there was an association between demographic and disease characteristics at first presentation to a paediatric rheumatologist and the length of time since first symptom onset.

Patients and methods

Patient selection

Children in this study were participants in the Childhood Arthritis Prospective Study (CAPS), an ongoing prospective longitudinal inception cohort study which aims to follow children presenting with new onset inflammatory arthritis for a minimum of 5 yrs. The overall aim of this study is to identify genetic and environmental predictors of short- and long-term outcomes of inflammatory arthritis (including response to treatment) in children and to identify the relative contributions of socio-demographic, clinical, psychological, laboratory and genetic factors and treatment in explaining outcome. The study was launched in September 2001 and aims to recruit 1100 children from five tertiary referral centres in England and Scotland: Royal Liverpool Children's Hospital, Liverpool; Booth Hall Children's Hospital, Manchester; Royal Victoria Infirmary, Newcastle; Royal Hospital for Sick Children,

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Glasgow; and Great Ormond Street Hospital, London. All children aged ≤ 16 yrs either presenting to the PRh outpatient clinic or admitted as inpatients, with newly diagnosed inflammatory arthritis in one or more joints, which had persisted, according to parent/child history for at least 2 weeks, are invited to participate. Exclusion criteria are septic arthritis, haemarthrosis, arthritis caused by malignancy or trauma, connective tissue disorders such as SLE, MCTD or dermatomyositis. The initial invitation was made by the paediatric rheumatologist and followed-up by the research nurse after the parent had had time to read the study information sheet.

CAPS was approved by the UK multicentre research ethics committee. Written informed consent was obtained from the parent(s)/guardian for all participant children according to the Declaration of Helsinki [6], and children, if considered able, were asked to provide assent.

Baseline data collection

Data for this study is collected from the PRh and the parent/child. All children undergo a rheumatological exam at their first appointment with the PRh (baseline). All children have an active and limited joint count recorded as well as a physician global assessment. At the first visit, the PRh is asked to assign a 'best guess' ILAR classification, if the child is felt to have JIA [7–9] or to indicate 'Other inflammatory arthritis' where appropriate. For this analysis, the ILAR classification is assigned at baseline (and for many children within the first weeks of disease) so can only be regarded as a predicted subtype. In addition, the children's clinical case notes are reviewed by a study research nurse using standard data collection forms. Here, other disease features relating to inclusion and exclusion criteria for ILAR classification, as recorded in the clinical case notes, are collected and include systemic rash, fever, lymphadenopathy, serositis, psoriasis, nail pitting, dactylitis, enthesitis, sacroiliitis and uveitis. Finally, the results from any laboratory investigations, if performed, are recorded from the clinical case notes and include, where undertaken, a full blood count, ESR and CRP, RF, ANA and HLA-B27. The parent or, where appropriate, the child completes a Childhood Health Assessment Questionnaire (CHAQ) [10] including a parent general evaluation and pain visual analogue scale (VAS).

Within 3 months of this PRh appointment, children and their parents are interviewed by the specialist rheumatology research nurse using a standard proforma and questionnaires either in the clinic or at home. Data collected includes demographic details, birth and health history as well as family history. The parent/child is asked to recall the date of first symptom onset related to the child's arthritis. If an exact date is not known, the month and year of symptom onset is recorded and the date set to the first of the month.

Analysis

This preliminary cross-sectional analysis focuses on the disease characteristics at presentation to PRh and their association with time since first symptom onset. The total symptom duration was calculated using the date of first reported onset of musculoskeletal symptoms and the date of the first paediatric rheumatologist visit. To further study the length of symptom duration in more detail, the time was divided into two components: symptom onset up to referral to PRh and the time between referral and PRh appointment date. This was subsequently analysed according to the source of the referral.

Presenting characteristics and median symptom duration are given for the group as a whole and for each ILAR subtype, where assigned. The total symptom duration was subsequently categorized as a dichotomous variable (short and long symptom duration) approximated to the cohort median and differences between the two groups were compared using Wilcoxon rank sum

statistics for continuous variables and Pearson's chi-squared test for proportional variables. A multivariable logistic regression model was developed to assess the independent association of presenting characteristics with long symptom duration. The resulting odds ratio (OR) is a measure of the probability of having a symptom duration greater than the cohort median. All analyses were undertaken using STATA version 9.2 (StataCorp, 4905 Lakeway Drive, College Station, TX 77845, USA).

