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Joint hypermobility syndrome in childhood. A not so benign multisystem disorder?

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***Objectives*. Joint hypermobility (JH) or 'ligamentous laxity' is felt to be an underlying risk factor for many types of musculoskeletal presentation in paediatrics, and joint hypermobility syndrome (JHS) describes such disorders where symptoms become chronic, often more generalized and associated with functional impairment. Clinical features are felt to have much in common with more severe disorders, including Ehlers–Danlos syndrome (EDS), osteogenesis imperfecta and Marfan syndrome, although this has not been formally studied in children. We defined the clinical characteristics of all patients with joint hypermobility-related presentations seen from 1999 to 2002 in a tertiary referral paediatric rheumatology unit.**

***Methods*. Patients were identified and recruited from paediatric rheumatology clinic and ward, and a dedicated paediatric rheumatology hypermobility clinic at Great Ormond Street Hospital. Data were collected retrospectively on the patients from the paediatric rheumatology clinics (1999–2002) and prospectively on patients seen in the hypermobility clinic (2000–2002). Specifically, historical details of developmental milestones, musculoskeletal or soft tissue diagnoses and symptoms, and significant past medical history were recorded. Examination features sought included measurements of joint and soft tissue laxity, and associated conditions such as scoliosis, dysmorphic features, cardiac murmurs and eye problems.**

***Results*. One hundred and twenty-five children (64 females) were included on whom sufficient clinical data could be identified and who had clinical problems ascribed to JH present for longer than 3 months. Sixty-four were from the paediatric rheumatology clinic and 61 from the hypermobility clinic. No differences were found in any of the measures between the two populations and results are presented in a combined fashion. Three-quarters of referrals came from paediatricians and general practitioners but in only 10% was hypermobility recognized as a possible cause of joint complaint. The average age at onset of symptoms was 6.2 yr and age at diagnosis 9.0 yr, indicating a 2- to 3-yr delay in diagnosis. The major presenting complaint was arthralgia in 74%, abnormal gait in 10%, apparent joint deformity in 10% and back pain in 6%. Mean age at first walking was 15.0 months; 48% were considered 'clumsy' and 36% as having poor coordination in early childhood. Twelve per cent had 'clicky' hips at birth and 4% actual congenital dislocatable hip. Urinary tract infections were present in 13 and 6% of the female and male cases, respectively. Thirteen and 14%, respectively, had speech and learning difficulties diagnosed. A history of recurrent joint sprains was seen in 20% and actual subluxation/dislocation of joints in 10%. Forty per cent had experienced problems with handwriting tasks, 48% had major limitations of school-based physical education activities, 67% other physical activities and 41% had missed significant periods of schooling because of symptoms. Forty-three per cent described a history of easy bruising. Examination revealed that 94% scored $\geq$4/9 on the Beighton scale for generalized hypermobility, with knees (92%), elbows (87%), wrists (82%), hand metacarpophalangeal joints (79%), and ankles (75%) being most frequently involved.**

***Conclusions*. JHS is poorly recognized in children with a long delay in the time to diagnosis. Although there is a referral bias towards joint symptoms, a surprisingly large proportion is associated with significant neuromuscular and motor development problems. Our patients with JHS also show many overlap features with genetic disorders such as EDS and Marfan syndrome. The delay in diagnosis results in poor control of pain and disruption of normal home life, schooling and physical activities. Knowledge of the diagnosis and simple interventions are likely to be highly effective in reducing the morbidity and cost to the health and social services.**

KEY WORDS: Joint hypermobility, Benign joint hypermobility syndrome, Heritable disorders of connective tissue, Mechanical pain.

Children possess an inherently greater range of motion in their joints than adults, with a gradual reduction in this range observed with age [1, 2]. The prevalence of hypermobility in children as a phenomenon [as opposed to joint hypermobility syndrome (JHS), i.e. symptomatic hypermobility] has been measured in a number of studies previously and, depending on the age or ethnicity of the study population or the inclusion criteria, has been reported to be between 2.3 and 30% [2–8]. Such high prevalence rates imply that hypermobility as a measured phenomenon in a significant majority of children will not normally lead to symptoms requiring medical attention. There are a number of studies that show the association between benign joint hypermobility syndrome and chronic health complaints in adults. Whilst arthralgia and chronic regional pain were the predominant symptoms, there

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were numerous extra-articular manifestations with dysautonomia and peripheral neuropathy, hernia and uterine/rectal prolapse, depression and anxiety, and chronic pain syndromes, to name a few [9, 10]. Numerous extra-articular manifestations of JHS have been similarly reported in children, including but not limited to chronic constipation and encopresis, enuresis and urinary tract infections (UTI), higher skin extensibility, lower systemic blood pressure, lower bone quantitative ultrasound measurements, chronic fatigue syndrome, temporomandibular joint disease, fibromyalgia, and gross motor developmental delay [11–14]. These studies also reported association between joint hypermobility and musculoskeletal disorders in children, whilst others did not find such a relationship [15].

