RISK FACTORS OF FUNCTIONAL CONSTIPATION AMONG THAI CHILDREN

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Abstract. Functional constipation is a common problem in pre-school children precipitated by intrinsic and extrinsic conditions. Risk factors associated with functional constipation among pre-school Thai children were identified in a case-control study employing a questionnaire based on Rome IV criteria among children 1-4 years of age (constipated, $n = 45$, non-constipated, $n = 45$) attending an outpatient department between September 2017 and January 2018. A significant common risk factor was a family history of constipation (p-value = 0.012). Univariate logistic regression analysis revealed significant differences between constipated and non-constipated group in exclusive formula feeding during the first year of life (odds ratio (OR) = 9.51, 95% confidence interval (CI): 1.14-79.6), daily vegetable or fruit ingestion of less than 1 ladle (OR = 9.63; 95% CI: 3.67-25.25), less than 250 ml daily water intake (OR = 4.42, 95% CI: 1.69-11.58), daily fruit juice intake of <250 ml (OR = 2.58; 95% CI: 0.62-10.69), weekly energetic (sweating) movement/activity of ≥4 days (OR = 8.11; 95% CI: 0.95-68.87), and major stressful event (OR = 9.51, 95% CI: 1.14-79.6). A multivariate logistic regression analysis indicated limited fruit or vegetable ingestion (adjusted OR = 11.07, 95% CI: 3.82-32.08) and water intake (adjusted OR = 5.47, 95% CI: 1.73-17.34) are significant independent risks for constipation in children. The study highlights recognition of these risk factors by parents or caregivers as well as physicians in order to modify feeding behavior and avoid pharmacological intervention of constipation in children in the country.

Keywords: functional constipation, children, risk factor, Thailand

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INTRODUCTION

Constipation constitutes one of the common problems encountered in general pediatric clinical practice and accounts for 3% of cases at primary care units (Singh and Conner, 2018).

The prevalence of constipation ranging between 0.5-32% in children <4 years of age in United State, Asian and European country (Koppen *et al*, 2018) and 2.4% in Songkhla Province, Thailand (Osatakul and Puetpaiboon, 2014). Moreover, a study by Voskuijl *et al* (2004) revealed as high as 64% prevalence of constipation in a tertiary care center in Amsterdam, Netherlands. Of these, the most frequent etiology being functional constipation (Tabbers *et al*, 2014), Overall, median age of children presenting symptoms of constipation is 2.3 years old, with no correlation observed between sex and constipation severity (Mugie *et al*, 2011; Turco *et al*, 2014).

Diagnosis of functional constipation is based on detailed interview of parents/caregivers on child's natural history and physical examination. Most frequent reference criteria for functional constipation are Rome IV diagnostic guidelines (Benninga *et al*, 2016), and definitive diagnosis in children <4 years of age is based on fulfilling two of the seven following criteria: (i) ≤2 defecations per week, (ii) history of excessive stool retention, (iii) history of painful or difficult bowel movement, (iv) history of large-diameter stool, (vi) presence of a large fecal mass in rectum, and (in toilet-trained children), (vi) at least one episode weekly of incontinence after acquiring toilet training skill, and (vii) history of large-diameter stools that may obstruct toilet flushing. A natural history of functional constipation can be prolonged and causes physical and emotional problems to affected children, and in addition, can create emotional stress to parents/caregivers (Rajindrajith *et al*, 2012). Common complications arising from functional constipation are anal pain, anal fissure, lower gastrointestinal bleeding, abdominal distension, chronic abdominal pain, failure to thrive, and psychosocial and learning problems.

The precipitating causes of functional constipation among children are multifactorial ranging from intrinsic factors to environmental conditions. These factors are an imbalance of fiber intake, amount of solid food ingestion, duration of breast milk feeding, daily amount of water or milk ingestion, improper age in switching from milk to solid food, low physical activity, prolonged screen time, previous medical condition or illness, medication use, too strict or inappropriate time for toilet training, switching to nursery care, time in daycare, socioeconomic status, number of family members, marital status of parents, and stressful conditions in family life (Yamada *et al*, 2019). Intrinsic factors are family history of constipation, allergic disorder, gender, experience of painful defecation and genetic predisposition.

