Where do people with Joint Hypermobility Syndrome present in secondary care? The prevalence in a general hospital and the challenges of classification.

May To, Jane Simmonds and Caroline Alexander

Word count: xxx

May To

Department of Therapies,

Charing Cross hospital

Fulham Palace road

London W6 8RF

0203 311 7844

may.to09@imperial.ac.uk

Dr Jane Simmonds

Institute of Child Health

30 Guilford Street

London WC1N 1EH

0207 905 2187 (ext 42187)

jane.simmonds@ucl.ac.uk

Dr Caroline Alexander

Department of Physiotherapy,

Charing Cross hospital

Fulham Palace road

London W6 8RF

0203 3111337

caroline.alexander@imperial.ac.uk

Keyword:

Joint hypermobility syndrome

Beighton score

Brighton criteria

Abstract

Aim

Joint Hypermobility Syndrome (JHS) is an inherited disorder of the connective tissue and can lead to widespread pain, joint instability and fatigue. In order to understand where patients with musculoskeletal symptoms and JHS present to secondary care we have established the prevalence of JHS within the pain management service, a general rheumatology clinic and an orthopaedic clinic of a single general hospital.

Method

A total of 138 patients attending the pain management service, a general rheumatology clinic and an orthopaedic clinic were surveyed for Joint Hypermobility Syndrome as part of their usual care using the Brighton criteria.

Results

The pain management and general rheumatology clinics both demonstrated a similar prevalence of 39.1% and 37.0% respectively. The orthopaedics clinic demonstrated a much lower prevalence of 10.9%.

Conclusion

There were a higher number of people with JHS presenting to the pain management and general rheumatology clinics than the orthopaedic clinic. This reflects an appropriate pathway for this multiple joint pathology. The difficulty in classifying people with JHS is discussed as these figures may reflect an over classification of the condition.

Introduction

Joint Hypermobility Syndrome (JHS) is an inherited disorder of the connective tissue. The common feature is pain but as this is a disorder of collagen that occurs throughout the body it has features such as varicose veins, uterine or rectal prolapse, hernias(1), cardiovascular, pulmonary, gastrointestinal and gynaecological problems (2). More surprising characteristics such as disturbances to pain perception (3;4), anxiety (5), fatigue (6) and osteoporosis (7) are also seen. Regarding the physical features, the spectrum is broad, with some people suffering very few symptoms and others with chronic long-standing joint pain, subluxations/dislocations, sprains, clumsiness and problems with activities ranging from sport to even simple writing tasks (8).

Classifying JHS is difficult because, unlike other hypermobility syndromes there are no specific genetic tests that define the syndrome (2). Further, there is some confusion as JHS may be the same condition as Ehlers Danlos Syndrome – Hypermobility Type (EDS-HT) formerly called Ehlers Danlos Syndrome – Type III (9). To add to the confusion, JHS has an asymptomatic counterpart that has been termed Generalised Joint Hypermobility (GJH). Classification is therefore important. The Beighton score is often

used to assess the degree of general joint flexibility, measuring specific areas of joint hypermobility. It is recognised as a somewhat crude scale but was originally designed as a quick tool to identify hypermobility in population studies (10;11). There are some disagreements as to the cut off score, which varies with age (12-15), but commonly a score of 4 or more out of 9 joints represents GJH in adults (16). Joint Hypermobility Syndrome is further classified using either the Brighton Criteria (17) or Villefranche Classification (Table 1). These classifications have the Beighton score embedded and also determine signs and symptoms commonly recognised as part of the syndrome. The Brighton criteria was originally designed in recognition of the extra articular features of joint hypermobility syndrome (Grahame et al., 2000), however its validity has been questioned (11). The Villefranche Classification focuses upon features of inheritance and was developed to identify EDS-HT; the Brighton Criteria focuses upon signs and symptoms and is used to classify JHS. The Brighton criterion has two major and eight minor criteria; one of the major criterion is a score of four or more using the Beighton score with the other major criterion being arthralgia for longer than three months in four or more joints. Joint Hypermobility Syndrome is classified based on two major criteria or one major criterion and two minor criteria or four minor criteria being fulfilled.

