

Joint hypermobility in children with and without functional constipation

Seyed Mohammadreza Fatemi Khorasgani¹, Neda Ramezani², Negar Ebrahimi Varnousfaderani²

¹Department of Pediatrics, Islamic Azad University, Najaf Abad Branch, Isfahan, Iran, ²Department of General Medicine, Islamic Azad University, Najaf Abad Branch, Isfahan, Iran

Background: Previous studies report an association between joint hypermobility (JH), as a hallmark of connective tissue disorder, and autonomic dysfunction, digestive problems, and irritable bowel syndrome. However, its association with functional constipation (FC) has not been evaluated. This study is run and implemented to justify this theme/topic. **Materials and Methods:** In this case-control study among 200 subjects, 100 were of FC according to the ROME III Criteria (case group) and each child was matched for age and gender with a healthy control that did not meet criteria for FC (control group). The demographic information and JH were assessed and compared in both groups, through a physical examination according to the Beighton score. **Results:** A total of 200 children with a mean age of 6.2 ± 2.2 years constituted the statistical population. The prevalence of JH was assessed to establish the Beighton score (≥ 4 was considered JH). There was no significant difference in JH between children with and without FC, odds ratio (OR) 1.13 (95% confidence interval [CI]: 0.65–1.98, $P = 0.669$). There was no significant difference in terms of gender and age between the two groups ($P = 0.887$, $P = 0.396$, respectively). JH was not significantly associated with gender ($P = 0.445$) while significantly associated with age ($P = 0.041$). Furthermore, there was no significant association between JH and FC ($P = 0.669$). Following multivariate logistic regression analysis between the presence of JH as the dependent variable and the measured variables as the independent variables, only age had significant independent predictive values in the development of JH ($P = 0.041$, OR = 0.88 [0.77–1]). The obtained adjusted OR in this study indicated that at each year age increase the JH risk decreased by 12%. **Conclusion:** Here, it is revealed that the relative frequency of JH in this age range, with and without FC, is not significantly different, and it is not significantly associated with gender while significantly associated with age.

Key words: Beighton score, functional constipation, functional gastrointestinal disorder, joint hypermobility, relative frequency

How to cite this article: Khorasgani SM, Ramezani N, Varnousfaderani NE. Joint hypermobility in children with and without functional constipation. J Res Med Sci 2020;25:28.

INTRODUCTION

Constipation, a common gastrointestinal disorder, imposes a high economic burden on the patient and society.^[1] This problem accounts for 3% of outpatient and 10%–25% of pediatric gastrointestinal referrals.^[2] Its prevalence in adults in Western and Asian countries varies from 10% to 20% and in children ranges from 0.7% to 29.6%.^[3] A review conducted on some studies in Iran (in Isfahan) discovered a constipation prevalence to be as high as 32.9%.^[4] The causes of constipation are divided into organic and functional categories.^[5] Majority of studies indicate that 90%–95%

of cases are not subject to specific organic cause.^[3] Joint hypermobility (JH) is suspected to be comorbidity in patients with gastrointestinal diseases.^[6–9] Alteration of the collagen fibers associated with JH is thought to be responsible for high prevalence of voiding dysfunction and constipation found in this group of children.^[8,10] JH is a relatively benign condition with excessive laxity involving multiple joints, allowing motion beyond the expected normal range, due to impaired collagen synthesis. JH may resemble Marfan syndrome, Ehlers–Danlos syndrome (EDS), and osteogenesis imperfecta, while being less severe. It is evident that JH indicates an increase in the normal joints' range of motion in the absence of connective tissue diseases.^[11] Although JH is

Access this article online

Quick Response Code:



Website:
www.jmsjournal.net

DOI:
10.4103/jrms.JRMS_881_19

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

Address for correspondence: Dr. Neda Ramezani, Department of General Medicine, Islamic Azad University, Najaf Abad Branch, Isfahan, Iran.
E-mail: n_ramezani227@yahoo.com

Submitted: 27-Nov-2019; **Revised:** 07-Dec-2019; **Accepted:** 24-Dec-2019; **Published:** 18-Mar-2020