The aim of this study was to characterize the historical and current clinical profile of a cohort of children with symptomatic joint hypermobility who had been referred to a paediatric rheumatology tertiary referral centre.

Methods

Study design and setting

The study was carried out in the outpatients and inpatients facilities of a paediatric rheumatology unit at a tertiary referral centre. The patients were recruited from two sources. The first group were the patients referred by general paediatricians or general practitioners, paediatric and adult rheumatologists, orthopaedic surgeons, physiotherapists, and the patient's own family to a dedicated hypermobility clinic at Great Ormond Street Hospital (GOSH), for whom data were collected prospectively (2000–2002). The second group of patients was identified by conducting searches in the electronic databases of the paediatric rheumatology department at GOSH. The latter group had been cared for in other paediatric rheumatology clinic or ward, and the relevant information was collected through review of their hospital case-notes (1999–2002).

Patients and case ascertainment

Inclusion criteria consisted of age <18 yr, the presence of joint hypermobility diagnosed by a consultant paediatric rheumatologist, and adverse symptom(s) related to the hypermobile joint(s). Patients were excluded if they were known or considered to have any other pathological condition with hypermobility as a known feature (e.g. specific collagen disorders, chromosomal abnormalities, metabolic disease), or if there was coexisting rheumatological illness which could account for at least some of their musculoskeletal symptoms.

Data collection and analysis

For the prospective cohort, relevant patient and family history was systematically sought by the use of a study questionnaire, and details of a complete systematic examination, including the musculoskeletal system, were similarly recorded on the study data collection sheets. Joint hypermobility was looked for in all of the possible joints, and the details of Beighton score [16] were recorded. For the retrospective cases, the same study questionnaire was completed using patient case-notes. Furthermore, information regarding previous referrals, diagnoses and treatments were enquired about and included. The management plan and interventions were similarly recorded and where patients were followed up for their hypermobility problem the response to intervention was sought and documented.

For statistical analysis the Stata™ 8.2 software program (Stata, College Station, TX, USA) was used. To compare the prevalence of congenital dislocatable hip (CDH), UTI, urinary tract dysfunction (vesico-ureteric reflux) and inguinal hernia with that of the normal population, 95% confidence intervals (CI) around the proportions in our cohort were calculated. The difference was deemed significant if the previously quoted rates were not within this interval. For comparing the median age of the cases with lower back pain with the cases without lower back pain, non-parametric tests were used. Similarly, to test the hypothesis that the degree of hypermobility varies with age, individual Beighton scores were calculated. The cases were divided into four age groups (Fig. 3) and non-parametric tests (Kruskal–Wallis) were used to compare the median for the Beighton score in each age subgroup.

Approval was obtained from the hospital's ethics committee, and all patients' parents/guardians were required to give informed consent to be included in the study.

Results

One hundred and eighty-nine patients were assessed for inclusion in the study, of whom 125 satisfied the inclusion criteria. All of the patients' parents/guardians who were approached to take part in the study agreed to join. For the majority of the patients complete data were available for all variables. However, in some cases part of the questionnaire was not answered, or, in the retrospective cases, some data were not available. As a result, where relevant, numbers are expressed as the fraction of available cases. Table 1 summarizes the demographic characteristics in this cohort. This was a predominantly Caucasian patient group, with a slight female majority. The 'Other White' category consisted of two Middle Eastern Arabs, one Egyptian, one Moroccan, one Iranian, one Turk and two Greek Cypriots. The 'Mixed' category included one Anglo-Mauritian, one Anglo-Pakistani, one Caucasian-Afro-Caribbean, two Caucasian-Moroccans and three Caucasian-unknowns. The median assessment age for the purposes of this study was one of mid-childhood to later childhood. The anthropometric data are summarized in Fig. 1, with height and weight distributions similar to that of a normal reference population. The bulk of the referrals (73.6%) were made by the children's general paediatrician or practitioner, but in only <10% (9/92) of cases was hypermobility given by them as the cause of symptoms (Table 2).

