

Bladder and bowel dysfunction in mothers and children: a population-based cross-sectional study

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ABSTRACT – Background – Recently it was shown an association between lower urinary tract symptoms in mothers and their children. However, the role of functional constipation in this binomial is unclear. **Objective** – To evaluate bladder and bowel dysfunction between mothers and children. **Methods** – A population-based cross-sectional study. Mothers and their children responded a self-administrated questionnaire composed by Rome IV criteria, International Consultation on Incontinence Questionnaire – Overactive Bladder, Dysfunctional Voiding Scoring System and demographic questions. **Results** – A total of 441 mother-child pairs was obtained. Children's mean age was 9.1 ± 2.7 years, with 249 (56.5%) female. Mothers' mean age was 35.7 ± 6.1 years. Isolated constipation was present at 35 (7.9%) children and 74 (16.8%) mothers. Isolated lower urinary tract symptoms were present in 139 (31.5%) children and 92 (20.9%) mothers and bladder bowel dysfunction occurred in 51 (11.6%) children and 78 (17.7%) mothers. There wasn't any association between isolated lower urinary tract symptoms in children and isolated lower urinary tract symptoms in mothers ($P=0.31$). In univariate analysis there were an association between bladder bowel dysfunction in children and bladder bowel dysfunction in mothers (OR=4.8 IC 95% 2.6–9.6, $P<0.001$) and isolated constipation in children and isolated constipation in mothers (OR=3.0 IC 95% 1.4–6.4, $P=0.003$). In multivariate analysis mothers with bladder bowel dysfunction was the only independent factor associated with bladder bowel dysfunction in children (OR=5.4 IC 95% 2.5–11.6, $P<0.001$). **Conclusion** – Mothers with bladder bowel dysfunction are more likely to have a child with bladder bowel dysfunction. Association between these two dysfunctions plays an important role in this familiar presentation.

HEADINGS – Constipation. Lower urinary tract symptoms. Child. Mothers.

INTRODUCTION

Bladder and bowel dysfunction (BBD) is present when there is co-occurrence of lower urinary tract symptoms (LUTS) and functional constipation (FC)⁽¹⁾. Approximately 50% of children who seek medical attention because of LUTS have FC at the moment of consultation⁽¹⁾. This is confirmed by a recent study proving that the presence of FC in children raised in 6.8 times the likelihoods of them to also present with LUTS⁽²⁾. Although BBD is a complex clinical condition because of its symptoms and its association with psychosocial problems, its physiopathology is yet to be clarified⁽³⁾.

BBD can result from pelvic organs cross-sensitization; when pathological stimuli from neighboring pelvic organs lead to altered bladder functioning as urinary urgency and dysfunctional voiding⁽³⁾. The common innervation and the common embryological origin of both organs, bladder and rectum, and their anatomical proximity can explain their cross-talk⁽³⁾. Furthermore, those children presenting with FC have an increased prevalence of urgency and urinary incontinence, lower urinary tract infections, enuresis and Vesicoureteral Reflux (VUR)⁽⁴⁾. Also, FC treatment in those children resulted in partial or complete improvement of LUTS⁽⁴⁾.

Many studies have demonstrated the influence of genetic and environmental factors over LUTS, such as enuresis⁽⁵⁾. Actually, we

have demonstrated LUTS family association between mothers and children previously⁽⁶⁾. However, the role of FC in the analysis was not evaluated, and the influence of family history in the development of BBD is yet to be determined^(6,7).

Therefore, a population-based study using validated diagnostic criteria can result in relevant information about family history of BBD, isolated LUTS (LUTS without FC) and isolated FC (FC without LUTS). The objective of the present study is to evaluate the family association between mothers and children for BBD, isolated LUTS and isolated FC.

METHODS

This is a cross-sectional study conducted in a Brazilian city from October 2016 to April 2017. Data collection was carried out in public squares and parks. Mothers were approached one by one randomly at collection points of different social-economic levels. We asked them to participate voluntarily through a self-administered questionnaire after signing the informed consent. The study was submitted to the Ethics Committee and obtained approval under the reference of CAAE 51086715.4.0000.5544.

