



# Treatment of Constipation in Children with Idiopathic Chest Pain and Constipation Could Resolve Their Chest Pain

Zahra Kheirandish<sup>1</sup>, Mozhgan Moghtaderi<sup>2,\*</sup>, Naser Honar<sup>2</sup> and Zahra Shah Amiri<sup>1</sup>

<sup>1</sup>Department of Pediatrics, Division of Cardiology, Faculty of Medicine, Islamic Azad University - Kazerun Branch, Kazerun, Iran

<sup>2</sup>Neonatal Research Center, Shiraz University of Medical Science, Shiraz, Iran

\*Corresponding author: Neonatal Research Center, Shiraz University of Medical Sciences, Zand St., 71348-45794, Shiraz, Iran. Tel/Fax: +98-7136281563, Email: moghtadery@sums.ac.ir

Received 2018 November 24; Revised 2019 May 11; Accepted 2019 May 15.

## Abstract

**Background:** Chest pain is one of the most frequent causes of a child's referral to a cardiologist.

**Objectives:** The present study aimed at determining whether treatment of constipation in 4 - 17-year-old children with idiopathic chest pain stops their chest pain.

**Methods:** The current descriptive study was conducted on all patients aged 4 - 17 years old with idiopathic chest pain referring to the Pediatric Cardiology Clinic of Hejazi Hospital, Shiraz, Iran in 2016. A diagnosis of idiopathic chest pain is established after a thorough history taking, physical examination, and appropriate laboratory investigations in patients with no abnormality in the heart, lung, musculoskeletal system, psychological condition, and upper gastrointestinal tract. The study patients were divided into two groups: 36 patients with constipation as cases and 27 patients without constipation as controls. Patients with constipation were supported with toilet training programs and pharmacological treatment. Relief of chest pain was evaluated in the two groups after four months.

**Results:** There were no significant differences in terms of age, gender, weight, and height between the patients with idiopathic chest pain with and without constipation. The number and length of chest pain were significantly different between the case and control groups ( $P < 0.001$  and  $0.047$ , respectively). After medical treatment of constipation, chest pain was significantly stopped in patients with constipation compared with the ones without constipation ( $P < 0.001$ ).

**Conclusions:** The current study showed that resolution of constipation stopped chest pain in the patients with idiopathic chest pain and constipation. Physicians should consider treatment of constipation as a first modality in each patient with idiopathic chest pain and constipation due to its easy assessment.

**Keywords:** Constipation, Chest Pain, Gastroesophageal Reflux

## 1. Background

Chest pain is a common complaint in children, which rarely raises concern for heart disease, in contrast to chest pain in adults for coronary ischemia. Pediatric chest pain is originally classified into cardiac and non-cardiac groups. Idiopathic chest pain occurs in more than 98% of children and is related to gastrointestinal (GI), musculoskeletal, and pulmonary systems, as well as unknown origin (1-4).

Many studies reported upper GI disorder such as gastroesophageal reflux disease, esophageal spasm, peptic ulcer disease, drug-induced esophagitis/gastritis, and cholecystitis as an etiology in developing chest pain (5-8). There are few elderly case reports to associate lower GI diseases with chest pain (9, 10).

Functional constipation (FC) is a prevalent condition

in children with multifactorial etiology. The definition of FC is based on Rome IV criteria; two or more of the following six criteria for at least one month for infants up to four years and at least two months for children older than four years: (a) two or fewer bowel movements per week, (b) at least one episode of fecal incontinence per week after the child has acquired complete bowel control, (c) history of extensive fecal retention or withholding behavior by the child, (d) hard and painful stool, (e) large fecal mass on digital rectal examination, (f) stools large in diameter that cause rectal outlet obstruction (11, 12).

Constipation has different management modalities; toilet training programs encourage the children older than four years to go to toilet after each meal and sit in toilet for at least five minutes to make an effort to defecate; if she/he could complete toilet training, reward her/him by

small gifts such as stickers. Changing their dietary habits to high fiber diets and fluid intake alongside physical activity is also helpful. If the child is experiencing chronic constipation even after the mentioned modalities, medication is needed to increase bowel movement (13, 14).