Up to 10% of a western population has GJH (18), with a declining prevalence with increasing age (19;20), a higher prevalence amongst women (20) and some ethnic groups (21). For example, the prevalence rises to 35% of males and 57% of females in a rural Nigerian population (22). With the JHS' population, the prevalence is estimated to be between 0.75% and 2% (23), but it has been reported to be as high as 45% of all people referred to rheumatologists (24) and 30% of all people referred to a British musculoskeletal triage clinic (25). This can vary with ethnicity (26), for example 55% of Omani women presenting to a woman's musculoskeletal physiotherapy service had JHS (27), and non-Caucasian women were diagnosed twice as frequently as Caucasian women in a UK general rheumatology clinic (24).

Discussions regarding the classification of JHS is a timely issue. Scheper *et al* (2015) (28) have set out a number of challenges that relate to phenotyping JHS and its difference to GJH. The reported numbers of people with JHS in musculoskeletal services would suggest that recruitment to such studies should be

straight forward. To assist our recruitment strategy we undertook a local survey to understand where people with JHS are referred within our secondary care setting. This was particularly relevant as our Consultant Rheumatologists' impression was that the prevalence of JHS was lower than suggested in the literature within our general rheumatology clinics. Therefore, our aim was to establish the prevalence of JHS within the pain management, general rheumatology and an orthopaedic lower limb clinic, in order to target our recruitment to future trials effectively.

Method

A sample size of 101 people was calculated, based upon the assumption that the proportion of JHS within our clinics will be between 15% and 25% of the population. The first author, a senior physiotherapist with a special interest in JHS and experience of using the Brighton Criteria attended outpatient services run by the pain management, general rheumatology and orthopaedic lower limb clinics in one general hospital. The hospital is part of a group of hospitals in North West London, UK. Thirty clinics in total were attended between October 2013 and September 2015. As a normal part of the patients' care the attendees were assessed for the presence of JHS using the Brighton Criteria noting the classification of the number of major and minor criteria. The percentage of attendees who had JHS was then recorded for each clinic.

Results

The results for 46 patients were sequentially recorded in each of the three clinics, thus a total of 138 people were assessed. This represents a higher sample size than our sample size calculation suggested; this occurred as the count took place for all patients attending clinic on the surveyed days, which accounted for more people than required.

The pain management and rheumatology clinics both demonstrated a similar prevalence for JHS; 39.1% and 37.0% respectively. The orthopaedics clinic demonstrated a much lower prevalence of 10.9%.

The percentages have been further analysed by noting the Beighton score and noting whether the classification was based upon major or minor criteria (see Table 2). The percentage of people who were

classified as having JHS with two major criteria in the pain management, rheumatology and orthopaedic clinics were 13.0%, 10.9% and 2.2% respectively. The percentage of people classified with a Beighton score of 4 or more and two minor criteria were 2.2%, 0% and 2.2%. The percentage of people classified with arthralgia for longer than 3 months in four or more joints and two minor criteria were 21.7%, 23.9% and 4.3% respectively. Finally, the percentage of people classified with four minor criteria was 2.2% in each group.

Discussion

More people with JHS presented to our pain management and general rheumatology clinics rather than the orthopaedic clinic. This reflects a more appropriate pathway for this multiple joint pathology, where orthopaedic surgery is rarely a chosen pathway of care.

Although the presence of JHS was high in the pain management and rheumatology clinics, it is similar to the percentage that others have found (24;25). The presence of joint hypermobility measured as a Beighton score of 4 or more, is approximately what one might expect within the general population in the pain management and rheumatology clinics, but far lower than expected in the orthopaedic clinic. If GJH is approximately 10% of a Western population (18), why are these findings lower? The population demographic, particularly the ethnic origin, sex and age was not collected, but local area population statistics collected in 2014 (www.IBHF.gov.uk), demonstrated that the population considered themselves 78.1% white and 31.9% from other ethnic groups. The majority of the other ethnic groups are Black African (5.8%), Mixed (5.5%), other Asian (4%) and Black Caribbean (3.9%). This does not suggest that the percentage of GJH in the local population should be particularly low.

The high percentage of people with JHS in two of the clinics is, in part, a reflection of classifying people who have a low Beighton score but have multiple joint pains from other sources. A low Beighton score may be a result of joints stiffening up with age. For example, people referred to the orthopaedic services may suffer with osteoarthritis and therefore represent a population with reduced range of motion.