Functional constipation is mainly a non-organic disorder needing long term management, such as dietary change, habitual and regular toilet training and behavioral modification; successful treatment depends on intensive reassurance, long term follow-up and appropriate medical therapy from physician and parents/caregivers (Nurko and Zimmerman, 2014). Laxative agents comprise the most widely prescribed

and effective therapy for functional constipation in pediatric age group (Bell and Wall, 2004; Gordon *et al*, 2016).

Several studies have described risk factors of pediatric functional constipation, such as personal or family history of atopy, paracetamol use in children, female gender, types of complimentary food *eg* gluten in diet during first year of life, allergy to cow milk, diet low in fruit and vegetables and inadequate liquid intake (Turco *et al*, 2014; Okuda *et al*, 2019; Boilesen *et al*, 2017). Successful treatment leads to amelioration of risk factors of constipation from the daily life of children.

Causes and risks of functional constipation vary among different countries due to race, genetic background, lifestyle, culture, eating habits and environmental factors (Rajindrajith *et al*, 2016). To the best of the authors' knowledge, this is the first study of identifying risk factors of functional constipation among Thai children, and eliminating or reducing these risks should assist in initiating successful treatment. The findings should allow development of appropriate educational programs for parents and forestall the occurrence of functional constipation among their children.

MATERIALS AND METHODS

Recruitment of participants

Children 1-4 years of age attending an outpatient pediatric department, Phramongkutklao Hospital, Bangkok, Thailand between September 2017 and January 2018 were enrolled. Children were allocated into constipation and control groups, the former based on Rome IV diagnostic criteria for functional constipation, namely, fulfilling at least 2 out of 7 criteria items (Benninga *et al*, 2016). Exclusion criteria were children with major intestinal or extra-intestinal disorders, which might cause constipation, and chronic use of medication affecting intestinal motility. Each group consisted of an equal number of at least 37 participants based on prevalence of breastfeeding for <6 months duration in constipation and non-constipation group of 92.3 and 62.7% respectively and with a power of 80% and level of significance at 5% (Park *et al*, 2016).

Study protocol was approved by the Ethics Committee, Phramongkutklao Hospital and Phramongkutklao College of Medicine (no. R090q/60). Prior written consent was obtained from parents or legal guardian of each participating child.

Study design

A case-control study was employed using a questionnaire developed by investigators. The questionnaire gathered demographic data of participants and family members, consisting of participant history of bowel movement, abnormal defecatory symptoms, lifestyle, eating habits and psychosocial problems that could cause of constipation, and history of constipation in family members (of any age) requiring long term laxative agents.

Statistical analysis

Continuous data in the questionnaire

were compared between constipated and control groups using Student's t-test and categorical data using chi-square and Fisher's exact test. Univariate logistic regression analysis was performed to identify significant risk factors and those with *p*-value <0.2 were subsequently subjected to a multivariate logistic regression analysis to identify independent risk factors. Statistical significance is accepted at *p*-value <0.050. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) Version 17.0 (SPSS Inc, Chicago, IL)

RESULTS

Children 1-4 years of age attending the pediatric outpatient department, Phramongkutklao Hospital, Bangkok between September 2017 and January 2018 were equally allocated into constipation and non-constipation (control) groups, 45 subjects each. Demographic profiles of the participating children and their parents/caregivers are not significantly different between the two groups except that children in the constipation group are older, with more numbers attending a nursery or kindergarten and from a family with history of constipation compared to those in control group (Table 1).