Results

Characteristics at presentation to PRh

Up to 20 December 2006, a total of 507 children with inflammatory arthritis were recruited to CAPS and included in this analysis. The median age at symptom onset was 6.8 yrs and the median age at first presentation was 7.8 yrs, 65% were female and 92% were Caucasian (Table 1). At presentation, 427 (84%) were assigned a JIA ILAR subtype: 233 (46%) children were classified as having oligoarthritis (children were not yet assigned to either persistent or extended oligoarthritis classifications), 68 (13%) had RF-negative polyarthritis and 27 (5.3%) had systemic onset arthritis (Table 1). Twenty-nine children (5.7%) were classified as having inflammatory arthritis other than JIA, including 17 children with reactive arthritis and 2 children with Down's syndrome-associated arthritis. In 51 children (10%), no specific diagnosis had been assigned and further investigations were awaited.

For all children, the median number of joints with active inflammation or limited range of movement were 1 [Interquartile range (IQR) 1, 4] and 1 (IQR 0, 3), respectively (Table 2). The median CHAQ score was 0.63 (IQR 0.13, 1.38). When the analysis was limited to those children who had been assigned a JIA subtype, CHAQ scores were higher in those with polyarthritis (RF-positive and -negative) and systemic arthritis compared with the other subtypes. Children presenting with systemic JIA had the highest median ESR (93 mm/h; IQR 60, 109) and CRP (98 mg/l; IQR 36, 246).

Symptom duration

The median symptom duration at the first presentation to PRh was 4.6 months (IQR 2.3, 9.5) (Table 1). However, 108 (21%) children had had symptoms longer than 1 yr. The shortest symptom duration was seen in those children presenting with systemic JIA (median 1.6 months; IQR 0.9, 5.6) and the longest in those presenting with PsA (median 8.6 months; IQR 3.2, 29.3) (Table 2).

The total symptom duration differed depending on the source of the referral to PRh (Table 3), although the number of physicians seen by the children prior to this referral was not known. Most children (155; 37%), were referred from a general paediatrician with a lesser proportion being referred via their GP, orthopaedic, Accident and Emergency or another medical specialist. The promptest referrals came via the Accident and Emergency Department. The total symptom duration was longest (median 7.8 months; IQR 4.6, 16.8) when children were referred from other medical specialists, for example, plastic surgery, neurology, ophthalmology, otolaryngology or adult rheumatologists. Once referred, 295 (62%) children were seen by a paediatric rheumatologist within 4 weeks. For 17 children, the source of the referral was missing. However, the median duration of symptoms in this group (3.8 months; IQR 2.6, 7.5) was similar to that seen among those children where the source was known.

Total duration of symptoms and presenting disease characteristics

As the median symptom duration was 4.6 months, the characteristics associated with symptoms of ≤ 4 and >4 months were

TABLE 1. Demographics and disease characteristics of children with inflammatory arthritis at first appointment with paediatric rheumatologist