These figures may be an over classification from people who had co-morbidities that do not reflect a hypermobility syndrome. For example, joint pain and soft tissue lesions are commonly associated with some immunological conditions, which may present alongside unrelated varicose veins, a hernia or a prolapse that can occur in an older population. Indeed, the Brighton Criteria has been validated against a healthy population and not yet against people with other musculoskeletal complaints (16). That is, the Brighton Criteria only excludes a classification of JHS in the presence of Marfan or Ehlers-Danlos Syndrome (other than ED-HT) rather than following the exclusion of other disorders. Therefore, the sensitivity and specificity of the criteria requires further investigation. Remvig et al (2011) have suggested that further investigations should include the determination of features that may contribute towards heterogeneity of JHS (11). This stresses the need for the Brighton Criteria to be considered alongside a thorough history taking, consideration of other differential diagnoses and careful clinical reasoning to avoid the risk of over classification. For example, a shoulder dislocation that was traumatic in origin could commonly re-dislocate due to a Hill-Sachs lesion but fulfil a minor criterion. Careful history needs to be taken to avoid attributing such an unrelated dislocation to JHS. This may also be the case for myopia, a hernia from a traumatic football injury, or a prolapse sustained by a mother during traumatic childbirth delivery. Sub-classifications of JHS have been demonstrated in children(29) and adults (30). The identification of these subtypes were based on symptoms such as fatigue, gastrointestinal problems and postural orthostatic tachycardia syndrome. It should be noted that these features (fatigue (6;31), gastrointestinal problems (26) and postural orthostatic tachycardia syndrome (32)) although associated (2) are not, as yet, considered part of the classification criteria.

In conclusion, recruitment to trials using the Brighton Criteria to achieve an accurate diagnosis of JHS from people with general hypermobility is challenging. Sensitivity and specificity testing of the Brighton Criteria against other populations is required, because this cohort of people who have widespread pain and symptoms requires accurate identification. This is important due to the significant affect it may have on their functional ability and quality of life and to ensure that they are directed to appropriate services.

Reference List

(1) BRAVO JF, WOLFF C. Clinical study of hereditary disorders of connective tissues in a Chilean population: joint hypermobility syndrome and vascular Ehlers-Danlos syndrome. Arthritis Rheum 2006; 54:515-523.

(2) CASTORI M. Ehlers-danlos syndrome, hypermobility type: an underdiagnosed hereditary connective tissue disorder with mucocutaneous, articular, and systemic manifestations. ISRN Dermatol 2012; 2012:751768.

(3) GRAHAME R. Joint hypermobility syndrome pain. Curr Pain Headache Rep 2009; 13:427-433.

(4) MULVEY MR, MACFARLANE GJ, BEASLEY M et al. Modest association of joint hypermobility with disabling and limiting musculoskeletal pain: results from a large-scale general population-based survey. Arthritis Care Res (Hoboken) 2013; 65:1325-1333.

(5) SMITH TO, EASTON V, BACON H et al. The relationship between benign joint hypermobility syndrome and psychological distress: a systematic review and meta-analysis. Rheumatology (Oxford) 2014; 53:114-122.

(6) CASTORI M, SPERDUTI I, CELLETTI C, CAMEROTA F, GRAMMATICO P. Symptom and joint mobility progression in the joint hypermobility syndrome (Ehlers-Danlos syndrome, hypermobility type). Clin Exp Rheumatol 2011; 29:998-1005.

(7) GRAHAME R, HAKIM AJ. Hypermobility. Curr Opin Rheumatol 2008; 20:106-110.

(8) ADIB N, DAVIES K, GRAHAME R, WOO P, MURRAY KJ. Joint hypermobility syndrome in childhood. A not so benign multisystem disorder? Rheumatology (Oxford) 2005; 44:744-750.

(9) ROSS J, GRAHAME R. Joint hypermobility syndrome. BMJ 2011; 342:c7167.

(10) FOLEY EC, BIRD HA. Hypermobility in dance: asset, not liability. Clin Rheumatol 2013; 32:455-461.

(11) REMVIG L, ENGELBERT RH, BERGLUND B et al. Need for a consensus on the methods by which to measure joint mobility and the definition of norms for hypermobility that reflect age, gender and ethnic-dependent variation: is revision of criteria for joint hypermobility syndrome and Ehlers-Danlos syndrome hypermobility type indicated? Rheumatology (Oxford) 2011; 50:1169-1171.