All children in the constipation group had a duration of defecation problems for >1 month with a mean duration of six months (Table 2). The most common finding among children with constipation was item 3 in Rome IV diagnostic criteria and least common was item 7 (Table 2). Stool withholding behaviors reported consisted of hiding (47%), holding onto furniture (42%), standing on toes (36%) and crossing of legs (13%). Based on a Bristol's stool scale, stool in children with constipation belonged either to type 1 or 2, while that of control children type 3 or 4; bloody stool was observed in nearly one-third of children with constipation but no soft or watery stool in both groups (Table 2).

Univariate logistic regression analysis revealed (i) exclusive formula feeding within the first year of life, (ii) daily vegetable/fruit ingestion of <1 ladle, (iii) daily water intake of <250 ml, (iv) daily fruit juice intake <250 ml, (v) weekly energetic (sweating) movement/activity ≥4 days, and (vi) presence of stressful events in family (one case of severe illness, one case of a new child and three cases of frequent long-distance (>2 hours) travels) are significant risk factors for constipation, and subsequent multivariate logistic regression analysis indicated items (ii) and (iii) are independent risk factors (Table 3). On the other hand, energetic (sweating) movement/activity ≥4 days per week marginally reduced risk of constipation.

DISCUSSION

Functional constipation is a common problem, especially among preschool children and can cause concern to both child and parents/caregivers (Kaugars *et al*, 2010). Many children with chronic constipation require long term management involving medical and intensive behavioral modification but children with appropriate compliance

can recover with excellent outcome within a short duration. The multitude of risk factors for developing functional constipation in children differ from those of adults and Identifying such risk factors will assist physicians and parents/caregivers in early identification of the problem enabling introduction of appropriate behavioral modifications. The present study identifies among Thai children 1-4 years of age four risk factors for constipation, two of which are independent factors, namely, daily vegetable/fruit ingestion of <1 ladle and daily water intake of <250 ml.

Several studies have shown an association between constipation and low fiber intake (Morais *et al*, 1999; Roma *et al*, 1999; Kranz *et al*, 2012). The American Academy of Family Physicians (AAFP) suggests a high fiber diet that includes whole grains, fruits and vegetables as part of dietary modification to treat functional constipation among infants and children (Nurko and Zimmerman, 2014). Insoluble fibers found in wheat bran, whole grains and some vegetables have a bulking action and help food pass more quickly through the intestine (Axelrod and Saps, 2018). In a review by Boilesen *et al* (2017), the authors noted a cut-off in daily water intake related to risk of constipation in children varies from 400 to 1,800 ml depending on age, but increase in daily water intake does not remedy the situation and is not included in current treatment recommendations (Koppen *et al*, 2015; Philichi, 2018; Yachha *et al*, 2018).

Exclusive formula feeding in the first year of life and stressful event in the family both were 10 folds more common among children with than without constipation. In breast milk, palmitic acid in triglycerides is positioned at sn-2 position, whereas in infant formula it is located at sn-1 and sn-3 positions, which are readily hydrolyzed by pancreatic lipase and the released palmitic acid form insoluble salts with calcium resulting in firmer stools (Quinlan *et al*, 1995). Stress can alter intestinal motility and visceral perception, disturb autonomic tone of the intestine and dysregulated the hypothalamic-pituitary-adrenal axis (Chang, 2011). Thus, children with psychosocial stress and emotional problems are more prone to manifest defecation anxiety and stool withholding leading to difficulty to achieve successful toilet training (Blum *et al*, 2004, Joinson *et al*, 2019). Training of mothers/caregivers in stress management methods of children with anxiety and depression ameliorates functional gastrointestinal disorders and severity of intestinal symptoms (Lu *et al*, 2019).

Genetic factors or familial predisposition is a possible cause of constipation in children as evidenced by presence in the constipation group of seven children from families with history of constipation while none was identified in control group. Some studies have reported this genetic association (Chan *et al*, 2007; Dehghani *et al*, 2015), but the actual genetic markers have yet to be identified (Peeters *et al*, 2011). However, environmental factors such as eating habits and cultural behavior regarding

toilet training cannot be ruled out.