There is evidence for association between FC and different diseases such as headache, migraine, overactive bladder, cow's milk allergy, rigid compulsive behavior, attention-deficit/hyperactivity disorder, nocturnal enuresis, and gastroesophageal reflux (15-20). However, a few investigations evaluating the relationship between pediatric chest pain and FC were found in the literature.

## 2. Objectives

The present study aimed at determining whether treatment of constipation in 4 - 17-year-old children with idiopathic chest pain stops their chest pain.

## 3. Methods

The present descriptive case-control study was conducted on all 4 - 17-year-old patients with idiopathic chest pain referred to Pediatric Cardiology Clinic of Hejazi Heart Center, Shiraz, Iran. The sampling procedure continued until all referral participants in 2016 (from January to December) enrolled in the study. After approval of the study protocol by Ethics Committee of Shiraz University of Medical Sciences, informed consent was obtained from each participant or his/her parents.

A diagnosis of idiopathic chest pain was established if the patient had no abnormality in the heart, lung, musculoskeletal system, psychological condition, and GI tract. Detailed history, physical examination, electrocardiography, and echocardiography were performed for all patients by the same cardiologist to rule out any cardiac diseases. In patients with no cardiac chest pain, information about the lung, musculoskeletal system, psychological condition, and GI involvement was collected via an interview. Cough and wheezing were considered as the pulmonary symptoms, trauma and point of tenderness were considered as musculoskeletal problems, and stress and anxiety as psychological problems. Symptoms were considered as upper GI disease if they accompanied by vomiting, difficult swallowing, heart burn, epigastric discomfort, and abdominal pain.

After the selection of patients with idiopathic chest pain, ibuprofen 4 mg/kg was started to control pain in all the subjects. A questionnaire was filled out to obtain some information about the heart disease and FC in all selected patients. The questionnaire had two parts: Part 1 included age, gender, the number of episodes of chest pain

in a week or a month, type of chest pain (sharp, squeezing, stab-like, tingling, and undefined), length and location of chest pain, accompanying symptoms (sighing, palpitation, dyspnea), and aggravating factors (respiration, change in position, exercise, eating, tenderness in palpation, awaking from sleep, heartburn). These questions were self-developed based on a review of related literature. Part 2 comprised of the number of bowel movement per week, number of fecal incontinence per week, diameter of the stool (small, punch), painful defecation, presence of blood in the stool, soiling, consistency of stool (hard, dry), withholding symptoms, abdominal pain, and abdominal distention. The second part questions were the modified form of Rome IV criteria (11, 12); each patient was diagnosed with FC if he/she had these characteristics.

After filling the questionnaire via interview, the patients with idiopathic chest pain were divided into two groups of with and without FC.

Patients in the case group with constipation were supported with toilet training programs and pharmacological treatment. Treatment regimen was started with polyethylene glycol (PEG) powder 0.3 g/kg once or twice daily, and in case of fecal disimpaction as 1 - 1.5 g/kg/day (for maximum four days); administration of Senna Gol syrup (Goldaru, Iran) 2.5 mg in the subjects 2 - 6 years, 7.5 mg in 6 - 12 years, and 15 mg in > 12 years, all once or twice daily. In patients with no improvement, magnesium hydroxide 1 mL/kg was prescribed. The patients with severe fecal impaction were treated with bisacodyl suppository (Tolidaru, Iran) 5 mg/day in children aged 2 - 10 years and 5 - 10 mg/day in subjects older than 10. If the patient experienced easy and frequent soft defecation for at least three months, medication was continued within the next month.

The patients were regularly followed up in both cardiology and GI clinics for four months. Weight and height were measured in all patients. Response to therapy was defined as relief of the initial symptoms of chest pain and constipation in the patients with this complaint.

### 3.1. Statistical Analysis

All the statistical analyses were performed using SPSS version 23.0 (IBM Corp.; Armonk NY, USA). Mean  $\pm$  standard deviation (SD) was used to describe continuous variables and independent t test to compare them. Frequencies and corresponding percentages of categorical variables were calculated and Pearson correlation and analysis of variance were used to assess their relationships. The comparison of chest pain before and after treatment of constipation was performed using chi-square test. P values of  $\leq 0.05$  were considered statistically significant.