known to be a symptom of collagen synthesis disorders, it is prevalent in healthy individuals. Its prevalence is within 7%–40% depending on age, gender, race, and methodology in different figures obtained from Beighton score or other related criteria.^[12,13] The available findings indicate that the prevalence of JH is significantly higher in constipation-predominant irritable bowel syndrome than in diarrhea (57.8% vs. 34.8%).^[9] According to previous studies, the prevalence of JH in gastrointestinal clinics is very high, which is associated with an increase in the severity of functional gastrointestinal symptoms, and can significantly decrease the patients' quality of life.^[14] In a study on patients within 5–24 years with a recent diagnosis of gastrointestinal disorders (having at least one of the criteria for gastrointestinal dysfunction), it is revealed that fibromyalgia and JH are commonly present in children and adults with gastrointestinal dysfunction, with a reported incidence of 56% for JH.^[15] In a study by Zeitoun *et al.*^[16] on patients with EDS, it is found that functional gastrointestinal symptoms are common in this group of patients and have a significant correlation with their quality of life. Available studies^[6-9] indicate that the correlation between joint softness as a prominent feature of connective tissue diseases, functional abdominal pain, and irritable bowel syndrome, given the possible association between functional constipation (FC) and JH in children. Because the treatment for gastrointestinal dysfunction is based on its symptoms, if there is a significant correlation between JH and FC, such conclusion will facilitate multidisciplinary medical management of gastrointestinal and extra-gastrointestinal manifestations in addition to improving patients' quality of life. Considering the importance of JH and the fact that different studies revealed controversial results according to the subject communities in terms of prevalence and forms of JH, there exists no study in this field in Iran. Consequently, thus, the aim of this study was to compare frequency of JH in children with and without FC.

MATERIALS AND METHODS

This was a case-control study that was conducted in Dr. Ali Shariatee Hospital in 2018. The statistical population consists of 200 children within 3–10 years of age range referred to the pediatric clinic. The case group consists of 100 children diagnosed by a pediatrician with FC based on the Rome III^[17] Criteria selected through sequential nonprobability sampling method, using a validated questionnaire in Persian.^[18]

In general, children with a history of constipation with organic causes, those with irritable bowel syndrome based on the ROME III Criteria,^[17] those treated for constipation within 2 weeks before enrollment, mental retardation or metabolic diseases (like hypothyroidism), Hirschsprung's

disease, spinal anomalies, anorectal pathology, rheumatic diseases, inflammatory bowel diseases, and bone metabolic disorders, children receiving medical treatment affecting gastrointestinal mobility or corticosteroid, and children undergoing stomach or bowel surgery are excluded in such studies.

Each child who met criteria for FC (case) was matched with another child of similar age and gender that did not meet the criteria for FC (control); the control groups were selected from the same population that the case groups came from.

According to the previous study of Reilly *et al.*,^[19] the equation was applied to estimate the sample size with consideration of the 95% confidence level and 80% power, $Z_1 = 1.96$, $Z_2 = 0.84$, $P_1 = 20\%$, and $P_2 = 38\%$, and d as the error coefficient of 0.06; yields $n = 100$, which 100 patients in case group and 100 in control group (total 200 patients). Based on the practical definition, any individual who had the following three criteria during the past 3 months is referred to having FC: (1) having two or more of the following symptoms: frequency of defecation less than three times a week, very hard or similar to dung stools, stool defecation with pressure, feeling incomplete emptying of bowels after stool defecation, feeling stool impaction in bowels, facilitating stool defecation using finger or toilet hose, (2) absence of loose and watery stools, and (3) not fulfilling criteria for irritable bowel syndrome based on the Rome III Criteria.

A physical examination was carried out by the researcher to diagnose JH based on the Beighton score, which is commonly used to measure general hypermobility. Beighton score determines the degree of hypermobility according to a severity scoring system between 0 and 9. In this scale, higher scores indicate more severe hypermobility (joint laxity) [Table 1].

In this study, score ≥ 4 was considered as JH. It should be noted that the researcher who examined the subjects was not aware that whether or not they have FC.

Table 1: Beighton criteria for joint hypermobility

	Right	Left
Passive dorsiflexion and hyperextension of the fifth MCP joint beyond 90°	1	1
Passive apposition of the thumb to the flexor aspect of the forearm	1	1
Passive hyperextension of the elbow beyond 10°	1	1
Passive hyperextension of the knee beyond 10°	1	1
Active forward flexion of the trunk with the knees fully extended so that the palms of the hands rest flat on the floor		1
Total		9

MCP= Metacarpophalangeal

Statistical analysis

Qualitative results are reported as absolute and relative frequency, while quantitative results are reported as mean \pm standard deviation. The obtained data were analyzed by IBM SPSS Statistics (version 24; IBM, New York, NY, USA)^[20] Chi-square and *t*-tests were used in this study, and where $P < 0.05$, the results were considered statistically significant. Univariate and multivariate regression analysis was conducted to investigate the possible effects of age and sex on the diagnosis of JH. Strength of association was calculated by odds ratio (OR) with its 95% confidence interval (CI).

This research study was approved by the local ethics committee with the following registration code "IR.IAU.NAJAFABAD.REC.1398.089." All stages of examinations and measurements were performed with informed consent of the parents.

RESULTS

Of 200 study participants within 3–10 years, with a mean age of 6.2 ± 2.2 years, 95 (47.5%) were males and 105 (52.5%) were females. The case group consists of 48 (48%) males and 52 (52%) females; the control group consists of 47 (47.3%) males and 53 (53.0%) females. There was no significant difference in terms of gender and age between the two groups ($P = 0.887$ and $P = 0.396$, respectively) [Table 2].