Regular physical activity was identified to be a protective factor against constipation among adults by improving rectosigmoid and colonic transit time among patients presenting chronic idiopathic constipation (De Schryver *et al*, 2005). In children, several reviews of the literature clearly indicate decreased physical activity as a risk factor for constipation (Inan *et al*, 2007; Driessen *et al* 2013; Olaru *et al*, 2016). Thus, parents/caregivers should be advised to include regular active physical activity as a preventive measure against onset of functional constipation.

In conclusion, the study has identified a small but significant number of risk factors for functional constipation in children, which family pediatricians should be aware of and inform parents/caregivers of appropriate measures not only to prevent the occurrence of this condition but also to provide advice on remediating the situation that can have profound adverse (but avoidable) consequences on their children physical and mental wellbeing.

Table 1

Demographic profiles of children in constipation and control groups enrolled at an outpatient pediatric department, Phramongkutklao Hospital, Bangkok, Thailand (September 2017 to January 2018)

Demographic profiles of children	Constipation group Number (%) (n = 45)	Control group Number (%) (n = 45)	p-value*
Female	24 (53)	19 (42)	0.291
Age, years (mean ± SD)	2.8 ± 0.9	2.2 ± 0.9	0.003
BMI, kg/m^2 (mean ± SD)	16 ± 2	16 ± 2	0.665
Gestational age, weeks (mean ± SD)	38 ± 2	38 ± 2	0.676
Birth weight, kg (mean ± SD)	3.0 ± 0.6	3.0 ± 0.4	0.848
Type of care			0.003
At home	*25 (55)*	39 (87)	
Nursery	8 (18)	4 (9)	
Kindergarten	12 (27)	2 (4)	
Number of siblings (including subject)			0.455
1	26 (58)	26 (58)	
2	17 (38)	14 (31)	
≤3	2 (4)	5 (11)	
Age of father, years (mean ± SD)	36 ± 7	35 ± 6	0.665

Table 1 (cont)

Demographic profiles of children	Constipation group Number (%) (n = 45)	Control group Number (%) (n = 45)	p-value*
Education of father			0.293
Up to primary education	3 (7)	3 (7)	
Up to 6th grade	5 (11)	7 (15)	
Up to 9th grade	9 (20)	10 (22)	
Up to 12th grade	9 (20)	7 (16)	
Vocational education	14 (31)	18 (40)	
Bachelor degree or higher	5 (11)	0 (0)	
Age of mother, years (mean ± SD)	33 ± 6	32 ± 6	0.609
Education of mother†			0.092
Up to primary education	4 (9)	1 (2)	
Up to 6th grade	3 (7)	5 (11)	
Up to 9th grade	10 (23)	9 (20)	
Up to 12th grade	4 (9)	9 (20)	
Vocational education	18 (41)	21 (47)	
Bachelor degree or higher	5 (11)	0 (0)	
Parent marital status			1.00
Married	41 (91)	40 (89)	
Separated	4 (9)	5 (11)	
Family with history of constipation	7 (16)	0 (0)	0.012
Family monthly income (THB)‡			0.552
<20,000	26 (58)	24 (53)	
≥20,000	19 (42)	21 (47)	
Category of housing			0.605
House	17 (38)	19 (42)	
Townhouse	5 (11)	8 (18)	
Condominium/flat	13 (29)	10 (22)	
Rented house	10 (22)	7 (16)	
Other	0	1 (2)	

*Significant at p <0.050; †Information not available from one mother in constipation group; ‡33.2 THB = USD1.00 (September, 2017)

BMI: body mass index; kg: kilogram; kg/m^2: kilogram per square meter; SD: standard deviation; THB: Thai Baht; USD: US dollars

Table 2

Abnormal defecation symptoms, stool characteristic and stool withholding behavior in constipated and control children groups enrolled at an outpatient pediatric department, Phramongkutklao Hospital, Bangkok, Thailand (September 2017 to January 2018)

