

Hypermobility Spectrum Disorders, Functional Constipation and Voiding Dysfunction in School-Aged Children: Are They Related to Each Other?

Okul Çağındaki Çocuklarda Hiper mobilite Spektrum Bozuklukları, Fonksiyonel Kabızlık ve İşeme Disfonksiyonu: Birbirleriyle İlişkili midir?

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Öz

Hiper mobilite spektrum bozuklukları, tanısı konmuş sistemik romatolojik bir hastalık olmaksızın kas-iskelet sistemi bulguları ve yaygın eklem hiper mobilitesi ile kendini gösterir. Hiper mobilite spektrum bozuklukları, disfonksiyonel işeme bozuklukları ve fonksiyonel kabızlık gibi klinik durumlar için risk oluşturabilir. Amacımız okul çağındaki çocuklarda hiper mobilite spektrum bozuklukları, işeme disfonksiyonu ve fonksiyonel kabızlık sıklığını saptamak ve birbirleriyle ilişkilerini değerlendirmektir. Bu kesitsel çalışmaya okul çağındaki 947 çocuk (6–15 yaş) dahil edildi. Bir pediatrik romatolog tüm çocukları hiper mobilite tanısı koymak için Beighton Hiper mobilite Skoru kullanarak muayene etmiş ve fonksiyonel kabızlık tanısı ise bir pediatrik gastroenterolog tarafından konulmuştur. İşeme disfonksiyonu tanısını koymak için bir pediatrik nefrolog tarafından Disfonksiyonel İşeme ve İnkontinans Semptomları Skorlaması kullanılmıştır. İşeme disfonksiyonu genç yaş grubunda, anne eğitimi düzeyi düşük olanlarda, gelir düzeyi düşük olanlarda ve idrar yolu enfeksiyonu öyküsü olanlarda daha sık görüldü (sırasıyla $p<0.001$, $p=0.027$, $p=0.035$, $p<0.001$). İdrar yolu enfeksiyonu öyküsü olan çocuklarda da kabızlık prevalansı daha yüksekti ($p=0.001$) ve kabızlık görülme sıklığı, işeme disfonksiyonu olan çocuklarda olmayanlara göre belirgin şekilde daha yüksekti ($p<0.001$). Hiper mobilitesi olan ve olmayan çocuklar arasında işeme disfonksiyonu ve kabızlık oluşumu açısından istatistiksel olarak anlamlı bir fark bulunamadı ($p>0.05$). Hiper mobilitesi olan çocuklarda fonksiyonel kabızlık ve işeme disfonksiyonu gibi şikayetlerin arttığı hipotezini doğrulamak için daha fazla çalışmaya ihtiyaç vardır. İşeme disfonksiyonu ve/veya idrar yolu enfeksiyonu olan çocuklarda kabızlık sorgulanmalı ve etkin bir şekilde tedavi edilmelidir.

Anahtar Kelimeler: Çocuklar, Fonksiyonel Kabızlık, Hiper mobilite Spektrum Bozuklukları, İşeme Disfonksiyonu

Abstract

Patients suffering from hypermobility spectrum disorders (HSDs) present with problems related to the musculoskeletal system and have generalized joint hypermobility without a diagnosed systemic rheumatological disease. HSDs represent an underlying risk factor for many clinical conditions, such as dysfunctional voiding disorders and functional constipation (FC). In this study, we investigated ways to detect the frequency of HSDs, voiding dysfunction (VD), and FC in school-aged children and assessed their relationship with each other. In this cross-sectional study, 947 school-aged children (6–15 years old) were included. A pediatric rheumatologist examined all children using the Beighton Hypermobility Score to diagnose hypermobility. FC was diagnosed by a pediatric gastroenterologist. The dysfunctional voiding and incontinence symptoms score questionnaire was used by a pediatric nephrologist to diagnose VD. VD was more frequently observed in the younger age group, those whose mothers had lower education levels, children from lower-income families, and those with a history of urinary tract infection ($p<0.001$, $p=0.027$, $p=0.035$, $p<0.001$, respectively). Children with a history of urinary tract infection also had a higher prevalence of constipation ($p=0.001$), and the incidence of constipation was significantly higher in children with VD compared to those without VD ($p<0.001$). The difference in the occurrence of VD and constipation between children with and without hypermobility was not significant ($p>0.05$). Further studies are needed to confirm the hypothesis that problems such as FC and VD are worse in children with hypermobility. Constipation should be investigated in children suffering from VD and/or urinary tract infections for effective treatment of these diseases.