(12) CLINCH J, DEERE K, SAYERS A et al. Epidemiology of generalized joint laxity (hypermobility) in fourteen-year-old children from the UK: a population-based evaluation. Arthritis Rheum 2011; 63:2819-2827.

(13) LAMARI NM, CHUEIRE AG, CORDEIRO JA. Analysis of joint mobility patterns among preschool children. Sao Paulo Med J 2005; 123:119-123.

(14) LEONE V, TORNESE G, ZERIAL M et al. Joint hypermobility and its relationship to musculoskeletal pain in schoolchildren: a cross-sectional study. Arch Dis Child 2009; 94:627-632.

(15) SECKIN U, TUR BS, YILMAZ O, YAGCI I, BODUR H, ARASIL T. The prevalence of joint hypermobility among high school students. Rheumatol Int 2005; 25:260-263.

(16) BEIGHTON P, SOLOMON L, SOSKOLNE CL. Articular mobility in an African population. Ann Rheum Dis 1973; 32:413-418.

(17) GRAHAME R, BIRD HA, CHILD A. The revised (Brighton 1998) criteria for the diagnosis of benign joint hypermobility syndrome (BJHS). J Rheumatol 2000; 27:1777-1779.

(18) GRAHAME R. Joint hypermobility and genetic collagen disorders: are they related? Arch Dis Child 1999; 80:188-191.

(19) HAKIM AJ, CHERKAS LF, GRAHAME R, SPECTOR TD, MACGREGOR AJ. The genetic epidemiology of joint hypermobility: a population study of female twins. Arthritis Rheum 2004; 50:2640-2644.

(20) LARSSON LG, BAUM J, MUDHOLKAR GS, SRIVASTAVA DK. Hypermobility: prevalence and features in a Swedish population. Br J Rheumatol 1993; 32:116-119.

(21) SEOW CC, CHOW PK, KHONG KS. A study of joint mobility in a normal population. Ann Acad Med Singapore 1999; 28:231-236.

(22) BIRRELL FN, ADEBAJO AO, HAZLEMAN BL, SILMAN AJ. High prevalence of joint laxity in West Africans. Br J Rheumatol 1994; 33:56-59.

(23) HAKIM AJ, SAHOTA A. Joint hypermobility and skin elasticity: the hereditary disorders of connective tissue. Clin Dermatol 2006; 24:521-533.

(24) GRAHAME R, HAKIM AJ. Joint Hypermobility Syndrome is highly prevalent in general rheumatology clinics, its occurrence and clinical presentation being gender, age and race-related. Ann Rheum Dis 2006; 65:263.

(25) CONNELLY E, HAKIM A, DAVENPORT S, SIMMONS J. A study exploring the prevalence of joint hypermobility syndrome in patients attending a musculoskeletal triage clinic. physiotherapy pratice and research 2015; 36:43-53.

(26) FIKREE A, AZIZ Q, GRAHAME R. Joint hypermobility syndrome. Rheum Dis Clin North Am 2013; 39:419-430.

(27) CLARK CJ, SIMMONDS JV. An exploration of the prevalence of hypermobility and joint hypermobility syndrome in Omani women attending a hospital physiotherapy service. Musculoskeletal Care 2011; 9:1-10.

(28) SCHEPER MC, DE VRIES JE, VERBUNT J, ENGELBERT RH. Chronic pain in hypermobility syndrome and Ehlers-Danlos syndrome (hypermobility type): it is a challenge. J Pain Res 2015; 8:591-601.

(29) PACEY V, ADAMS RD, TOFTS L, MUNNS CF, NICHOLSON LL. Joint hypermobility syndrome subclassification in paediatrics: a factor analytic approach. Arch Dis Child 2015; 100:8-13.

(30) DE W, I, ROMBAUT L, MALFAIT F, DE BT, DE PA, CALDERS P. Clinical heterogeneity in patients with the hypermobility type of Ehlers-Danlos syndrome. Res Dev Disabil 2013; 34:873-881.

(31) HAKIM AJ, GRAHAME R. Non-musculoskeletal symptoms in joint hypermobility syndrome. Indirect evidence for autonomic dysfunction? Rheumatology (Oxford) 2004; 43:1194-1195.