Table 3 illustrates the age characteristics of this cohort in relation to symptom onset, diagnosis and referral. In the majority there was a significant time lapse between the onset of symptoms and the establishment of hypermobility as the cause, whilst this interval is much shorter when comparing age at diagnosis with age at first attendance at the paediatric rheumatology facilities.

Table 1. Demographics and patient characteristics of 125 patients with benign joint hypermobility syndrome

	Number (%)
Gender	
Female	67 (54)
Male	58
Ethnicity	
Caucasian	99 (79)
Other White	8 (6)
South Asian	6 (5)
Afro-Caribbean	3 (2)
Oriental	1 (1)
Mixed	8 (6)
Median age at assessment (range)	12 (3–17) yr
Assessment setting	
Paediatric rheumatology clinic	64 (51)
Hypermobility clinic	61

Table 4 summarizes other associated clinical characteristics in this patient group. Clumsiness and poor coordination, easy bruising, clicky joints and family history of significant or problematic joint laxity were reported most frequently. Family history of joint laxity in a first degree relative included nine fathers, 18 mothers, five parent pairs, 15 parent–sibling pairs, three parents–sibling trios and seven siblings. This history was also present in 24 second-degree relatives. The mean age of first walking in this cohort was 15.0 months (range 8.5–36.0), which is considerably later than the usual average age reported in most populations, which is between 11 and 12 months [17].

The prevalence of CDH was 4.8% (95% CI 1.6–10.8%), significantly higher in this cohort than the 1% reported in the normal population [18]. The proportions having a history of UTI were measured in each gender. The mean for the females was 13.2% (95% CI 5.5–25.3%) and that for males was 6% (95% CI 1.2–16.2), both significantly greater than the rates in normal population: 1% for boys and 2–5% for girls [19].

Other clinical history, such as inguinal hernia (4%, 95% CI 1–9.8%) and urinary tract dysfunction (4%, 95% CI 0.6–8.6%), although possibly increased in occurrence amongst our cohort, did not reach significance when compared with rates (1–2 and 1%, respectively) in the normal population [20], perhaps as a result of small numbers. When other medical history was sought, there were 12 cases (10%) with asthma. This parallels the prevalence of this disorder (12–24%) amongst the source paediatric population [21].

Joint pain followed by coordination problems and reduced joint movement range, were the most common presenting features in this patient group (Table 5). Knees and ankles were the most frequently reported joints with adverse symptoms. Although pain in the spine was recorded in 23 patients, this was a major presenting complaint in only seven (5.6%). The median age of patients with lower back pain was significantly higher than that of cases free of back pain (9.0 *vs* 6.0 yr, $P = 0.04$).

Exercise-related pain and anterior knee pain were reported with disproportionately greater frequency than any other symptoms in this cohort (Table 6), whilst joint swelling and back and foot pains came next in frequency. In all of the cases reporting exercise-related pain, the pain occurred within 24 h of activity. Immediate postexercise pain was reported in 52/80, with 47/80 and 40/80 reporting late evening and morning after pain, respectively. Joint stiffness was present in almost one-third, and among the 41 reporting joint swelling 18 also reported joint stiffness. One-third also reported sleep disturbance due to musculoskeletal symptoms. More than half of patients reported missing school, and a similar

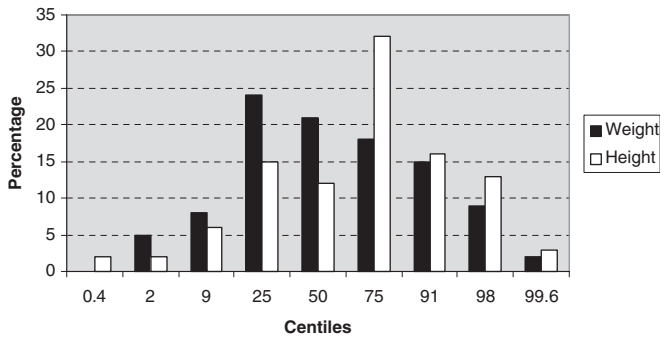

FIG. 1. Percentage of cases for height and weight centiles. The anthropometric measurements in this cohort followed nearly those of their source population.