Keywords: Children, Functional Constipation, Hypermobility Spectrum Disorders, Voiding Dysfunction

Introduction

Hypermobility spectrum disorders (HSDs) are a group of inherited diseases of the connective tissue

that present with problems in the musculoskeletal system and generalized joint hypermobility without a diagnosed systemic rheumatological disease. The incidence of HSDs varies between 5% and 45% according to the age, sex, and ethnic origin of the patients (1-3).

In children, HSD is diagnosed based on the Beighton Hypermobility Score (4,5). In HSD, the most common complaint is pain that is often felt in the shoulders, arms, elbows, back, neck, and temporomandibular joint (6,7). Arthralgia, recurrent joint dislocation, subluxation, and carpal tunnel syndrome, as well as, several other conditions, such as vesicoureteral reflux, voiding dysfunction (VD), urinary tract infections (UTIs), striae gravidarum, varicocele, abdominal herniation, and mitral valve

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prolapse may accompany HSD (8,9). Pelvic floor dysfunction influences the etiopathogenesis of VD, and the incidence of VD is higher in patients with HSD than in healthy children (8,9).

Functional constipation (FC) is a clinical condition frequently reported in childhood and affects the quality of life of children and their parents. An increase in intestinal laxity due to HSD may lead to a decrease in intraluminal pressure and result in relatively slow intestinal passage. Previous studies have reported that the incidences of rectal evacuation disorders, slow transit constipation, and gastrointestinal system disorders, such as functional abdominal pain and FC, were higher in patients with HSD compared to their incidences in healthy children (10,11).

In this study, we investigated the frequency of HSD, FC, VD, and their relationships with each other in school-aged children. We hypothesized that lax pelvic floor ligaments in HSD may lead to functional gastrointestinal system disorders and dysfunctional voiding problems. As studies in this field are limited, we examined the reciprocal relationships (if any) between HSD, FC, and VD.

Material and Method

Study Design

This prospective study was conducted at Trabzon Farabi Hospital between April 2017 and June 2020. Students were screened from four different schools, which were located in different regions of Trabzon Province. The students were primary and secondary school children who were 6–15 years old. The students who met the inclusion criteria were included in the study. Primary and secondary school students in Trabzon Province were individually examined, and questionnaires were distributed among them. In total, 947 children participated in this cross-sectional study. We excluded children from the study with chronic kidney and urinary tract anomalies that cause VD, those with chronic diseases involving the gastrointestinal system that cause FC, and those with chronic rheumatological diseases. All participants were healthy and were not under any drug therapy regimen. The questionnaires requested demographic information from participants on their age, sex, education status of the parents, family income, number of siblings, voiding habits, history of UTI, constipation, and any learning or behavioral problems. The questionnaires were filled out by the parents and collected two weeks later.

Evaluation of Hypermobility Spectrum Disorders

A pediatric rheumatologist examined the physical condition of all participants and used the Beighton Hypermobility Score to diagnose HSD. For children who were 5–9 years old and those ≥ 10 years old, Beighton Hypermobility Score ≥ 5 and ≥ 4

were defined as the criteria for HSD, respectively. These scores were calculated based on the following criteria: (i) dorsiflexion of the metacarpophalangeal joint to $\geq 90^\circ$, (ii) hyperextension of the elbow to $\geq 10^\circ$, (iii) hyperextension of the knee to $\geq 10^\circ$, and (iv) placement of hands flat on the floor without bending the knees (4-5).