Previously trained physicians and medical students conducted the study. The self-reported questionnaires were easy to understand, and there was no need for the questions to be read out loud, ensur-

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ing privacy. Mothers went to a quieter and more private location of the square or park to answer the questionnaires which were answered in about 15 minutes.

Inclusion criteria were children aged 5-14 years-old whose mothers lived with them and agreed to participate. Our exclusion criteria were (1) illiterate mothers, once questionnaires were self-administered, (2) children and mothers with neurological conditions or urinary tract or gastrointestinal malformations that could affect correct bladder functioning, and (3) mothers who did not answer the forms completely.

Questionnaires contained social-demographic information: mothers' education level, children's age, gender and ethnicity and whether the child attended a private or a public school. It also contained Dysfunctional Voiding Scoring System (DVSS) for children's LUTS whereas mothers' were asked through International Consultation on Incontinence Questionnaire – Overactive Bladder (ICIQ-OAB). ROME IV criteria (children's and adults') evaluated FC symptoms. All questionnaires were validated for the language in use⁽⁸⁻¹¹⁾.

DVSS contains ten questions including nine items concerning clinical symptoms and one item about psychosocial stress⁽⁸⁾. In questions one to nine, numerical answers were taken based on a Likert scale with scores from 0–3 according to the presence and severity of symptoms⁽⁸⁾. In the 10th item, no stressful events in the child's life meant zero points and three points if they were present⁽⁸⁾. Children were considered with LUTS when urinary symptoms were present at least one or two times a week: score one at items 1,2,5,6,7,8 and 9 of DVSS⁽⁸⁾. Items 3 and 4 were not used to define LUTS because they refer to bowel symptoms⁽⁸⁾. The 10th item also was kept out of the analysis because it refers to psychosocial symptoms⁽⁸⁾.

ICIQ-OAB contains four questions about daily urinary frequency, nocturia, urinary urgency and urinary incontinence⁽⁹⁾. Answers were scored from 0–4 in a Likert scale also according to the presence and severity of symptoms⁽⁹⁾. Mothers were positive for urinary urgency or urinary incontinence when presented them at least "sometimes" (score two)⁽⁹⁾. Nocturia was defined as at least two micturitions at night (score two). Increased daily urinary frequency happened when mothers had nine or more micturitions a day (score two)⁽⁹⁾. Mothers with LUTS had either nocturia or urgency or incontinence or increased daily urinary frequency⁽⁹⁾.

ROME IV criteria, adults' and children's, contain six questions adapted to each version^(10,11). Child/Adolescent ROME IV criteria are: (1) Two or fewer defecations in the toilet per week; (2) At least one episode of fecal incontinence per week; (3) History of retentive posturing or excessive volitional retention; (4) History of painful or hard bowel movements; (5) Presence of a large fecal mass in the rectum; (6) History of large diameter stools which may obstruct the toilet⁽¹⁰⁾. Children were constipated when they presented at least two positive criteria⁽¹⁰⁾.

Adults' ROME IV criteria are: (1) Straining during at least 25% of defecations; (2) Lumpy or hard stools in at least 25% of defecations (3) Sensation of incomplete evacuation for at least 25% of defecations (4) Sensation of anorectal obstruction/blockage for at least 25% of defecations (5) Manual maneuvers to facilitate at least 25% of defecations (6) Fewer than three defecations per week⁽¹¹⁾. Mothers were constipated when they presented at least two positive criteria⁽¹¹⁾.

According to those urinary and intestinal symptom definitions, we established the following groups:

- FC: as the group of individuals we disregarded the presence or the absence of LUTS;
- LUTS: as the group of those we disregarded the presence or the absence of FC;
- Isolated LUTS: when urinary symptoms were present in the absence of constipation;
- Isolated FC: when constipation was present in the absence of LUTS;
- BBD: when there was the co-occurrence of LUTS and FC.

Statistical analysis

We used SPSS 20.0 version for statistical analysis. The normality of numerical variables was evaluated using descriptive statistics, graphics analysis, and the Kolmogorov-Smirnov test. Numerical variables (mothers' and children's ages) were expressed as mean and standard deviation. Categorical variables (social-demographic variables, LUTS, FC, isolated LUTS, isolated FC, and BBD) were described as absolute numbers and proportions.