	Whole cohort	Systemic	Oligoarthritis	Polyarthritis RF negative	Polyarthritis RF positive	Enthesitis- related arthritis	PsA	Undifferentiated
	507	27	233	68	12	32	35	20
Demographics								
Age at onset (yrs)	6.8 (3.0, 10.0)	6.4 (4.2, 9.8)	5.0 (2.4, 9.7)	6.7 (2.3, 9.6)	11.8 (9.4, 13.1)	11.6 (10.4, 13.3)	10.1 (6.3, 11.5)	6.4 (2.7, 11.9)
Female (%)	65	70	66	78	83	9	69	60
Caucasian (%)	92	96	92	97	84	97	100	89
Total symptom duration (months)	4.6 (2.3, 9.5)	1.6 (0.9, 5.6)	4.4 (2.5, 8.6)	5.9 (2.6, 19.3)	6.2 (2.9, 33.2)	7.5 (3.6, 12.7)	8.6 (3.2, 29.3)	2.5 (1.2, 21.6)
Disease features								
Number of joints with active inflammation	1 (1, 4)	2 (0, 5)	1 (1, 2)	9 (5, 14)	9 (3, 25)	2 (1, 4)	3 (2, 10)	1 (1, 4)
Number of joints with limited movement	1 (0, 3)	0 (0, 3)	1 (0, 2)	6 (1, 10)	7 (1, 16)	2 (1, 4)	2 (0, 6)	1 (1, 3)
CHAQ score (0–3)	0.63 (0.13, 1.38)	1 (0.25, 0.2)	0.63 (0.13, 1.25)	1.25 (0.38, 1.88)	1.0 (0.13, 1.75)	0.56 (0.13, 1.13)	0.56 (0.13, 1.38)	0.19 (0, 1.19)
Physician global assessment (0–100)	35 (20, 60)	70 (57, 76)	26 (17, 47)	49 (30, 67)	50 (32, 81)	42 (29, 56)	30 (18, 57)	37 (21, 39)
Parent general evaluation (0–100)	20 (5, 46)	32 (7, 48)	15 (3, 43)	32 (10, 53)	19 (15, 50)	30 (20, 53)	18 (4, 31)	21 (2, 48)
Pain (0–100)	34 (9, 60)	29 (9, 52)	30 (7, 50)	35 (13, 68)	55 (10, 68)	50 (38, 68)	28 (10, 64)	39 (2, 67)
ESR (<i>n</i> =389) (mm/h)	21 (6, 46)	93 (60, 109)	17 (6, 35)	22 (5, 54)	15 (4, 30)	10 (5, 23)	26 (9, 47)	7 (2, 46)
ESR ≤10 mm/h, <i>n</i> (%)	137 (35)	0	66 (38)	22 (36)	4 (36)	10 (50)	9 (28)	8 (53)
CRP (<i>n</i> =328) (mg/l)	9 (<5, 33)	98 (36, 246)	7 (<5, 16)	14 (4, 52)	12 (5, 33)	3 (<5, 21)	7 (<5, 15)	2 (<5, 59)
Acute uveitis, <i>n</i> (%)	7 (1.6)	0	4 (1.8)	1 (1.5%)	0	2 (6.3)	0	0
Chronic uveitis, <i>n</i> (%)	10 (2.0)	0	5 (2.2)	1 (1.5)	0	1 (3.1)	1 (2.7)	0

All results presented as median (interquartile range) unless otherwise specified.

TABLE 2. Source of referral to first PRh appointment and total symptom duration in months prior to first assessment by PRh: median (IQR)

Source of referral	<i>n</i> (% of whole cohort) ^a	Symptom duration between symptom onset and referral to rheumatology care ^b	Duration from date of referral to PRh to first PRh appointment ^b	Total symptom duration ^b
Total ^a	490 (97)	3.3 (1.5, 8.1)	0.8 (0.3, 1.7)	4.7 (2.2, 9.4)
Accident and emergency	44 (9)	1.1 (0.3, 3.2)	0.3 (0, 0.9)	1.7 (0.9, 4.3)
General practitioner	85 (17)	3.8 (1.6, 11.3)	1.3 (0.8, 2.3)	5.3 (3.2, 13.7)
Orthopaedic surgeon	147 (29)	3.3 (1.7, 7.8)	1.0 (0.5, 1.9)	5.1 (2.6, 9.7)
General paediatrician	185 (36)	3.3 (1.8, 8.3)	0.6 (0.2, 1.3)	4.6 (2.3, 9.0)
Other ^c	29 (6)	5.4 (2.8, 13.3)	0.9 (0.3, 2.1)	7.5 (4.6, 14.3)
Not recorded	17 (3)	–	–	3.8 (2.6, 7.5)

^aDate and source of referral only available for 490 children. ^bDifferences between referral sources statistically significant (Kruskal–Wallis equality-of-populations rank test, $P < 0.001$). ^cIncludes plastic surgery, ophthalmology, otolaryngology, neurology, physiotherapy, adult rheumatology and direct parent referral.