#### 4. Results

A total of 36 patients (16 females, 20 males) with idiopathic chest pain and FC with in the age range of 4 to 17 years (mean:  $9 \pm 2.9$ ) as the case group and 27 (13 females, 14 males) patients within the same age range (mean  $11 \pm 2.4$ ) with idiopathic chest pain without FC as the control group were included in the study. Demographic data in the case and control groups are shown in Table 1; there were no significant differences in age, weight, and height between the two groups.

Characteristics of chest pain in patients with and without FC are shown in Table 2. The number of episodes and length of chest pain were significantly different between patients with and without constipation ( $P$  value  $< 0.001$  and  $0.047$ , respectively).

Characteristic	ICP with Constipation (N = 36), Mean $\pm$ SD	ICP Without Constipation (N = 27), Mean $\pm$ SD	P Value
Age, y	$9 \pm 2.9$	$11 \pm 2.4$	0.07
Weight, kg	$28.3 \pm 11.7$	$41.6 \pm 15.6$	0.21
Height, cm	$129.0 \pm 17.8$	$143.2 \pm 14.1$	0.45

Abbreviation: ICP, idiopathic chest pain.

The most frequent symptoms related to constipation in patients with chest pain were respectively abdominal pain, painful defecation, abdominal distension, and hard stool (Table 3).

Pharmacological management of FC was performed based on the protocol mentioned in the method section. Dietary changes alone led to resolution of constipation in four (11%) out of 36 patients. PEG was administered in 30 (83.3%) patients of whom two (5.6%) needed treatment with other laxatives.

After medical treatment of constipation, chest pain significantly stopped in patients with constipation compared with the ones without constipation ( $P < 0.001$ ) (Table 4).

#### 5. Discussion

It is well known that gastrointestinal diseases can be a reason for non-cardiac chest pain of unknown origin (20, 21). The current study results showed that treatment of children with constipation who referred with idiopathic chest pain significantly led to their relief.

Upper GI diseases such as gastroesophageal reflux disease, hypercontractile esophageal motility disorders with nutcracker, jackhammer esophagus, and distal esophageal spasm or achalasia are considered as identified causes of chest pain (6, 21). By endoscopic examination, many

studies found that gastritis, chronic duodenitis, and duodenogastric reflux can be a cause for chest pain (22). Sabri et al., conducted a study on 44 patients with chest and epigastric pain, showing 41 (93.2%) subjects with positive finding in endoscopy including gastritis, duodenitis, and esophagitis (23).

Lower GI diseases are observed in some case reports as a reason of chest pain. Fisher and Davis (9) reported an 81-year-old male patient admitted for fractured neck of his right femur. About 10 days after the surgery, he had recurrent episodes of retrosternal and right lower chest pain accompanied by nausea, dyspnea, sweating, and hiccup. No abnormality was detected in the heart and other examinations except for five days of constipation. Treatment of constipation led to the improvement of his chest pain.

Di Saverio et al., reported an 89-year-old female patient with chest pain and constipation (10). Luder et al., mentioned a 10-year-old male patient with acute respiratory distress, chest pain, and abdominal pain. Following the treatment of constipation, all symptoms were completely resolved in both cases (24).

Most importantly, the association of constipation with cardiac diseases is still questionable. Salmoirago-Blotcher revealed that postmenopausal females with constipation had an increased risk for cardiovascular diseases (25).

Out of 36 patients with chest pain and constipation, 25 reported improvement of chest pain after treating the constipation. Neural pathway of the heart and GI tract appear similar; this mechanism is proposed to explain constipation as a cause to develop chest pain (26). Another possible mechanism can be the increased plasma levels of serotonin in patients with constipation; elevated plasma levels of serotonin can indirectly cause chest pain across psychiatric diagnoses. Also, it might be filling of intestinal loops that push the diaphragm upward and stretching of the diaphragm, which cause pain usually in the left lower part of the chest.

Children in the current study complained of chest pain and constipation with chest pain less than two times per week for a few minutes or seconds. Non-cardiac organic chest pain often lasts for hours (27); however, most children in the current study did not like to talk about their pain.