For the sample size calculation, we estimated a BBD prevalence of 10% in children⁽²⁾. In mothers, a higher number of FC is expected in comparison to children's population⁽¹¹⁾; therefore, we estimated the prevalence of BBD no greater than 20%. It was necessary to estimate this percentage since there are few studies concerning BBD in adults. Then, to attain a power of 80% and a 95% confidence level, we needed a sample of, at least, 216 children and 384 mothers.

To analyze the association between numerical variables (mothers' and children's ages) and BBD in children we used t-student test. Pearson chi-square test was used to calculate the association between categorical variables: social-demographic variables and BBD in children; isolated FC in mothers and isolated FC in children; isolated LUTS in mothers and isolated LUTS in children; BBD in mothers, isolated LUTS in mothers and isolated FC in mothers and BBD in children. Associations were significant when $P < 0.05$.

Afterward, all social-demographic variables and mothers' clinical characteristics (isolated LUTS, isolated FC, and BBD) were inserted into a logistic regression model in which BBD in children was the dependent variable as we tried to adjust for confounding variables. LUTS in mothers and FC in mothers were not inserted in this model because BBD in mothers is strongly correlated to them. It would interfere in the integrity of the results if they were all together in this analysis.

RESULTS

We interviewed 526 mothers and 526 children, but only 441 mother-child pairs presented their questionnaires fully answered. Children's mean age was 9.1 ± 2.7 years-old whereas mothers' was 35.7 ± 6.1 years-old. The mean ages did not differ significantly between groups of children with and without BBD, $P = 0.80$ for children's mean age and $P = 0.80$ for mothers' mean age. The study population is described in TABLE 1.

LUTS were present in 190 (43.1%) children and 170 (38.5%) mothers while FC was present in 86 (19.5%) children and 152 (34.5%) mothers. Isolated FC was observed in 35 (7.9%) children and 74 (16.8%) mothers whereas isolated LUTS were found in 139 (31.5%) children and 92 (20.9%) mothers. The co-occurrence of FC and LUTS, known as BBD, was present in 51 (11.6%) children and 78 (17.7%) mothers.

There was a positive association between mothers and children with LUTS; mothers with LUTS had 1.6 times more chance to

TABLE 1. Social-demographic characteristics of children (n=441) according to the presence of bladder and bowel dysfunction.

Variables	Children with BBD n (%)	CI 95%	Children without BBD n (%)	CI 95%	P-value
Gender					
Feminine	216 (55.5)	50.6–60.4	33 (63.5)	49.8–75.7	0.28
Masculine	173 (44.5)	39.6–49.4	19 (36.5)	24.3–50.2	0.28
Ethnicity					
White	75 (19.3)	15.6–23.4	10 (19.2)	10.2–31.6	0.99
Afro-American	102 (26.2)	22.0–30.8	13 (25.0)	14.7–38.0	0.85
Brown	199 (51.2)	46.2–56.1	24 (46.2)	33.0–59.7	0.50
Indigene	13 (3.3)	1.9–5.5	5 (9.6)	3.6–20.0	0.05
School attended					
Public	165 (42.4)	37.6–47.4	23 (44.2)	31.2–57.9	0.80
Private	224 (57.6)	52.6–62.4	29 (55.8)	42.1–68.8	0.80
Mothers' education level					
≤ High school	247 (63.5)	58.6–68.2	33 (63.5)	49.8–75.7	0.99
≥ Higher education	142 (36.5)	31.8–41.4	19 (36.5)	24.3–50.2	0.99

BBD: bladder and bowell dysfunction; CI: confidence interval.

have children with the same condition (OR 1.6 CI 95% 1.0–2.3, $P=0.00$). FC in mothers was also associated with FC in children; they had three times more chance to have children with FC (OR 3.0 CI 95% 1.9–4.95, $P=0.00$). Both analyses disregarded individuals with and without BBD.