TABLE 3. Association between baseline disease characteristics^a and symptom duration at first PRh assessment

	Total cohort (<i>n</i> =507)						
	Symptoms ≤4 months 228	Symptoms >4 months 279	<i>P</i> -value	Symptoms >6 months 215	<i>P</i> -value (compared with ≤4 months)	Symptoms >12 months 108	<i>P</i> -value compared with ≤4 months
Age, (yrs)	6.5 (2.9, 10.8)	7.3 (3.2, 10.9)	NS	7.4 (3.1, 11.2)	NS	6.6 (2.9, 10.3)	NS
Female, <i>n</i> (%)	141 (62)	186 (66)	NS	140 (65)	NS	68 (63)	NS
Active joint count	1 (1, 3)	2 (1, 6)	0.005	2 (1, 6)	0.006	2 (1, 8)	0.001
Limited joint count	1 (0, 2)	1 (0, 4)	0.007	1 (1, 4)	0.005	2 (1, 4)	0.009
CHAQ (0–3)	0.75 (0.13, 1.38)	0.63 (0.13, 1.5)	NS	0.63 (0.13, 1.50)	NS	0.56 (0, 1.50)	NS
Physician global assessment (0–100)	37 (20, 64)	33 (20, 56)	NS	34 (20, 58)	NS	35 (26, 57)	NS
Parent global assessment (0–100)	18 (4, 47)	20 (5, 46)	NS	20 (5, 45)	NS	21 (5, 48)	NS
Pain (0–100)	34 (6, 61)	34 (10, 60)	NS	33 (10, 57)	NS	33 (10, 60)	NS
ESR (mm/h) ^b	32 (12, 57)	14 (5, 32)	<0.001	11 (5, 30)	<0.001	8 (4, 22)	<0.001
ESR ≤10 mm/h, <i>n</i> (%)	39 (23)	98 (46)	<0.001	79 (48)	<0.001	45 (56)	<0.001
CRP (mg/l)	12 (4, 48)	7 (3, 20)	0.002	7 (0, 19)	0.0002	5 (0, 14)	<0.001
Acute uveitis, <i>n</i> (%)	4 (1.8)	3 (1.3)	NS	3 (1.4)	NS	2 (1.9)	NS
Chronic uveitis, <i>n</i> (%)	3 (1.4)	7 (2.6)	NS	5 (2.4)	NS	3 (2.9)	NS

^aResults are presented as median (interquartile range) unless stated otherwise. ^bESR available in 389 children only (174 with oligoarthritis).

examined (Table 3). Additional analysis of those children with >6 and >12 months was also performed. For the cohort as a whole, a total of 279 children (55%) had symptoms >4 months. Those with longer symptoms had higher active and limited joint counts but lower ESR and CRP compared with children with symptoms ≤4 months. Overall, 35% of the cohort had a normal ESR (defined as ≤10 mm/h) at first presentation to a paediatric rheumatologist.

However, only 22% of children with shorter symptom duration (≤4 months) had a normal ESR at presentation compared with 46% of children with longer symptoms at first presentation ($P < 0.001$). There was no difference in the predominance for either upper limb or lower limb joint involvement between those with shorter or longer total symptom duration (data not shown). There was a trend towards those children with a longer symptom

TABLE 4. Association between baseline disease characteristics^a and symptoms duration at first PRh assessment (oligoarthritis only)

	JIA: oligoarthritis only (n = 233)						
	Symptoms ≤4 months 107	Symptoms >4 months 126	P-value	Symptoms > 6 months 92	P-value (compared with ≤4 months)	Symptoms >12 months 46	P-value compared with ≤4 months
Age, (yrs)	4.3 (2.4, 8.3)	6.1 (2.7, 10.2)	0.03	6.1 (2.5, 10.3)	0.05	6.1 (3.0, 10.2)	NS
Female, n (%)	73 (68)	81 (64)	NS	58 (63)	NS	28 (61)	NS
Active joint count	1 (1, 2)	1 (1, 2)	NS	1 (1, 2)	NS	1 (1, 2)	NS
Limited joint count	1 (1, 1)	1 (0, 2)	NS	1 (1, 2)	NS	1 (1, 2)	NS
CHAQ (0–3)	0.75 (0.13, 1.25)	0.5 (0, 1.13)	0.04	0.5 (0, 1.0)	0.02	0.25 (0, 0.75)	0.0046
Physician global assessment (0–100)	29 (19, 52)	27 (10, 43)	NS	30 (10, 53)	NS	33 (21, 62)	NS
Parent global assessment (0–100)	12 (4, 43)	15 (4, 39)	NS	15 (2, 40)	NS	13 (2, 40)	NS
Pain (0–100)	30 (5, 55)	26 (10, 50)	NS	30 (10, 50)	NS	30 (6, 48)	NS
ESR (mm/h) ^b	25 (10, 42)	10 (5, 22)	<0.001	10 (4, 26)	0.0003	7 (4, 22)	<0.001
ESR ≤10 mm/h, n(%)	20 (26)	46 (48)	0.003	35 (52)	0.003	19 (56)	0.002
CRP (mg/l)	7 (1,16)	7 (0,16)	NS	7 (0, 12)	NS	7 (0, 10)	NS
Acute uveitis, n(%)	3 (2.9)	1 (0.8)	NS	1 (1.1)	NS	1 (2.2)	NS
Chronic uveitis, n(%)	2 (1.9)	3 (2.4)	NS	2 (2.2)	NS	1 (2.2)	NS