TABLE 3. Ages at onset, first attendance and diagnosis (yr)

	Mean	Median	Range
Age at onset	6.23	6.50	0.5–15.0
Age at diagnosis	8.95	9.29	1.75–18.75
Interval symptoms–diagnosis	2.75	2.29	0.1–12.66
Age at first attendance	8.39	8.90	0.6–16.5

TABLE 4. Associated clinical history in proportions of cases where this information was available

Associated clinical feature	Proportion (%)
Congenital dislocatable hips (CDH)*	4/103 (3.9)
Clicky hip	12/103 (12)
Walked after 15 months	19/57 (33)
Poor coordination	30/86 (36)
Clumsy	44/92 (48)
Learning difficulty	13/91 (14)
Dyslexia	2/88 (2)
Dyspraxia	6/87 (7)
Hernias	4/101 (4)
Constipation	9/85 (11)
UTI	
Females*	7/53 (13)
Males*	3/51 (6)
Urinary tract dysfunction (Vesico-ureteric reflux 3, urge-incontinence 1)	4/99 (4)
Heart murmur	5/104 (5)
Easy bruising	39/91 (43)
Clicky joints	25/84 (30)
Joint laxity in 1° relative	57/90 (63)

*Significantly higher result than for normal population.

TABLE 2. Referral details and the number of cases

Who requested referral	Cases in which hypermobility was noted *n* (%)	Joint hypermobility recognized as cause of symptoms *n* (%)	Who referred patient to paediatric rheumatologist/hypermobility clinic *n* (%)
Paediatric rheumatologist	71 (57)	85 (68)	2 (2)
Adult rheumatologist	3 (2)	6 (5)	9 (7)
General paediatrician	8 (6)	8 (6)	48 (38)
Orthopaedic surgeon	4 (3)	4 (3)	3 (2)
Other specialist	7 (6)	4 (3)	10 (8)
General practitioner	2 (2)	1 (1)	44 (35)
Therapist (external)	4 (3)	2 (2)	–
Family	19 (15)	7 (6)	–
Other	2 (2)	2 (2)	–
Unknown	5 (4)	6 (5)	9 (7)
Total	125 (100)	125 (100)	125 (100)

The first column includes details of who requested the referral; the last column shows who actually made the referral.

proportion did not take part in physical education on a regular basis because of the symptoms.

Tables 7 and 8 demonstrate the extent to which investigations and treatment had been carried out prior to treatment. With the exception of plain radiographs revealing anatomical abnormalities (two scoliosis, one dysplasia, one bifid rib and one transitional L5 vertebra), the majority of these investigations were either normal or reported an incidental and transient abnormality. Reported abnormalities on MRI scan consisted of possible discitis at multiple spinal levels, mild gluteal wasting, and subdural haemorrhage without any evidence of blood vessel aneurysm, in one case each. Positive bone scintigraphy results included mild increased tracer uptake at the third lumbar vertebra, and an ankle, in two separate cases. Amongst other investigations were karyotype and specific gene testing (fragile X, Marfan syndrome, hereditary sensorimotor neuropathy and Beckwith–Wiedemann syndrome), skin and muscle biopsy, pH-probe and barium meal, electromyography and nerve conduction studies, echocardiography and various urine and blood metabolic screens, the results of which were all normal. Non-steroidal anti-inflammatory drugs (NSAIDs) and paracetamol were the two most frequently used medications, only 21/51 patients reporting any benefit from NSAIDs. Steroid courses and sulphasalazine were used in four separate cases, without obvious benefit.

Many patients had seen local therapists prior to their referral. This included physiotherapy in 49%, occupational therapy in 13% and podiatry in 11%.

Pain on examination was elicited most frequently in the knees, ankles and hips, in that order, these joints also featuring as having the highest rate for increased movement range (Table 9). The joint movement range was most frequently decreased in the thoracolumbar region. The Beighton score at assessment was used as a measure of hypermobility. The distribution of the Beighton score was skewed towards the higher range and is presented in Fig. 2. There was a predilection for the three highest categories, 61/90 cases scoring ≥ 7. In the majority of patients without a formal Beighton score, the presence or absence of ability to perform forward bending (to put the hands on the floor) was the item omitted. In order to assess if hypermobility was highest at any age, the cases were divided into four age groups (Fig. 3) and the medians for the Beighton scores were compared. The trend seems to be that of decreasing score with age, although there was an increase in the 'pubertal' age quartile. Using non-parametric tests for the equality of the populations (Kruskal–Wallis test), the latter age group was not any different in Beighton score compared with the rest of the cases (median 7.3 for both, $\chi^2 = 0.021$ with 1 degree of freedom, $P = 0.88$), nor was there any significant difference in this variable between the four age groups ($\chi^2 = 6.3$ with 3 degrees of freedom, $P = 0.08$).