Mothers with isolated FC had more children with isolated FC, $P=0.003$ (TABLE 2), although there was no association between mothers and children with isolated LUTS (TABLE 3), $P=0.31$. Also, mothers with BBD raised in 4.8-fold the chance of their children to have BBD (OR=4.8 IC 95% 2.6–9.6, $P=0.000$) (TABLE 4). Isolated FC and isolated LUTS in mothers weren't associated to BBD in children (OR=0.9 IC 95% 0.4–2.00, $P=0.83$, and OR=0.6 IC 95% 0.2–1.3, $P=0.16$, respectively) (TABLE 4).

In multivariate analysis, BBD in mothers was the only independent factor associated with BBD in children (OR=5.4 IC 95% 2.5–11.6, $P=0.00$).

TABLE 2. Univariate analysis of isolated functional constipation between mothers and children.

Variables	Mothers with isolated FC n (%)	Mothers without isolated FC n (%)	OR	CI 95%	P-value
Children with isolated FC	12 (16.2)	22 (6)	3.0	1.4–6.4	0.003
Children without isolated FC	62 (83.8)	345 (94)			

Isolated FC: FC without LUTS; OR: odds ratio; CI: confidence interval.

TABLE 4. Frequency of children with and without bladder and bowel dysfunction according to mother's clinical characteristics.

	Mothers								
	BBD n (%)			Isolated FC n (%)			Isolated LUTS n (%)		
	with	without	P-value	with	without	P-value	with	without	P-value
Children with BBD	23 (29.5)	29 (8)	0.00	8 (10.8)	44 (12)	0.83	7 (7.6)	45 (12.9)	0.16
Children without BBD	55 (70.5)	334 (92)		66 (89.2)	323 (88)		85 (92.4)	304 (87.1)	

BBD: bowel and bladder dysfunction; Isolated FC: FC without LUTS; Isolated LUTS: LUTS without FC.

DISCUSSION

This study aimed to evaluate the role of FC in the family association of LUTS, so we separated mothers and children with BBD, isolated FC, and isolated LUTS. We found positive associations between mothers and children with LUTS and between those with FC, groups in which we did not separate individuals with and without BBD. However, we only observed a positive association between mothers and children with isolated FC, but not with isolated LUTS. Also, mothers with BBD increased independently in 5.4-fold the chances of their children to have BBD.

A recent study from our research group showed a positive association of LUTS between mothers and children, although we did not evaluate the role of FC in that analysis^(6,7). Mothers with LUTS had 2.5 more chance to have children with LUTS while mothers with Overactive Bladder (OAB) had 2.8 more chance to have chil-

TABLE 3. Univariate analysis of isolated lower urinary tract symptom between mothers and children.

Variables	Mothers with isolated LUTS n (%)	Mothers without isolated LUTS n (%)	OR	CI 95%	P-value
Children with isolated LUTS	33 (35.9)	108 (30.9)	1.25	0.8–2.0	0.31
Children without isolated LUTS	59 (64.1)	241 (69.1)			

Isolated LUTS: LUTS without FC; OR: odds ratio; CI: confidence interval.

dren with OAB⁽⁶⁾. The present study, though, failed to encounter an association of isolated LUTS between mothers and children.

Other trial found that maternal urinary incontinence (UI) increased in 2.28 the likelihoods of their children to also have UI, whereas UI in fathers increased in 9.1 the likelihoods of their children to develop the same condition⁽¹²⁾. Likewise, children with a family history of enuresis also present with an increased risk of developing this dysfunction, mainly if both of their parents have a history of enuresis⁽⁵⁾. However, it is common knowledge that environmental influences can trigger LUTS in children^(5,6).

These findings suggest an interaction between hereditary and environmental factors in the development of LUTS^(13,14). Most studies, though, have failed to determine gene loci related to Lower Urinary Tract Dysfunction (LUTD)⁽¹⁵⁾. One paper found an association between a polymorphism in the Arg allele of the β -adrenoreceptor (β 3-AR) gene and an increased susceptibility in developing OAB⁽¹⁵⁾. Studies involving twins demonstrated that urinary incontinence, increased or decreased daily urinary frequency and nocturia were LUTS with the strongest hereditary behavior^(16,17). OAB and urinary urgency were the ones most associated with environmental influences^(16,17). Therefore, the Hereditary Component of LUTS remains uncertain.

