Joint Hypermobility: A Common Association with Complex Functional Gastrointestinal Disorders

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Objective To evaluate the prevalence of joint hypermobility (JH) and comorbid conditions in children and young adults referred to a tertiary care neurogastroenterology and autonomic disorders clinic for functional gastrointestinal complaints.

Study design This was a retrospective chart review of 66 new patients aged 5-24 years who fulfilled at least 1 pediatric Rome III criteria for a functional gastrointestinal disorder (FGID) and had a recorded Beighton score (n = 45) or fibromyalgia tender point score (n = 45) based on physician examination. Comorbid symptoms were collected and autonomic testing was performed for evaluation of postural tachycardia syndrome (POTS).

Results The median patient age was 15 years (range, 5-24 years), 48 (73%) were females, and 56% had JH, a significantly higher rate compared with population studies of healthy adolescents ($P < .001$; OR, 10.03; 95% CI, 5.26-19.13). POTS was diagnosed in 34% of patients and did not correlate significantly with hypermobility. Comorbid conditions were common, including sleep disturbances (77%), chronic fatigue (93%), dizziness (94%), migraines (94%), chronic nausea (93%), and fibromyalgia (24%).

Conclusion JH and other comorbid symptoms, including fibromyalgia, occur commonly in children and young adults with complex FGIDs. POTS is prevalent in FGIDs but is not associated with hypermobility. We recommend screening patients with complex FGIDs for JH, fibromyalgia, and comorbid symptoms such as sleep disturbances, migraines, and autonomic dysfunction. *(J Pediatr 2014;165:973-8)*.

Children and adolescents with unexplained gastrointestinal (GI) symptoms typically fall under the umbrella of functional GI disorders (FGIDs). FGIDs represent a major health burden, with patients often suffering from a variety of comorbidities and no distinct explanatory model to guide diagnosis and treatment.[1] These comorbidities frequently entail multisystem complaints that share many qualities with a connective tissue disorder known as joint hypermobility syndrome (JHS). Some of these complaints include chronic fatigue, sleep disturbances, migraine, fibromyalgia, and chronic nausea. The Rome III criteria have evolved as discrete symptom-based diagnoses to help classify FGIDs based mainly on GI symptomatology.[2] The Rome criteria do not take into account the comorbid conditions that may cause even greater debilitation, school absenteeism, and high health care utilization.[3,4]

JHS is part of a group of hereditary connective tissues disorders that includes Marfan syndrome, Ehlers-Danlos syndrome (EDS), and osteogenesis imperfecta. JHS shares phenotypic overlap with these disorders (and has been termed EDS hypermobility type), but historically has been considered a more benign form.[5] JHS is defined as musculoskeletal symptoms in the presence of generalized joint hypermobility (JH) not attributable to a systemic rheumatologic disease.[6,7] Prevalence rates vary greatly according to race, age, and sex, with higher rates in Asians, younger individuals, and females.[6] In Western adolescent populations, the rate of generalized JH is approximately 10%-20%.[8,9] Fibromyalgia, a chronic condition characterized by a constellation of complaints, including musculoskeletal pain, poor sleep, and fatigue,[10,11] is associated with high prevalence rates of JH, in up to 64% of adults,[12] and with heightened pain sensitivity in these individuals.[13] Conversely, children with JH have a 40% rate of fibromyalgia.[14]

JHS shares many comorbid symptoms with FGIDs, including sleep disturbances, fibromyalgia, psychological illness, and migraine headaches, as well as a similar demographic profile.[15] Autonomic nervous system (ANS) dysfunction also has

ANS	Autonomic nervous system
BP	Blood pressure
EDS	Ehlers-Danlos syndrome
FGID	Functional gastrointestinal disorder
GI	Gastrointestinal
HR	Heart rate
IBS	Irritable bowel syndrome
JH	Joint hypermobility
JHS	Joint hypermobility syndrome
POTS	Postural tachycardia syndrome

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been reported in patients with JHS who have undergone ANS testing.[16] Studies in adults have identified an association between JHS and GI symptomatology, including abdominal pain, bloating, nausea, diarrhea, and constipation.[6,15,17-20] We hypothesized that children and young adults with complex FGIDs may satisfy the criteria for JH and suffer numerous extraintestinal functional complaints overlapping with those of patients with JHS. The present study aimed to evaluate the prevalence of JH, orthostatic intolerance, and 7 other comorbid conditions, including fibromyalgia, in children and young adults with complex FGIDs.

Methods

This Institutional Review Board–approved, cross-sectional review of retrospective data from 75 subjects included physician-performed Beighton scores and fibromyalgia tender points. Participants included all new pediatric and young adult patients consecutively seen by a joint gastroenterology-neurology physician team in the outpatient pediatric neurogastroenterology and autonomic disorders clinic at Children's Hospital of Wisconsin between February 2012 and February 2013.