Table 10 summarizes the associated clinical findings of this study group. The majority of the cases had pes planus, with muscle weakness as the next common finding. Furthermore, muscle wasting was evident in more than a quarter of cases where this was assessed. Of those cases with Marfanoid body habitus, 7/10 had arachnodactyly and two had a heart murmur. The majority of the cases with high-arched palate (4/5) and pectus carinatum (2/3) were not Marfanoid, although the numbers were very small.

Table 5. Main presenting complaints in 125 cases with JHS

Major presenting complaints	Number (%)	Main joints complained of	Number (%)
Arthralgia	92 (74)	Knees	82 (66)
Back pain	7 (6)	Ankles	33 (26)
Problems with gait, falls, coordination	13 (10)	Spine	23 (18)
		Hips	11 (9)
Reduced joint movement range	12 (10)	Elbows	11 (9)
		Shoulders	8 (6)
Problems with handwriting	4 (3)	Feet	5 (4)
Clicky hips	3 (2)		

Table 7. Investigations performed prior to referral and diagnosis

Investigations	Number (%)	Number with abnormality (%)
Plain radiographs, MRI	46 (37), 10 (8)	5 (11), 3 (33)
Inflammatory markers (ESR/CRP)	65 (52)	3 (5) mildly-elevated
Full blood count	68 (54)	2 (3)
Nucleotide bone scan	8 (6)	2 (25)
Autoantibodies	24 (19)	1 (4) ANA 1:40

Table 8. Treatment received before being seen by the paediatric rheumatologist

Medications/treatment	Number (%)
NSAIDs	51/102 (50)
Sulphasalazine	2/102 (2)
Paracetamol	37/90 (41)
Steroids	2/102 (2)
Physiotherapy	37/94 (39)
Hydrotherapy	11/110 (10)
Occupational therapy	15/112 (13)
Podiatry	13/114 (11)

The proportions for which this information was available are shown.

Table 6. Clinical symptoms and associated features in the proportions of cases for whom this information was available

Clinical symptom/feature	Proportion (%)	Associated symptom/feature	Proportion (%)
Joint swelling	41/107 (38)	Pain exacerbated by exercise	80/99 (81)
Back pain	46/116 (40)	Pain exacerbated by infection	30/83 (39)
Joint sprains	21/110 (19)	Infection at beginning of symptoms	22/86 (26)
Foot pain	37/110 (34)	School missed	42/102 (41)
Anterior knee pain	85/116 (73)	Problems at school	21/88 (24)
Dislocation/subluxation episodes	12/116 (10)	Handwriting problems	42/106 (40)
'Growing pains' diagnosed	32/98 (33)	PE missed	49/103 (48)
Sleep disturbance	41/111 (37)	Sport hobbies	35/52 (67)
Joint stiffness	31/103 (30)	Wheelchair/crutches used	27/107 (25)
Diffuse musculoskeletal pain	15/107 (14)	Benefits applied for	12/69 (17)
Pain amplification	25/121 (21)	Benefits received	7/69 (10)

PE, physical education.

TABLE 9. Joint examination results in proportions of cases where this information was available

Joints	Pain on examination (%)	Swollen (%)	Joint range of movement		
			Increased (%)	Decreased (%)	Normal (%)
Hips	23/118 (20)	–	75 (60)	5 (4)	28 (22)
Knees	48/119 (40)	12/121 (10)	102 (82)	3 (2)	6 (5)
Ankles	29/119 (24)	7/122 (6)	77 (62)	2 (2)	24 (19)
Subtarsal	8/116 (7)	0	74 (59)	1 (1)	26 (21)
Tarsal	9/87 (10)	0	–	–	–
Toes	8/116 (7)	–	66 (53)	0	31 (25)
Cervical spine	10/117 (9)	–	58 (46)	0	42 (34)
Thoracolumbar spine	13/118 (11)	0	60 (48)	6 (5)	39 (31)
Shoulders	10/118 (9)	0	64 (51)	0	37 (30)
Elbows	14/117 (12)	1/122 (1)	97 (78)	0	14 (11)
Wrists	15/117 (13)	1/122 (1)	89 (71)	0	19 (15)
MCPs	14/117 (12)	0	97 (78)	0	11 (9)
PIPs	12/117 (10)	0	81 (65)	0	22 (18)
DIPs	3/117 (3)	0	74 (59)	0	29 (23)
Thumbs	10/117 (9)	0	90 (72)	0	14 (11)
TMJ	3/89 (3)	–	–	–	–