Evaluation of Functional Constipation

Participants were evaluated, and FC was diagnosed by a pediatric gastroenterologist who assessed the gastrointestinal symptoms of participants based on the Rome III Diagnostic Criteria for Irritable Bowel Syndrome (12). All participants filled out a questionnaire based on the Rome III criteria to assess FC. According to the Rome III criteria, complaints of irritable bowel syndrome should be present for at least three months, recurrent abdominal pain or discomfort (an uncomfortable sensation not described as pain) associated with two or more of the following: improvement with defecation, and/or onset associated either with a change in the frequency of stool, and/or in the form or appearance of stool that should be present for at least six months.

Evaluation of Voiding Dysfunction

The diagnosis of VD was based on the questionnaire for the Dysfunctional Voiding and Incontinence Symptoms Score (DVISS) of The International Children's Continence Society. The results were evaluated by a pediatric nephrologist. The obtainable DVIS scores ranged from 0 to 35 points. A DVIS score of ≥ 9 points suggested VD (13).

Evaluation of Urinary Tract Infection

Whether participants had a history of UTI or started antibiotherapy due to UTI was also determined by the questions asked in the questionnaire.

Statistical Analysis

All data were analyzed using SPSS 26.0. The descriptive variables are presented as numbers and percentages. The differences between categorical variables in independent groups were determined by Chi-square tests. The differences between subgroups were determined by post hoc tests. All differences were considered to be statistically significant at $p < 0.05$. Power analysis was not performed at the beginning of the study. A posterior power analysis was performed and calculated using the relationship between VD and constipation as the primary hypothesis. The G*Power 3.1.9.2 program was used to perform the power analysis, and the post hoc power was found to be 99.9%.

Results

Demographic characteristics

In this cross-sectional study, 947 children (6–15 years old) were included. Among them, 52.4% were girls. Most participants (60.4%) were between 6 and 10 years old. The questions on the mother's education level, father's education level, monthly income of the family, and the number of children in the family were answered by 942, 932, 910, and 937 participants, respectively. The mothers of 335 (35.6%) children and fathers of 366 (39.3%) children were high school graduates. The families of 379 (41.6%) children had a monthly income three times the minimum wage (in Turkish liras), and 754 (80.5%) children had 2–3 siblings.

Frequency and Clinical Features of Functional Constipation, Voiding Dysfunction, and Hypermobility Spectrum Disorders

Hypermobility was observed in 155 (16.4%) children, VD in 139 (14.7%) children, and constipation in 174 (18.4%) children. Children with hypermobility most commonly had left (89.7%) and right (82.6%) metacarpophalangeal joint hypermobility. The most common complaints in children with VD were urgency (72.7%) and enuresis (56.8%). Lumpy or hard stool (54.6%) and painful defecation (45.4%) were the most common complaints in children with constipation (Table 1). When the factors affecting the frequency of VD were examined, VD was more frequently associated with younger children (6–10 years old), lower education level of the mother, lower family income level (minimum wage and below), and children with a history of UTIs ($p<0.001$, $p=0.027$, $p=0.035$, and $p<0.001$, respectively). Constipation was more common in children with a history of UTIs ($p=0.001$). The difference in the incidence of VD and constipation between children with and without hypermobility was not significant. The frequency of constipation was higher in children with VD compared to those without VD ($p<0.001$) (Table 2). Comparison within the subgroups showed that the frequency of VD differed significantly based on the maternal education level, and its frequency increased as the education level decreased ($p=0.027$). The results of post hoc tests showed that the frequency of VD differed significantly between those whose mothers received secondary school education and high school education ($p=0.040$), between those whose mothers received secondary school education and university education ($p=0.019$), between those whose mothers received primary school education and high school education ($p=0.042$), and between those whose mothers received primary school education and university education ($p=0.020$). The frequency of VD differed significantly according to the monthly income level of the family, and the frequency increased as the income level decreased

($p=0.035$). The results of post hoc tests showed a significant difference between those whose families earned the minimum wage or below and those whose families earned three times the minimum wage ($p=0.010$). The frequency of hypermobility differed significantly according to the monthly income of the family; the frequency increased with an increase in the income level ($p=0.003$). The results of the post hoc test showed a significant difference between those whose families earned the minimum wage or less and those whose families earned two times the minimum wage ($p=0.002$); the difference was also significant between those whose families earned two times and three times the minimum wage ($p=0.037$).