Of 200 study participants, 113 (56.5%) had JH while 87 (43.5%) did not. Table 3 describes the univariate and multivariate regression analysis of the prevalence of JH in relation to gender, age, and FC functions. JH was not significantly associated with gender ($P = 0.445$) while significantly

associated with age ($P = 0.041$). Furthermore, there was no significant association between JH and FC ($P = 0.669$).

Following multivariate logistic regression analysis between the presence of JH as the dependent variable and the measured variables as the independent variables, only age had significant independent predictive values in the development of JH ($P = 0.041$, OR =0.88 [0.77–1]). The obtained adjusted OR in this study indicated that at each year age increase the JH risk decreased by 12%.

DISCUSSION

The main idea of this study was to determine the association between FC and JH.

According to the results of this study, the frequency percentage of JH in all children is 56.5%, indicating a high prevalence of this disease among 3–10-year-old children. JH is observed in 58% of the case group and 55% of the controls. In this study, we found out that JH in 3–10-year-old children does not have statistically significant correlation with FC.

According to Kovacic *et al.*,^[15] 56% of the patients with gastrointestinal dysfunction had JH, which is very close to the findings here, while it should be considered that these two studies had different methods. According to Fikree *et al.*,^[14] JH in patients with gastrointestinal functional symptoms was significantly higher compared to patients with organic gastrointestinal symptoms, which is inconsistent with the findings of this study; such inconsistencies may be due to different methods and demographics, age range, and sample size.

The study of Zweig *et al.*^[9] revealed that the prevalence of JH in children with constipation-predominant irritable bowel syndrome was significantly higher than diarrhea, which confirmed the association between FC and JH. These results are inconsistent with our findings, which is due to the differences in the nature of functional gastrointestinal diseases.

Saps *et al.*^[21] conducted a cross-sectional case-control study and revealed that the prevalence of JH between children

Table 2: Characteristic of children with and without functional constipation

Parameters	FC (n=100)	Controls (n=100)	P
Gender, n (%)			
Male	48 (48)	47 (47)	0.887
Female	52 (52)	53 (53)	
Age, mean \pm SD	6.08 \pm 2.18	6.35 \pm 2.35	0.396

FC=Functional constipation; SD=Standard deviation

Table 3: Comparison of children with and without joint hypermobility for gender, age, and functional constipation

Factors	Joint hypermobility		Crude OR ^a		Adjusted OR ^b	
	BS \geq 4 (n=113)	BS <4 (n=87)	OR (95%CI)	P	OR (95% CI)	P
Gender, n (%)						
Male	51 (53.7)	44 (46.3)	0.804 (0.46-1.41)	0.445	0.79 (0.45-1.39)	0.409
Female	62 (59)	43 (41)	1		1	
Age, mean \pm SD	5.93 (2.28)	6.59 (2.21)	0.88 (0.77-1)	0.041*	0.88 (0.77-1)	0.041*
FC, n (%)						
FC	58 (58)	42 (42)	1.13 (0.65-1.98)	0.669	1.1 (0.62-1.93)	0.751
Controls	55 (55)	45 (45)	1		1	

^aUnivariate logistic regression; ^bMultivariate logistic regression; *Significant at 0.05 level. BS=Beighton score; OR=Odds ratio; CI=Confidence interval; FC=Functional constipation

with and without functional gastrointestinal disorders was not significantly different, which corresponds with the results in this study.

Some of the major strengths of our study include the use of validated questionnaires to diagnose FC and the setting of our investigation that allowed us to obtain data from community children without the selection bias inherent to consultation patterns. To the best of our knowledge, this is the first study to assess JH in children with FC in Iran using the Beighton score. By studying a group of children without primary joint problems, the study minimized selection and response bias. Similarly to other studies, we found a significant association between JH and young age.^[22]

Limitations of this study consists of (1) the results here are not generalizable to children with other age groups, (2) impossibility in determining the causal correlation between FC and JH, (3) encountering problems during examination such as the absence of a completely standardized examination condition, and (4) we did not obtain data on other comorbidities that would have been useful to assess the impact of JH and FC.

CONCLUSION

We concluded that there was no significant difference in the frequency of JH between the groups of with and without constipation. It should be noted that confounding effects of age and gender were neutralized by matching the subjects in control and case groups.

In general, the mean age of the children with JH is significantly lower than that of the children without JH (regardless of whether or not they had FC). With these results in mind, more studies are necessary to determine the actual correlation between FC and JH.

Furthermore, other potential clinical factors affecting the development of JH in children with FC (e.g., severity of FC) should be assessed in future studies.

Clinical features of JH in patients with and without FC in other age groups and other gastrointestinal dysfunctions (such as irritable bowel syndrome) should also be compared with the results of this study.