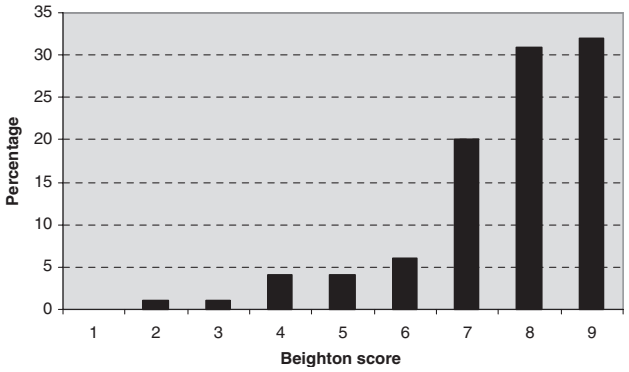

FIG. 2. Frequency and percentage of cases categorized by their Beighton score. Whilst inclusion in the study did not require more than 1 joint to be involved, the majority of the cases had high scores.

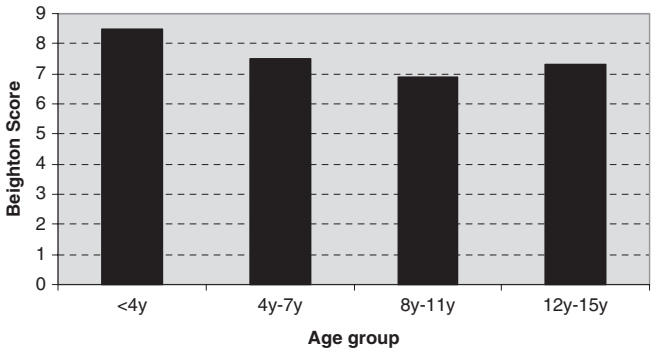

FIG. 3. Beighton score by age groups. The groups were not significantly different in terms of hypermobility score.

Limited information was available at the time of reporting this cohort regarding subsequent management and referrals. Fourteen patients required inpatient hospital admission and an intensive rehabilitation programme. Formal physiotherapy and home exercise programme have been documented in 69 and 86 cases, respectively; 51 reporting definite improvement. The basis of the physical therapy was a very gradual reconditioning and re-establishment of normal muscle power, by means of isometric exercises, and power building activities. Where joint contractures and loss of movement range were encountered, appropriate splints alongside stretching (active and passive) exercises were carried out to improve mobility. Of 43 cases referred for podiatry evaluation and management, 27 reported some benefit, whilst 13 denied any improvement (three were awaiting foot orthoses).

TABLE 10. Associated clinical features on examination in the proportion of cases where this information was available

Clinical feature	Number (%)
Mild dysmorphic features	7/121 (6)
Marfanoid habitus	10/120 (8)
Arachnodactyly	7/120 (6)
Pectus excavatum	2/123 (2)
Pectus carinatum	3/123 (2)
High arched palate	5/60 (8)
Abnormal bruising	24/117 (21)
Abnormal scarring	15/116 (13)
Skin distensibility increased	27/87 (31)
Heart murmur	7/119 (6)
Blue sclerae	2/72 (3)
Gait abnormal	17/113 (15)
Scoliosis	10/118 (9)
Pes planus	88/99 (89)
Weakness	41/106 (39)
Muscle wasting	27/106 (26)

Discussion

The aim of this study was to characterize the historical clinical referral patterns, investigation details and treatment in a paediatric cohort with symptomatic joint hypermobility.

This cohort contains cases with more severe end of the spectrum of JHS. It represents an important group of children whose persistent symptoms and loss of function have caused a great deal of anxiety amongst both family and the health professionals, requiring the utilization of significant time and resources. Their demographic and anthropometric characteristics are not dissimilar from their normal source population (Table 1 and Fig. 1). Referral patterns and the time delay between symptom onset and paediatric rheumatologist assessment suggest that in most cases a timely connection between symptomatology and the hypermobility as a

cause was not established. In contrast, the short interval between referral date and identification of joint hypermobility as the cause for their adverse symptoms indicates that this diagnosis can be readily made in the clinical setting, provided that the required skill and knowledge are present. Indeed, historical features of this symptom complex (e.g. its intimate relationship with physical activity and its characteristic worsening after exercise), along with the findings on thorough clinical examination, are sufficient in nearly all cases to make the correct diagnosis. This obviates the need for the costly, sophisticated and mostly unnecessary investigations meted out to many children in this series.