Questions about bowel movement habits should be considered when evaluating a child with chest pain. Abdominal pain (88.9%), painful defecation (75%), and hard stool (66.7%) were the most common complaints in the patients with constipation.

All patients were recruited from one cardiology referral center in Shiraz; multicenter studies could help to have a larger sample size.

**Table 2.** The Characteristics of Chest Pain in the Study Participants

Characteristic	ICP with Constipation, No. (%)	ICP Without Constipation, No. (%)	P Value
<b>Episodes of pain</b>			< 0.001
2-3 times/mo	7 (19.4)	16 (59.2)	
Less than 2 times/wk	15 (41.6)	7 (25.9)	
More than 3 times/wk	14 (38.8)	4 (25.9)	
<b>Type of pain</b>			0.403
Sharp	6 (16.6)	1 (3.7)	
Squeezing	3 (8.3)	10 (37)	
Stab like	4 (11.1)	6 (22.2)	
Tingling	22 (61.1)	10 (37)	
Undefined	1 (2.7)	0	
<b>Length of pain</b>			0.047
Few seconds	9 (25)	2 (7.4)	
Few minutes	25 (69.4)	19 (70.3)	
Few hours	2 (5.5)	6 (22.2)	
<b>Location of pain</b>			0.371
Left sided	27 (75%)	21 (77.7)	
Bilateral	0	1 (3.7)	
Left hand	5 (13.8)	5 (18.5)	
Right hand	0	1 (3.7)	
Epigastric area	1 (2.7)	2 (7.4)	
Substernal area	4 (11.1)	3 (11.1)	
<b>Accompanying symptoms</b>			0.501
Sighing	1 (2.7)	0	
Palpitation	1 (2.7)	0	
Dyspnea	1 (2.7)	0	
<b>Aggravating factors</b>			0.271
Respiration	19 (52.7)	16 (59)	
Change in position	8 (22.2)	2 (7.4)	
Exercise	15 (41.6)	8 (29.6)	
Eating	4 (11.1)	0	
Tenderness in palpation	4 (11.1)	2 (7.4)	
Awakening from sleep	2 (5.5)	1 (3.7)	
Heartburn	2 (5.5)	1 (3.7)	

Abbreviation: ICP, idiopathic chest pain.

**Table 3.** The Characteristics of Bowel Habits in Patients with Idiopathic Chest Pain and Constipation

Characteristic	No. (%)
<b>Two or fewer bowel movements per week</b>	17 (47.2)
<b>One episode of fecal incontinence per week</b>	15 (41.7)
<b>Diameter of stool</b>	
Small	15 (41.7)
Punch	21 (58.3)
<b>Painful defecation</b>	27 (75)
<b>Presence of blood in stool</b>	3 (8.3)
<b>Soiling</b>	7 (19.4)
<b>Consistency of stool</b>	
Hard	24 (66.7)
Dry	12 (33.3)
<b>Withholding behavior</b>	3 (8.3)
<b>Abdominal pain</b>	32 (88.9)
<b>Abdominal distension</b>	26 (72.2)

**Table 4.** The Relief of Chest Pain After Treatment of Constipation in Patients with Idiopathic Chest Pain and Constipation

Chest Pain	ICP with Constipation and Pharmacological Therapy, No. (%)	ICP Without Constipation and Pharmacological Therapy, No. (%)	P Value
<b>Relieved</b>	25 (69.4)	4 (14.8)	
<b>Decreased</b>	6 (16.6)	1 (3.7)	< 0.001
<b>Not changed</b>	5 (13.8)	22 (81.4)	

Abbreviation: ICP, idiopathic chest pain.

### 5.1. Conclusions

The study data suggest that constipation should be considered in the evaluation of each child with idiopathic chest pain since assessment and treatment of constipation is easy. Treatment of constipation in children with idiopathic chest pain results in the relief of chest symptoms.