(32) MATHIAS CJ, LOW DA, IODICE V, OWENS AP, KIRBIS M, GRAHAME R. Postural tachycardia syndrome--current experience and concepts. Nat Rev Neurol 2012; 8:22-34.

London Borough of Hammersmith and Fulham website (2016) http://www.IBHF.gov.uk

TABLE I. Diagnostic Criteria for Joint Hypermobility Syndrome (JHS) and Ehlers–Danlos Syndrome, Hypermobility Type (EDS-HT)

Brighton criteria (JHS)

Major criteria
- Beighton score ≥4/9
- Arthralgia for >3 months in >4 joints

Minor criteria
- Beighton score of 1–3
- Arthralgia in 1–3 joints
- History of joint dislocations
- Soft tissue lesions >3
- Marfan-like *habitus*
- Skin striae, hyperextensibility, or scarring
- Eye signs, lid laxity
- History of varicose veins, hernias, visceral prolapses

From [Grahame et al., 2000]

The diagnosis of JHS is fixed by the presence of both major, or one major and two minor, or four minor criteria, as well as of two minor criteria plus one or more first-degree affected relative(s). The diagnosis of JHS needs clinical/molecular exclusion of partially overlapping heritable connective tissue disorders

Villefranche criteria (EDS-HT)

Major criteria
- Beighton score ≥5/9
- Skin involvement (hyperextensibility and/or smooth, velvety skin)

Minor criteria
- Recurring joint dislocations
- Chronic joint/limb pain
- Positive family history

From [Beighton et al., 1998]

To date, there is no consensus on the minimum criteria for the diagnosis of EDS-HT. Clinical practice suggests to fix the diagnosis of EDS-HT by the presence of both major criteria (with or without minor criteria) in sporadic cases and to use minor criteria for at-risk relatives not satisfying both major criteria. The exclusion of other heritable connective tissue disorders is indicated also for EDS-HT

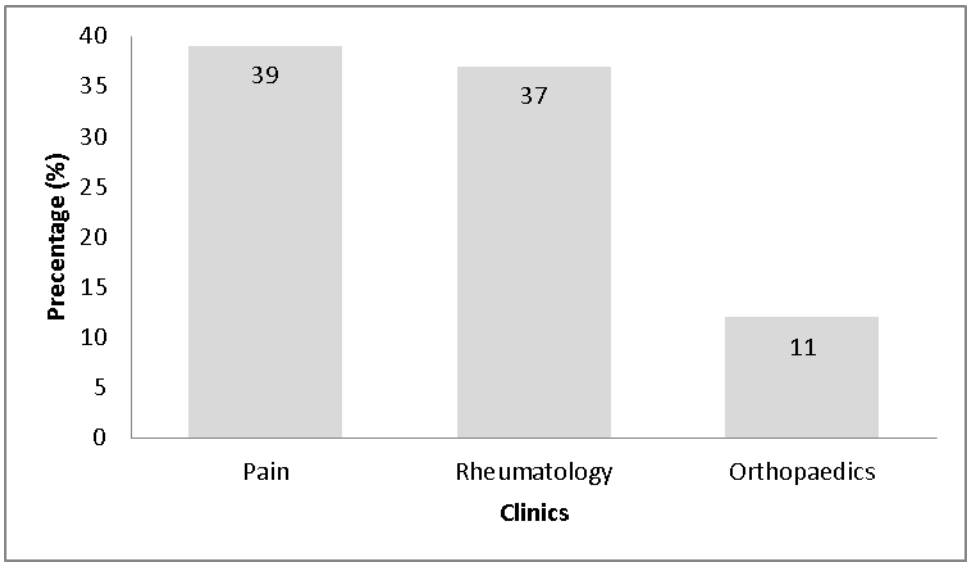

Figure1: Bar chart showing the percentage of people classified with Joint Hypermobility Syndrome using the Brighton criteria in the three different clinics.

	2 major	Beighton + 2 minor	Arthralgia + 2 minor	4 minor
Pain management	13.0	2.2	21.7	2.2

Rheumatology	10.9	0	23.9	2.2
Orthopaedics	2.2	2.2	4.3	2.2

Table 1. Demonstrates the percentage of people classified with the four different criteria in the pain management, general rheumatology and orthopaedic clinics.