Clumsiness, poor coordination and late walking represent difficulties with fine and gross motor development and may be related to the central nervous system or proprioceptive control. The relatively high rate of learning difficulties, dyslexia and dyspraxia also suggests possibility of central nervous system involvement in this condition, although in the absence of scientific evidence these observations should merely serve to suggest areas for future research. The rates for CDH and UTI were significantly higher amongst this cohort, whilst for hernia, urinary tract dysfunction and heart murmur the results did not reach significance, possibly as a consequence of insufficient case numbers. These observations suggest that, in addition to the more obvious musculoskeletal features in joint hypermobility, other organ systems are clearly involved, a finding also reported by others in hypermobile adults and children [22, 23]. Boys with generalized joint hypermobility have been found to have constipation almost five times as often and faecal soiling twice as often as controls, whilst urinary incontinence and infections were more prevalent in girls with this condition [24]. Others showed higher skin extensibility, lower quantitative ultrasound measurements in bones, and significantly increased urinary excretion of collagen degradation products compared with the reference group [25]. The collagen content of the umbilical cords from newborns with CDH was reduced in comparison with controls, and the collagen III/I ratio was increased. Mutations in the fibrillin genes are found in a proportion of Marfan syndrome and congenital contractural arachnodactyly [26] and several mutations in collagen genes have been described in osteogenesis imperfecta [27], two conditions sharing overlapping clinical features with JHS [16, 28] as well as an autosomal dominant mode of inheritance. There were many shared clinical features between our cohort and other heritable disorders of connective tissue (HDCT), although such characteristics (e.g. blue sclerae, arachnodactyly) were not uniformly present in every case. Such heterogeneity in the phenotype may be explained by gene polymorphism, incomplete expression and/or penetrance, not dissimilar to other HDCTs. A family history of joint laxity in the first-degree relatives was present in 63% of our cohort. In addition, there were 24 (27%) second-degree relatives with this history and a significant number of kindreds. These findings favour a dominant mode of inheritance.

One of the main characteristics in the reported symptoms from this group is its intimate association with exercise. Although joint stiffness was reported in a minority, resting relieved the symptoms. This is in contrast to the inflammatory rheumatological conditions where resting or inactivity promotes 'gelling' or stiffness. Exercise-induced pain is not exclusive to the 'mechanical' conditions, however, and may be observed in the inflammatory condition, e.g. juvenile idiopathic arthritis. Similar in these two conditions is perhaps disuse atrophy in the muscles, which may also explain at least some of the coordination problems encountered in our cohort. Repetitive pain-related muscular inhibition can result in reduced muscle bulk, with resultant muscle deconditioning and loss of movement range in joints. Furthermore, loss of motion at certain joints or areas is seen (especially lumbar spine, but also tendo-achillis or gastrocnemii), which may represent post-traumatic response or an 'adaptive postural stabilizing' response. Tenderness and pain on examination is an important finding, implying that such a feature does occur in JHS (as it does in inflammatory arthritides) and may occur for many reasons, such as tissue sensitivity, recent sprain/strain injury, or an exaggerated perceived discomfort. Another aspect of reduced exercise tolerance is the impact on play and social activities. A significant proportion of our group did not engage in routine exercise, such as physical education at school. Indeed, a significant number did not attend school altogether, this adding support to our observation regarding the profound impact of this condition on the child's function. In addition, pain amplification was perceived to be present by the clinician in 21% of the cases. The relationship between joint hypermobility and chronic pain is well known and has been frequently reported [29–31].

Joint hypermobility is common in children, although in a small proportion it may manifest as pathology, resulting in morbidity and loss of function. It is of great importance to promote the knowledge of this common condition at all levels of health-care provision. Further research into the genetic aspects of this disorder will aid with prognosis and in the counselling of families. Finally, the variable response rate to physiotherapy, occupational therapy and podiatry seen amongst this cohort highlights the heterogeneity of the condition, and calls for the pressing need to conduct well-designed prospective therapeutic trials.

The authors have declared no conflicts of interest.

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