Functional Gastrointestinal Disorders (FGID) also seem to suffer from genetic and environmental influences^(7,18). Individuals with constipated first-degree relatives have an increased chance of being constipated⁽⁷⁾. Chances are even higher if there are more than one case in family⁽⁷⁾. Children whose mothers report hard stools, encopresis and abdominal pain have more chances of also reporting the same symptomatology⁽¹⁸⁾. Furthermore, IBS which FC is one of its main clinical manifestations is commonly known to aggregate in families and affect multiple generations.

As it is for LUTD, the influence of genetic components over FC remains uncertain, and few studies tried to identify related genes, the majority of them with negative results⁽²²⁾. A recent paper demonstrated lower serum motilin levels in constipated children and it was also possible to associate those serum levels of this hormone to the Bristol stool scale⁽²³⁾. Other study compared the colonic epithelium of non-constipated individuals with those of patients with refractory constipation⁽²⁴⁾. Lower numbers of Cajal cells, higher numbers of macrophages and reduced miRNA-128 expression were found in the colonic specimens from the constipated patients⁽²⁴⁾. miRNA-128 regulates macrophages recruitment, and macrophages can cause Cajal cells death⁽²⁴⁾. Therefore, genetics may influence the development of gastrointestinal disorders, including FC⁽¹⁸⁻²⁵⁾.

Despite all the recent findings, genetic factors cannot be the only responsible for these dysfunctions (gastrointestinal and urinary)⁽¹³⁾. Environmental influences as psychosocial stress, dietary intake, history of infections and individual microflora may also be related to BBD, isolated FC and isolated LUTS⁽¹³⁾. They might be responsible for the phenotypic expression of a common genotype⁽²⁵⁻²⁹⁾.

The interaction between genetic and hereditary factors could explain our findings. The existence of genetic mutations would make those individuals affected by them more susceptible to these functional disorders (gastrointestinal and urinary). Then, the environment to which they would be exposed would help later to determine different clinical manifestations that exist (epigenetic). BBD and FC could be two manifestations of a common genetic mutation. We observed that BBD in mothers is an independent factor associated with BBD in children. Also, isolated FC in mothers was associated with isolated FC in children. Genetic influences over LUTS are yet to be explained.

As a limitation, this study collected only mothers' opinion about children's urinary and intestinal symptoms, which could lead to overemphasized or minimized data. However, the age range included here are mainly of children and pre-adolescents, ages in which the family still plays a significant role in their lives⁽³⁰⁾. So, we believe that most children reported their urinary or gastrointestinal symptoms to their mothers⁽³⁰⁾. Also, little evidence is available concerning BBD in children and adults; therefore, it is complicated to infer direct comparisons with the results found in this study. Most information came indirectly from studies about FC only or LUTS only.

CONCLUSION

BBD in mothers was an independent factor associated with BBD in children. Therefore, family history of BBD should be investigated routinely in pediatric care.

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Authors' contribution

Substantial contributions to conception and design: Ribeiro RS, Abreu GE, Barroso Jr U, Veiga ML, Lobo VA. Acquisition of data: Dourado ER. Analysis and interpretation of data: Ribeiro RS, Abreu GE, Barroso Jr U, Veiga ML. All authors have drafted revised and approved the article.

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RESUMO – Contexto – Recentemente foi demonstrada associação entre sintomas do trato urinário inferior entre mães e filhos. No entanto, o papel da constipação funcional neste binômio não é claro. **Objetivo** – Avaliar a disfunção vesíco-intestinal entre mães e filhos. **Métodos** – Estudo transversal de base populacional. As mães e os filhos responderam a um questionário de autorresposta, composto pelos critérios de Roma IV, *International Consultation on Incontinence Questionnaire – Overactive Bladder, Dysfunctional Voiding Scoring System* e perguntas sociodemográficas. **Resultados** – Foram estudados 441 pares mãe-filho. A idade média dos filhos foi de 9,1±2,7 anos, sendo 249 (56,5%) do sexo feminino. A idade média das mães foi de 35,7±6,1 anos. A constipação sem sintomas do trato urinário inferior estava presente em 35 (7,9%) crianças e 74 (16,8%) mães. Sintomas do trato urinário inferior isolados estavam presentes em 139 (31,5%) crianças e 92 (20,9%) mães e a disfunção vesíco-intestinal ocorreu em 51 (11,6%) crianças e 78 (17,7%) mães. Não houve associação entre sintomas isolados do trato urinário inferior em crianças e sintomas isolados do trato urinário inferior em mães ($P=0,31$). Na análise univariada, houve associação entre disfunção vesíco-intestinal em crianças e disfunção vesíco-intestinal em mães ($OR=4,8$ IC 95% 2,6–9,6; $P<0,001$) e constipação isolada em crianças e constipação isolada em mães ($OR=3,0$ IC 95% 1,4–6,4; $P=0,003$). Na análise multivariada, mães com disfunção vesíco-intestinal foi o único fator de associação independente para disfunção vesíco-intestinal em crianças ($OR=5,4$ IC 95% 2,5–11,6; $P<0,001$). **Conclusão** – Mães com disfunção vesíco-intestinal têm maior probabilidade de ter filhos com disfunção vesíco-intestinal. A associação entre constipação e sintomas do trato urinário inferior desempenha um papel importante nesta apresentação familiar.