### Footnotes

**Authors' Contribution:** The study concept: Zahra Kheirandish, Naser Honar, and Zahra Shah Amiri; the study design: Zahra Kheirandish, Naser Honar, and Zahra Shah Amiri; supervision of the study: Mozghan Moghtaderi, Zahra Kheirandish, Naser Honar, and Zahra Shah Amiri; data collection and/or processing: Mozghan Moghtaderi, Zahra Kheirandish, and Zahra Shah Amiri; analysis and/or interpretation of data: Mozghan Moghtaderi, Zahra Kheirandish, and Naser Honar; literature review: Mozghan

Moghtaderi, Zahra Kheirandish, and Naser Honar; writing of the manuscript: Mozghan Moghtaderi and Zahra Kheirandish; critical revision of the manuscript for important intellectual content: Zahra Kheirandish, Mozghan Moghtaderi, Naser Honar, and Zahra Shah Amiri.

**Conflict of Interests:** The authors declared no conflict of interest.

**Ethical Approval:** The study protocol was approved by Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran.

**Funding/Support:** The research received no specific grant from any funding, commercial, or not-for-profit organization.

**Patient Consent:** Informed consent was obtained from each participant or his/her parents.

## References

- Danduran MJ, Earing MG, Sheridan DC, Ewalt LA, Frommelt PC. Chest pain: Characteristics of children/adolescents. *Pediatr Cardiol.* 2008;**29**(4):775-81. doi: [10.1007/s00246-008-9200-9](https://doi.org/10.1007/s00246-008-9200-9). [PubMed: [18305982](https://pubmed.ncbi.nlm.nih.gov/18305982/)].
- Hussain MZ, Ishrat S, Salehuddin M, Mahmood M, Islam MT. Chest pain in children: An update. *Mymensingh Med J.* 2011;**20**(1):165-70. [PubMed: [21240184](https://pubmed.ncbi.nlm.nih.gov/21240184/)].
- Husser D, Bollmann A, Kuhne C, Molling J, Klein HU. Evaluation of noncardiac chest pain: Diagnostic approach, coping strategies and quality of life. *Eur J Pain.* 2006;**10**(1):51-5. doi: [10.1016/j.ejpain.2005.01.011](https://doi.org/10.1016/j.ejpain.2005.01.011). [PubMed: [16291298](https://pubmed.ncbi.nlm.nih.gov/16291298/)].
- Khairandish Z, Jamali L, Haghbin S. Role of anxiety and depression in adolescents with chest pain referred to a cardiology clinic. *Cardiol Young.* 2017;**27**(1):125-30. doi: [10.1017/S104795116000238](https://doi.org/10.1017/S104795116000238). [PubMed: [26979465](https://pubmed.ncbi.nlm.nih.gov/26979465/)].
- Wang TL, Peng KR, Jiang MZ, Yu JD, Zhou XL. [Noncardiac chest pain and gastroesophageal reflux in children]. *Zhonghua Jie He He Hu Xi Za Zhi.* 2006;**29**(8):563-6. Chinese. [PubMed: [17074273](https://pubmed.ncbi.nlm.nih.gov/17074273/)].
- Kim YJ, Shin EJ, Kim NS, Lee YH, Nam EW. The importance of esophageal and gastric diseases as causes of chest pain. *Pediatr Gastroenterol Hepatol Nutr.* 2015;**18**(4):261-7. doi: [10.5223/pghn.2015.18.4.261](https://doi.org/10.5223/pghn.2015.18.4.261). [PubMed: [26770901](https://pubmed.ncbi.nlm.nih.gov/26770901/)]. [PubMed Central: [PMC4712539](https://pubmed.ncbi.nlm.nih.gov/PMC4712539/)].
- Durning SJ, Nasir JM, Sweet JM, Cation LJ. Chest pain and ST segment elevation attributable to cholecystitis: a case report and review of the literature. *Mil Med.* 2006;**171**(12):1255-8. doi: [10.7205/milmed.171.12.1255](https://doi.org/10.7205/milmed.171.12.1255). [PubMed: [17256696](https://pubmed.ncbi.nlm.nih.gov/17256696/)].