^aResults are presented as median (interquartile range) unless stated otherwise. ^bESR available in 389 children only (174 with oligoarthritis).

duration being older at symptom onset (7.3 vs 6.5 yrs) although this did not reach statistical significance. There were no significant differences in CHAQ, physician's global assessment, parent's general evaluation and pain scores between the two groups. Very few children had a diagnosis of uveitis at first presentation (7 with acute uveitis and 10 with chronic uveitis), which did not differ between those with longer and shorter symptom duration. It was not known as to how many children had been referred to an ophthalmologist prior to the first PRh consultation, but only three children had been referred directly from an ophthalmologist to PRh.

Using a multivariable logistic regression model, only ESR remained an independent factor associated with total symptom duration. In those children with a normal ESR at presentation, the odds of a total symptom duration >4 months between symptom onset and first appointment with PRh was 3.32 (95% CI 1.93, 5.69).

As some of these findings could be explained by the very short symptom duration in those children presenting with systemic JIA, a further analysis limited to those children assigned to the JIA subtype oligoarthritis, the largest ILAR subtype, was undertaken (Table 4). Again, longer total symptom duration was associated with a lower ESR at presentation (10 vs 25 mm/h; $P < 0.001$). Those children with longer symptoms were also older at symptom onset (6.1 vs 4.3 yrs; $P = 0.03$) but had a lower median CHAQ score at presentation (0.50 vs 0.75; $P = 0.04$). There was also a trend towards lower pain scores in patients with longer symptom duration at first presentation, although this did not reach statistical significance. Using a multivariable logistic regression model, the strong association between a normal ESR and longer symptom duration at presentation remained (OR 2.71; 95% CI 1.24, 5.92). In addition, the odds of longer symptom duration increased by 9% for each increasing year of age at symptom onset (OR 1.09; 95% CI 1.00, 1.19). CHAQ score was not independently associated with a longer total symptom duration (OR 0.77; 95% CI 0.45, 1.31).

Discussion

The results of this study demonstrate that many children have had a long duration of symptoms prior to first assessment by a paediatric rheumatologist, with a median total duration of 4.6 months. For >20% of children, this duration was >1 yr. An interesting association between normal ESR at presentation and longer duration of symptoms at first presentation might suggest that a diagnosis of inflammatory arthritis may not be considered in the setting of normal inflammatory markers, thus delaying a referral to specialist PRh care. The symptom duration

was shortest in those presenting with systemic JIA, presumably because these children are typically very unwell with high inflammatory markers. The longest symptom duration was seen among children with PsA. Although it is difficult to draw any firm conclusions from this observation, the possibility exists that if children are undergoing treatment for psoriasis, joint complaints may be initially overlooked.

An audit of the delay in diagnosis of inflammatory arthritis in 42 children who presented over a 12-month period in Western Australia found similar patterns to our study. The mean delay was 39.9 weeks (range 1–208 weeks) [11]. As in CAPS, Manners [11] noted that the delay to diagnosis was significantly decreased if ESR at presentation was high and the child had signs of active inflammation. They found that the factors that did not affect delay included subtype of inflammatory arthritis, the discipline of referring practitioner, age at disease onset, presence of ANA, HLA-B27, RF, visible swelling of joints, involvement of any particular joint, number of joints and place of residence (rural vs urban).