To avoid biases, we considered all children and young adults referred to the pediatric neurogastroenterology and autonomic disorders clinic with suspected FGIDs of a minimum 2 months duration, with no evidence of an inflammatory, metabolic, or anatomic process. Of 75 new clinic patients classified according to the pediatric 2006 Rome III criteria for FGIDs,[2] 66 met at least 1 pediatric Rome criterion and were included in the study (Figure 1). The remaining 9 patients were excluded. Of these 9 patients, 4 suffered from chronic nausea and the other 5 had a constellation of symptoms, including chronic fatigue, diarrhea without abdominal pain, dizziness, sleep disturbance, and migraine headache. Because chronic idiopathic nausea is not a Rome III pediatric diagnosis, the 4 patients with nausea were excluded. Six of the 66 subjects were adults (aged ≥19 years). These 6 subjects were excluded in a comparison of results of this study with those of a previous study of 861 healthy adolescents,[8] but were included in the remaining analyses. We also intended to exclude any patients with a documented medical condition explaining the presentation. However, no further patients were excluded based on a number of clinically determined tests, including biochemical, endoscopic, and motility studies, which provided no medical diagnoses.

We collected data on demographics, medical history, family medical history, diagnostic imaging, motility studies, and mucosal endoscopic biopsy analyses from systematic chart reviews, and data on comorbid symptoms, including sleep disturbances, chronic fatigue, dizziness, syncope, chronic nausea, and migraine headache, as documented in the medical record by the clinic physician. Sleep disturbance was defined as the presence of at least 2 of the following 3 criteria: time to fall asleep >30 minutes, frequent nighttime awakening, and not feeling refreshed on awakening in the morning. Chronic fatigue required a minimum of 6 months duration,[21] and chronic nausea required a minimum of 2 months of symptoms, as used for all pediatric Rome criteria.[2] Dizziness was considered present if a subject complained of recurrent dizziness while in upright sitting/standing position, and syncope was defined as at least 3 episodes of temporary loss of consciousness in a lifetime. Migraine headaches required documentation in the chart of a diagnosis by the clinic neurologist in accordance with the International Headache Society's 1997 pediatric migraine criteria.[22] We also retrieved physician-performed hypermobility scores based on the validated 1999 Beighton scale[23] (0-9; 45 subjects) (Table) and fibromyalgia tender point scores (0-18; 45 subjects) (Figure 1) as defined by the 1990 American College of Rheumatology criteria.[10]

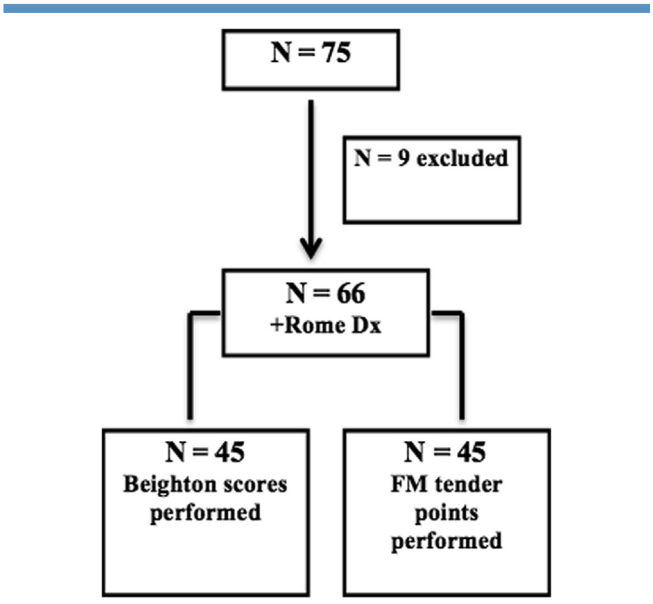

Figure 1. Subject selection process. *FM*, fibromyalgia.

Autonomic testing was performed as a clinical tool in nearly all patients according to our clinical practice, as reported previously.[24] A tilt table test assessed for postural tachycardia syndrome (POTS) and other orthostatic diagnoses, with the patient lying supine for 10 minutes on a motorized tilt table before being subjected to a head-up tilt to 70° for 30 minutes (or 40 minutes in patients with a history of syncope). Continuous beat-to-beat blood pressure

Table. Nine-point Beighton hypermobility score

Beighton score	Maneuver
1	Passive dorsiflexion of fifth metacarpophalangeal joint to ≥90°
2	Opposition of thumb to volar aspect of ipsilateral forearm
3	Hyperextension of elbow to ≥10°
4	Hyperextension of knee to ≥10°
5	Place hands flat on floor without bending knees

One point is given for each body side on maneuvers 1-4, with a total of 9 possible points. A score of ≥4 out of 9 is consistent with JH.