DESCRIPTORIOS – Constipação intestinal. Sintomas do trato urinário inferior. Criança. Mães.

REFERENCES

- Burgers R, De Jong TPVM, Visser M, Di Lorenzo C, Dijkstra MGW, Benninga MA. Functional defecation disorders in children with lower urinary tract symptoms. *J Urol.* Elsevier Inc. 2013;189:1886-90.
- Sampaio C, Sousa AS, Fraga LGA, Veiga ML, Bastos Netto JM, Barroso U. Constipation and Lower Urinary Tract Dysfunction in Children and Adolescents: A Population-Based Study. *Front Pediatr.* 2016;4:1-6.
- Malykhina AP, Brodie KE, Wilcox DT. Genitourinary and gastrointestinal co-morbidities in children: The role of neural circuits in regulation of visceral function. *J Pediatr Urol.* Elsevier. 2017;13:177-82.
- Halachmi S, Farhat WA. Interactions of constipation, dysfunctional elimination syndrome, and vesicoureteral reflux. *Adv Urol.* 2008;2008:828275.
- Arnell H, Hjälmås K, Jägervall M, Läckgren G, Stenberg A, Bengtsson B, et al. The genetics of primary nocturnal enuresis: inheritance and suggestion of a second major gene on chromosome 12q. *J Med Genet.* 1997;34:360-5.
- Sampaio AS, Fraga LGA, Salomão BA, Oliveira JB, Seixas CL, Veiga ML, et al. Are lower urinary tract symptoms in children associated with urinary symptoms in their mothers? *J Pediatr Urol.* 2017;13:269.e1-269.e6.
- Chan AOO, Hui WM, Lam KF, Leung G, Yuen MF, Lam SK, et al. Familial aggregation in constipated subjects in a tertiary referral center. *Am J Gastroenterol.* 2007;102:149-52.
- Calado AA, Araujo EM, Barroso Jr U, Netto JMB, Zerati Filho M, Macedo Jr A, et al. Cross-cultural adaptation of the dysfunctional voiding score symptom (DVSS) questionnaire for Brazilian children. *Int Braz J Urol.* 2010;36:458-63.
- Pereira SB, Thiel R do RC, Ricetto C, Silva JM, Pereira LC, Herrmann V, et al. Validação do International Consultation on Incontinence Questionnaire Overactive Bladder (ICIQ-OAB) para a língua portuguesa. *Rev Bras Ginecol e Obs.* 2010;32:273-8.
- Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, Van Tilburg M. Childhood functional gastrointestinal disorders: Child/adolescent. *Gastroenterology.* W.B. Saunders. 2016;150:1456-1468.e2.
- Mearin F, Lacy BE, Chang L, Chey WD, Lembo AJ, Simren M, Spiller R. Bowel Disorders. *Gastroenterology.* 2016 pii: S0016-5085(16)00222-5. doi: 10.1053/j.gastro.2016.02.031.
- Von Gontard A, Heron J, Jonsson C. Family history of nocturnal enuresis and urinary incontinence: Results from a large epidemiological study. *J Urol.* 2011;185:2303-6.
- Olaru C, Diaconescu S, Trandafir L, Gimiga N, Stefanescu G, Ciubotariu G, et al. Some Risk Factors of Chronic Functional Constipation Identified in a Pediatric Population Sample from Romania. *Gastroenterol Res Pract.* 2016;2016:3989721.
- Dehghani SM, Moravej H, Rajaei E, Javaherzadeh H. Evaluation of familial aggregation, vegetable consumption, legumes consumption, and physical activity on functional constipation in families of children with functional constipation versus children without constipation. *Gastroenterol Rev.* 2015;2:89-93.