- Ottavanger JP, Wilson JH, Stricker BH. Drug-induced chest pain and myocardial infarction. Reports to a national centre and review of the literature. *Eur J Clin Pharmacol.* 1997;**53**(2):105-10. [PubMed: [9403280](https://pubmed.ncbi.nlm.nih.gov/9403280/)].
- Fisher AA, Davis MW. An elderly man with chest pain, shortness of breath, and constipation. *Postgrad Med J.* 2003;**79**(929):180. 183-4. doi: [10.1136/pmj.79.929.180](https://doi.org/10.1136/pmj.79.929.180). [PubMed: [12697928](https://pubmed.ncbi.nlm.nih.gov/12697928/)]. [PubMed Central: [PMC1742652](https://pubmed.ncbi.nlm.nih.gov/PMC1742652/)].
- Di Saverio S, Lombardi R, Bianchi E, Tugnoli G, Jovine E. An elderly woman with chest pain and constipation. *BMJ.* 2015;**350**:h166. doi: [10.1136/bmj.h166](https://doi.org/10.1136/bmj.h166). [PubMed: [25601597](https://pubmed.ncbi.nlm.nih.gov/25601597/)].
- Simren M, Palsson OS, Whitehead WE. Update on Rome IV criteria for colorectal disorders: Implications for clinical practice. *Curr Gastroenterol Rep.* 2017;**19**(4):15. doi: [10.1007/s11894-017-0554-0](https://doi.org/10.1007/s11894-017-0554-0). [PubMed: [28374308](https://pubmed.ncbi.nlm.nih.gov/28374308/)]. [PubMed Central: [PMC5378729](https://pubmed.ncbi.nlm.nih.gov/PMC5378729/)].
- Beckic S. [Functional bloating, constipation and diarrhea]. *Acta Med Croatica.* 2015;**69**(4):253-62. Croatian. [PubMed: [29083560](https://pubmed.ncbi.nlm.nih.gov/29083560/)].
- Bharucha AE, Dorn SD, Lembo A, Pressman A; American Gastroenterological Association. American Gastroenterological Association medical position statement on constipation. *Gastroenterology.* 2013;**144**(1):211-7. doi: [10.1053/j.gastro.2012.10.029](https://doi.org/10.1053/j.gastro.2012.10.029). [PubMed: [23261064](https://pubmed.ncbi.nlm.nih.gov/23261064/)].
- Tabbers MM, DiLorenzo C, Berger MY, Faure C, Langendam MW, Nurko S, et al. Evaluation and treatment of functional constipation in infants and children: Evidence-based recommendations from ESPGHAN and NASPGHAN. *J Pediatr Gastroenterol Nutr.* 2014;**58**(2):258-74. doi: [10.1097/MPG.0000000000000266](https://doi.org/10.1097/MPG.0000000000000266). [PubMed: [24345831](https://pubmed.ncbi.nlm.nih.gov/24345831/)].
- Inaloo S, Dehghani SM, Hashemi SM, Heydari M, Heydari ST. Comorbidity of headache and functional constipation in children: A cross-sectional survey. *Turk J Gastroenterol.* 2014;**25**(5):508-11. doi: [10.5152/tjg.2014.6183](https://doi.org/10.5152/tjg.2014.6183). [PubMed: [25417610](https://pubmed.ncbi.nlm.nih.gov/25417610/)].
- Le Gal J, Michel JF, Rinaldi VE, Spiri D, Moretti R, Bettati D, et al. Association between functional gastrointestinal disorders and migraine in children and adolescents: A case-control study. *Lancet Gastroenterol Hepatol.* 2016;**1**(2):114-21. doi: [10.1016/S2468-1253\(16\)30038-3](https://doi.org/10.1016/S2468-1253(16)30038-3). [PubMed: [28404068](https://pubmed.ncbi.nlm.nih.gov/28404068/)].