One limitation of this study was the accuracy with which the date of symptom onset was recorded. It has been shown that the ability of adults to recall the date of symptom onset becomes less reliable with time since symptom onset [12], and therefore, is likely to be most accurate for those with a very short duration. In addition, for younger children, the date of symptom onset was provided by the parent, who may have had difficulty in assigning an accurate date. This may have affected our estimated median symptom duration, although most likely this would have affected the extremes of the estimates, for which the median would be least affected. Our study is also limited by the lack of details regarding the features present in the child when the disease first manifested, and therefore, those presenting symptoms recorded in the CAPS database may not necessarily be an accurate reflection of how ill the child was in the early days/weeks of the disease. It is therefore possible that certain characteristics, such as ESR, may have been affected by interventions or therapies received before rheumatology care, particularly if these children with a longer symptom duration had received care by other medical specialists first. However, this is unlikely to be the case for such a large proportion of the cohort. For many of these children, they may have been symptomatic for a significant length of time even before the parent sought primary care. Delay in presenting to medical care after onset of symptoms may arise because onset can be insidious and signs and symptoms can be non-specific and parents may be unaware of the severity of the problem. Other factors, such as socio-economic status, may also influence this delay and could be analysed in further studies.

Delays in referral to PRh may also occur after the child enters medical care. Three published case reports describe children in which diagnosis of inflammatory arthritis was delayed because of non-recognition of early symptoms by parents and physicians [11]. UK trainees in paediatrics and primary care have reported low self-confidence in their ability to assess a child's musculoskeletal system and poor documentation of musculoskeletal assessment possibly as a result of inadequate training in rheumatology [13]. Based on the adult Gait, Arms, Legs, Spine screen, a musculoskeletal screening examination for children (pGALS) has now been developed, which could be used to improve paediatric clinical rheumatology skills [14]. Therefore, the delay will consist in both the parent and child recognizing the illness, and subsequently, the appropriate referral being made. A Brazilian study found that a mean of 3.6 physicians (range 1–20) were consulted between onset of symptoms and first consultation with paediatric rheumatologist, with a time interval ranging from a few days to 10 yrs (mean 1.4) [15]. More recently, a UK study also found that children with JIA had been referred to a median of 3 (0–5) medical specialists prior to consultation with PRh. Despite this, most children had untreated active disease at presentation and no child had been referred for an ophthalmological assessment [16]. In our study, the longest delay occurred in those children who were referred from routes other than general or musculoskeletal care. Once referral was made, however, most children were seen within 4 weeks, according to ARMA standards.

Overall, we found that those children with the most severe disease presented earlier and as a result, we could not demonstrate a significant detrimental effect of prolonged symptom duration prior to the first PRh visit. It is possible that those children with the longest symptom duration had received at least some appropriate treatment elsewhere. However, all children still had some evidence of active disease at the time of this first consultation, suggesting that any prior treatment had not been definitive. What this study has not yet shown is whether or not this 'delay' in reaching a paediatric rheumatologist will have long-term detrimental effects. When 683 Italian children with JIA were followed for 10 yrs, the probability of attaining remission decreased in proportion to delay in entering tertiary care [17]. Children referred within 1 yr from disease onset had a statistically significant higher remission rate than children referred 1–5 yrs or >5 yrs of onset (35.7, 32.4, 22.8, respectively, $P=0.0124$). Further follow-up of our cohort will address this issue in the future.

In conclusion, this analysis has demonstrated that many children subsequently diagnosed with inflammatory arthritis have a significantly long period of symptoms prior to referral to specialist care. Children with distinct signs and symptoms were referred more quickly, particularly in the setting of raised inflammatory markers. This is of concern as institution of appropriate medical therapies and referral for ophthalmological assessment may therefore be delayed, possibly resulting in poorer long-term outcomes such as irreversible joint deformity and subsequent functional loss. Increased public awareness of this condition as well as improvements to musculoskeletal training for physicians may reduce the time taken to initial contact by patients with the medical system as well as expedite appropriate referrals. The strength of CAPS lies in its design. As a prospective inception cohort of children presenting with inflammatory arthritis to PRh, the influence of this 'delay to presentation' as well as other disease- and treatment-related factors on outcome can be fully assessed. Recruitment and follow-up of children to CAPS continues.

Rheumatology key messages

- Many children with inflammatory arthritis have a significantly long period of symptoms prior to referral to rheumatology.
- Normal blood tests, including ESR, do not preclude the diagnosis of inflammatory arthritis.

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