Table 1. The frequencies and characteristics of hypermobility, voiding dysfunction, and constipation in children.

	n	%
Hypermobilities	155	16.4
Left metacarpal	139	89.7
Right metacarpal	128	82.6
Left knee	105	67.7
Left elbow	101	65.2
Right knee	99	63.9
Right elbow	83	53.5
Left thumb	72	46.5
Right thumb	62	40.0
Trunk	15	9.7
Voiding Dysfunction	139	14.7
Urgency	101	72.7
Enuresis	79	56.8
Squatting	57	41.0
Urinary incontinence	48	34.5
Staccato urination	42	30.2
>7 urination in a day	41	29.5
Discontinuous urination	38	27.3
Painful voiding	29	20.9
Hesitancy	20	14.4
Functional Constipation	174	18.4
Lumpy or hard stool	95	54.6
Painful defecation	79	45.4
Sensation of incomplete evacuation	64	36.8
≤2 defecation in a week	48	27.6
Fecal incontinence	28	16.1
Urinary tract infection	240	25.3

Discussion

In this study, the results related to FC and VD were not significantly different between children with and without HSD. Some studies have reported that the frequency of FC and VD is higher among children with HSD, while other studies did not find a significant increase (14-16). Chelimsky et al. (14) showed that an increase in intestinal laxity leads to a decrease in intraluminal pressure and results in slow intestinal passage. Similar to the findings of our study, Khorasgani et al. (15) found no significant difference in the incidence of HSD between patients with and without FC. Zaleski et al. (17) conducted a study with 411 children and showed that FC is significantly more common in girls with HSD

($p < 0.05$). Adib et al. (3) conducted a similar study in a pediatric rheumatology clinic in the United Kingdom and detected chronic constipation in 30% of the patients with HSD. In this study, we detected FC in 20% of cases with HSD; however, the difference in the frequency of FC between the HSD group and the healthy control group was not significant ($p = 0.647$). Velasco-Benitez et al. (16) evaluated 1,630 children who were 10–18 years old using the Rome IV criteria and detected functional gastrointestinal tract disorders in 267 (16.2%) patients and HSD in 306 (28.4%) patients. The differences in the results of the studies investigating the relationship between FC and HSD might be due to genetic variations associated with HSD. Variations in incidence rates may be caused by differences in sex, age, ethnic and regional

characteristics of the patients, and the types of questionnaires used to detect FC (4). Unlike the findings of our study, Shulman et al. (18) did not find a significant difference between patients with and without generalized joint hypermobility in terms of the development of irritable bowel syndrome and functional abdominal pain. We speculated that dietary, oral hydration, and defecation habits are also important factors associated with the development of FC. Information on these aspects should be obtained from patients when evaluating FC. The differences between the studies may also be due to the different scoring systems used to evaluate HSD. Some researchers argue that the Beighton scoring system is insufficient to define HSD and that it needs to be improved (19).

Table 2. Comparison of hypermobility, voiding dysfunction, and constipation in children based on the contributing factors.