Acknowledgments

Appreciations are extended to Shariati Hospital supervisors for their assistance and cooperation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Sharma A, Rao S. Constipation: Pathophysiology and current therapeutic approaches. *Handb Exp Pharmacol* 2017;239:59-74.
- Waterham M, Kaufman J, Gibb S. Childhood constipation. *Aust Fam Physician* 2017;46:908-12.
- Iwańczak B, Iwańczak F. Functional gastrointestinal disorders in children and adolescents. The Rome IV criteria. *Pol Merkur Lekarski* 2017;43:75-82.
- Adibi P, Behzad E, Pirzadeh S, Mohseni M. Bowel habit reference values and abnormalities in young Iranian healthy adults. *Dig Dis Sci* 2007;52:1810-3.
- Tabbers MM, Benninga MA. Constipation in children: Fibre and probiotics. *BMJ Clin Evid* 2015;2015: pii: 0303.
- Castori M, Morlino S, Pascolini G, Blundo C, Grammatico P. Gastrointestinal and nutritional issues in joint hypermobility syndrome/Ehlers-Danlos syndrome, hypermobility type. *Am J Med Genet C Semin Med Genet* 2015;169C:54-75.
- 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.
- Kajbafzadeh AM, Sharifi-Rad L, Seyedian SS, Mozafarpour S, Paydary K. Generalized joint hypermobility and voiding dysfunction in children: Is there any relationship? *Eur J Pediatr* 2014;173:197-201.
- Zweig A, Schindler V, Becker AS, van Maren A, Pohl D. Higher prevalence of joint hypermobility in constipation predominant irritable bowel syndrome. *Neurogastroenterol Motil* 2018;30:e13353.
- de Kort LM, Verhulst JA, Engelbert RH, Uiterwaal CS, de Jong TP. Lower urinary tract dysfunction in children with generalized hypermobility of joints. *J Urol* 2003;170:1971-4.
- Morlino S, Dordoni C, Sperduti I, Venturini M, Celletti C, Camerota F, *et al.* Refining patterns of joint hypermobility, habitus, and orthopedic traits in joint hypermobility syndrome and Ehlers-Danlos syndrome, hypermobility type. *Am J Med Genet A* 2017;173:914-29.
- Beckers AB, Keszthelyi D, Fikree A, Vork L, Masclee A, Farmer AD, *et al.* Gastrointestinal disorders in joint hypermobility syndrome/Ehlers-Danlos syndrome hypermobility type: A review for the gastroenterologist. *Neurogastroenterol Motil* 2017;29:e13013.
- Castori M, Hakim A. Contemporary approach to joint hypermobility and related disorders. *Curr Opin Pediatr* 2017;29:640-9.
- Fikree A, Aktar R, Grahame R, Hakim AJ, Morris JK, Knowles CH, *et al.* Functional gastrointestinal disorders are associated with the joint hypermobility syndrome in secondary care: A case-control study. *Neurogastroenterol Motil* 2015;27:569-79.
- Kovacic K, Chelimsky TC, Sood MR, Simpson P, Nugent M, Chelimsky G. Joint hypermobility: A common association with complex functional gastrointestinal disorders. *J Pediatr* 2014;165:973-8.
- Zeitoun JD, Lefèvre JH, de Parades V, Séjourné C, Sobhani I, Coffin B, *et al.* Functional digestive symptoms and quality of life in patients with Ehlers-Danlos syndromes: Results of a national cohort study on 134 patients. *PLoS One* 2013;8:e80321.
- Lewis ML, Palsson OS, Whitehead WE, van Tilburg MA. Prevalence of functional gastrointestinal disorders in children and adolescents. *J Pediatr* 2016;177:39-43.e3.
- Ghalichi F, Ghaemmaghami J, Malek A, Ostadrahimi A. Effect

- of gluten free diet on gastrointestinal and behavioral indices for children with autism spectrum disorders: A randomized clinical trial. *World J Pediatr* 2016;12:436-42.
19. Reilly DJ, Chase JW, Hutson JM, Clarke MC, Gibb S, Stillman B, *et al.* Connective tissue disorder – A new subgroup of boys with slow transit constipation? *J Pediatr Surg* 2008;43:1111-4.
 20. Cor IS. IBM SPSS Statistics for Windows, version 24.0. IBM Corp.: Armonk, NY, USA. 2016.
 21. Saps M, Blom PJ, Velasco-Benitez CA, Benninga MA. Functional gastrointestinal disorders and joint hypermobility: A school-based study. *J Pediatr Gastroenterol Nutr* 2018;66:387-90.
 22. Hasija RP, Khubchandani RP, Shenoi S. Pediatric rheumatology-joint hypermobility in Indian children. *Clin Exp Rheumatol* 2008;26:146.