- Qu HC, Zhang W, Liu YL, Wang. Association between polymorphism of β 3- adrenoceptor gene and overactive bladder: a meta-analysis. *Genet Mol Res Mol Res.* 2015;14:2495-251.
- Wennberg A, Altman D, Lundholm C, Klint Å, Peeker R, Fall M, et al. Genetic Influences Are Important for Most But Not All Lower Urinary Tract Symptoms: A Population-Based Survey in a Cohort of Adult Swedish Twins. *Eur Urol.* 2011;59:1032-8.
- Rohr G, Kragstrup J, Gaist D, Christensen K. Genetic and environmental influences on urinary incontinence: A Danish population-based twin study of middle-aged and elderly women. *Acta Obstet Gynecol Scand.* 2004;83:978-82.
- Lewis ML, Palsson OS, Whitehead WE, van Tilburg MAL. Prevalence of Functional Gastrointestinal Disorders in Children and Adolescents. *J Pediatr.* 2016;177:39-43.e3.
- Saito YA. The Role of Genetics in IBS. *Gastroenterol Clin North Am.* Elsevier Ltd; 2011;40:45-67.
- Bonfiglio F, Nag MHA, Zheng FHT, Tigchelara MCCE, Reznichenko FWA, Homuth NVRG, et al. A GWAS meta-analysis from 5 population-based cohorts implicates ion channel genes in the pathogenesis of irritable bowel syndrome. 2018;30:e13358.
- Fukudo S, Kanazawa M, Mizuno T, Hamaguchi T, Kano M, Watanabe S, et al. Impact of serotonin transporter gene polymorphism on brain activation by colorectal distention. *Neuroimage.* Elsevier Inc. 2009;47:946-51.
- Peeters B, Benninga MA, Hennekam RC. Childhood constipation; An overview of genetic studies and associated syndromes. *Best Pract Res Clin Gastroenterol.* 2011;25:73-88.
- Ulusoy E, Arslan N, Kume T, Ulgenalp A, Cirah C, Bozkaya O, et al. Serum motilin levels and motilin gene polymorphisms in children with functional constipation. *Minerva Pediatr.* 2016. [Internet]. [cited 2018 Jun 9]. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/27706119>
- Liu W, Zhang Q, Li S, Li L, Ding Z, Qian Q, et al. The Relationship Between Colonic Macrophages and MicroRNA-128 in the Pathogenesis of Slow Transit Constipation. *Dig Dis Sci.* 2015;60:2304-15.
- Sagawa T, Okamura S, Kakizaki S, Zhang Y, Morita K, Mori M. Functional gastrointestinal disorders in adolescents and quality of school life. *J Gastroenterol Hepatol.* 2013;28:285-90.
- Logan BA, Correia K, McCarthy J, Slattery MJ. Voiding dysfunction related to adverse childhood experiences and neuropsychiatric disorders. *J Pediatr Urol.* 2014;10:634-8.
- Appak YÇ, Sapmaz ŞY, Doğan G, Herdem A, Özyurt BC, Kasirga E. Clinical findings, child and mother psychosocial status in functional constipation. *Turkish J Gastroenterol.* 2017;28:465-70.
- Farnam A, Rafeey M, Farhang S, Khodjastefajari S. Functional constipation in children: does maternal personality matter? *Ital J Pediatr.* 2009;35:25.
- Kilincaslan H, Abali O, Demirkaya SK, Bilici M. Clinical, psychological and maternal characteristics in early functional constipation. *Pediatr Int.* 2014;56:588-93.
- Breinbauer C. Youth: Choices and Change. Promoting Healthy Behaviors in Adolescents. *Adolescence.* 2005;40:231.