Abnormal defecation symptoms and stool characteristic	Constipation group Number (%) (n = 43)	Control group Number (%) (n = 45)	p-value*
Functional constipation in infant/childhood†			
1. ≤2 defecations per week	14 (33)	1 (2)	<0.001
2. History of excessive stool retention	16 (37)	0 (0)	<0.001
3. History of painful or hard bowel movements	36 (84)	1 (2)	<0.001
4. History of large-diameter stools	24 (56)	0 (0)	<0.001
5. Presence of a large fecal mass in the rectum	4 (9)	0 (0)	0.053
6. At least one episode/week of incontinence after acquisition of toilet skills	6 (14)	0 (0)	0.011
7. History of large-diameter stools that may obstruct toilet flushing	3 (7)	0 (0)	0.112
Duration of constipation (month ± SD)	6 ± 6	NA	NA
Presence of bloody stool	14 (31)	0 (0)	<0.001
Presence of stool withholding behavior	37 (82)	0 (0)	<0.001
Stool characteristic‡			<0.001
Type 1: separate hard lumps (difficult to excrete)	21 (49)	0 (0)	
Type 2: lumpy sausage-shaped	22 (51)	0 (0)	
Type 3: sausage-shaped with cracks on surface	0 (0)	13 (29)	
Type 4: smooth and soft sausage- or snake-shaped	0 (0)	32 (71)	
Type 5: soft blob with clear-cut edge	0 (0)	0 (0)	
Type 6: fluffy or mushy with ragged edge	0 (0)	0 (0)	
Type 7: watery with no solid piece or entirely liquid	0 (0)	0 (0)	

*Significant at p <0.050; †Rome IV criteria; ‡Bristol's stool scale

NA: not applicable; SD: standard deviation

Table 3

Univariate and multivariate logistic regression analyses of risk factors for functional constipation in constipated and control children groups attending an outpatient pediatric department, Phramongkutklao Hospital, Bangkok, Thailand (September 2017 to January 2018)

Variable	Constipation group Number (%) (n = 45)	Control group Number (%) (n = 45)	Univariate analysis OR (95% CI)	p-value*	Multivariate analysis Adjusted OR (95% CI)	p-value*
Exclusive breastfeeding within first year of life	17 (38)	14 (31)	1.34 (0.56-3.22)	0.506		
Exclusive formula feeding within first year of life	8 (18)	1 (2)	9.51 (1.14-79.6)	0.038		
No breastfeeding or cessation of breastfeeding before six months of age	19 (42)	19 (42)	1.00 (0.43-2.31)	1.000		
Formula milk introduction before six months of age	20 (44)	22 (49)	0.84 (0.37-1.92)	0.673		
Complimentary food introduction before six months of age	10 (22)	11 (24)	1.13 (0.43-3.01)	0.803		
Daily vegetable/fruit ingestion <1 ladle	35 (78)	12 (27)	9.63 (3.67-25.25)	<0.001	11.07 (3.82-32.08)	<0.001
Daily water intake <250 ml	22 (49)	8 (18)	4.42 (1.69-11.58)	0.003	5.47 (1.73-17.34)	0.004
Daily milk intake >250 ml	39 (87)	42 (93)	2.15 (0.5-9.21)	0.301		
Daily fruit juice intake <250 ml	42 (93)	38 (84)	2.58 (0.62-10.69)	0.192		
Weekly energetic (sweating) movement/activity ≥4 days	38 (84)	44 (98)	8.11 (0.95-68.87)	0.055		
Sedentary activity ≥2 hours per day	31 (69)	36 (80)	0.55 (0.21-1.45)	0.230		
Defecation in a standing position	21 (47)	20 (44)	0.96 (0.41-2.23)	0.929		
Presence of stressful events in family	8 (18)	1 (2)	9.51 (1.14-79.6)	0.038		

*Significant at p <0.050

CI: confidence interval; ml: milliliter; OR: odds ratio

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