	Hypermobility			Voiding dysfunction			Constipation		
	n	%	p*	n	%	p*	n	%	p*
Age groups (years)									
6-10	78	13.6	0.005	111	19.4	<0.001	103	18.0	0.719
11-15	77	20.5		28	7.5		71	18.9	
Sex									
Female	91	18.3	0.084	71	14.3	0.740	94	19.0	0.630
Male	64	14.2		68	15.1		80	17.7	
Maternal education									
Illiterate	1	9.1	0.066	3	27.3	0.027	3	27.3	0.514
Primary school	28	12.6		41	18.5		47	21.2	
Secondary school	23	15.3		29	19.3		24	16.0	
High school	52	15.5		41	12.2		55	16.4	
University	50	22.3		24	10.7		43	19.2	
Paternal education									
Illiterate	1	12.5	0.099	2	25.0	0.078	1	12.5	0.905
Primary school	17	12.8		21	15.8		28	21.1	
Secondary school	21	14.4		27	18.5		27	18.5	
High school	54	14.8		57	15.6		65	17.8	
University	60	21.5		27	9.7		49	17.6	
Monthly income									
Minimum wage or below	18	9.9	0.003	36	19.8	0.035	27	14.8	0.290
Minimum wage x 2	52	14.9		53	15.2		71	20.3	
Minimum wage x 3	79	20.8		44	11.6		68	17.9	
Number of siblings									
Single	16	18.8	0.199	17	20.0	0.097	18	21.2	0.266
2-3	127	16.8		101	13.4		131	17.4	
>3	10	10.2		19	19.4		23	23.5	
History of UTI									
Yes	46	19.2	0.153	53	22.1	<0.001	62	25.8	0.001
No	105	15.2		82	11.9		111	16.1	
Hypermobility									
Yes				18	11.6	0.291	31	20.0	0.647
No				121	15.3		143	18.1	
Voiding dysfunction									
Yes	18	12.9	0.291				55	39.6	<0.001
No	137	17.0					119	14.7	
Constipation									
Yes	31	17.8	0.647	55	31.6	<0.001			
No	124	16.0		84	10.9				

*Chi-square test. UTI: urinary tract infection.

Abdol-Mohammad et al. (20) evaluated 226 children (113 patients with HSD and 113 control subjects; 5–14 years old) and detected HSD in 45% of patients with VD and 17% of control subjects. The most common complaints in that study were related to UTI in girls and constipation in boys. In our study, HSD was detected in 12.9% of patients with VD, and its prevalence was not significantly different from that of the control subjects ($p=0.291$). de Kort et al. (9) showed that children with HSD have a higher frequency of VD and daytime urinary incontinence than healthy children because of the laxity of their pelvic floor ligaments. In girls with HSD, the frequencies of UTI, nocturnal enuresis, and daytime urinary incontinence were higher than their respective frequencies in the controls. The frequency of constipation and fecal incontinence was higher in boys with HSD. We did not find a significant relationship between HSD and VD in this study, probably because of the differences in the study populations, ethnicity, regional characteristics, sex, and age of the participants investigated in other studies. These differences in the results between studies may also suggest that voiding disorders have a multifactorial etiology involving central, spinal, and sympathetic-parasympathetic neural mechanisms, which affect functions of detrusor and sphincter, bladder filling and emptying phases, and the physiology of urination. We found that enuresis occurred in 56.8% and daily urinary incontinence occurred in 34.5% of patients with VD. In our study, the frequency of UTI was significantly higher in patients with VD and constipation ($p<0.05$ for both). The frequency of VD was significantly higher (31.6%) in patients with FC than those without FC ($p<0.001$), which was also found in other studies. Lower urinary tract symptoms are more prevalent in patients with constipation (21). We found UTI at a significantly higher (22.1%) rate in patients with VD ($p<0.001$) than those without VD. As shown in other studies, the frequency of UTI was significantly higher (25.8%) in patients with FC relative to that in healthy participants ($p=0.001$). However, UTI rates were similar in patients with and without HSD. Some researchers have reported higher incidence rates of lower urinary tract symptoms (vesicoureteral reflux, UTI, VD, etc.) in patients with a more complicated syndrome known as Ehlers-Danlos syndrome (22).

Limitations of the Study

As this study was conducted in one city, the conclusions derived based on the collected data cannot be generalized to the whole population. Thus, multicenter studies need to be conducted to investigate generalized hypermobility in childhood. If information on the three-day diet and fluid intake of the patients could be obtained, additional factors triggering FC might have been identified. If patients with VD who maintained a voiding diary were

evaluated, we may have identified other factors affecting its etiology.

Conclusion

VD and FC are common in childhood. The relationship between HSD and these disorders is not clear. Constipation should be investigated in children with VD and/or UTIs, and the factors causing FC in these patients should be identified and treated. Some studies have shown that diffuse joint hypermobility increases problems such as FC and VD. More information might help diagnose and treat patients with HSD in future.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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