- Abreu GE, Dourado ER, Alves DN, Araujo MQ, Mendonca NSP, Barroso Junior U. Functional constipation and overactive bladder in women: A population-based study. *Arq Gastroenterol.* 2018;**55**Suppl 1(Suppl 1):35-40. doi: [10.1590/S0004-2803.201800000-46](https://doi.org/10.1590/S0004-2803.201800000-46). [PubMed: [30184023](https://pubmed.ncbi.nlm.nih.gov/30184023/)].
- Miceli Sopo S, Arena R, Greco M, Bergamini M, Monaco S. Constipation and cow's milk allergy: A review of the literature. *Int Arch Allergy Immunol.* 2014;**164**(1):40-5. doi: [10.1159/000362365](https://doi.org/10.1159/000362365). [PubMed: [24853450](https://pubmed.ncbi.nlm.nih.gov/24853450/)].
- McKeown C, Hisle-Gorman E, Eide M, Gorman GH, Nylund CM. Association of constipation and fecal incontinence with attention-deficit/hyperactivity disorder. *Pediatrics.* 2013;**132**(5):e1210-5. doi: [10.1542/peds.2013-1580](https://doi.org/10.1542/peds.2013-1580). [PubMed: [24144702](https://pubmed.ncbi.nlm.nih.gov/24144702/)]. [PubMed Central: [PMC4530301](https://pubmed.ncbi.nlm.nih.gov/PMC4530301/)].
- Baran M, Ozgenc F, Arikan C, Cakir M, Ecevit CO, Aydogdu S, et al. Gastroesophageal reflux in children with functional constipation. *Turk J Gastroenterol.* 2012;**23**(6):634-8. doi: [10.4318/tjg.2012.0454](https://doi.org/10.4318/tjg.2012.0454). [PubMed: [23794297](https://pubmed.ncbi.nlm.nih.gov/23794297/)].
- Frieling T, Bergdoldt G, Allescher HD, Riemann JF. [Chest pain - not always the heart! Clinical impact of gastrointestinal diseases in noncardiac chest pain]. *Z Gastroenterol.* 2015;**53**(2):120-4. German. doi: [10.1055/s-0034-1385770](https://doi.org/10.1055/s-0034-1385770). [PubMed: [25668714](https://pubmed.ncbi.nlm.nih.gov/25668714/)].
- Berezin S, Medow MS, Glassman MS, Newman LJ. Chest pain of gastrointestinal origin. *Arch Dis Child.* 1988;**63**(12):1457-60. doi: [10.1136/adc.63.12.1457](https://doi.org/10.1136/adc.63.12.1457). [PubMed: [3232993](https://pubmed.ncbi.nlm.nih.gov/3232993/)]. [PubMed Central: [PMC1779185](https://pubmed.ncbi.nlm.nih.gov/PMC1779185/)].
- Sabri MR, Ghavanini AA, Haghghat M, Imanieh MH. Chest pain in children and adolescents: Epigastric tenderness as a guide to reduce unnecessary work-up. *Pediatr Cardiol.* 2003;**24**(1):3-5. doi: [10.1007/s00246-002-0077-8](https://doi.org/10.1007/s00246-002-0077-8). [PubMed: [12399900](https://pubmed.ncbi.nlm.nih.gov/12399900/)].
- Luder AS, Segal D, Saba N. Hypoxia and chest pain due to acute constipation: An underdiagnosed condition? *Pediatr Pulmonol.* 1998;**26**(3):222-3. [PubMed: [9773918](https://pubmed.ncbi.nlm.nih.gov/9773918/)].
- Salmoirago-Blotcher E, Crawford S, Jackson E, Ockene J, Ockene I. Constipation and risk of cardiovascular disease among postmenopausal women. *Am J Med.* 2011;**124**(8):714-23. doi: [10.1016/j.amjmed.2011.03.026](https://doi.org/10.1016/j.amjmed.2011.03.026). [PubMed: [21663887](https://pubmed.ncbi.nlm.nih.gov/21663887/)]. [PubMed Central: [PMC3144272](https://pubmed.ncbi.nlm.nih.gov/PMC3144272/)].
- Bassotti G, Villanacci V, Cretoiu D, Cretoiu SM, Becheanu G. Cellular and molecular basis of chronic constipation: Taking the functional/idiopathic label out. *World J Gastroenterol.* 2013;**19**(26):4099-105. doi: [10.3748/wjg.v19.i26.4099](https://doi.org/10.3748/wjg.v19.i26.4099). [PubMed: [23864772](https://pubmed.ncbi.nlm.nih.gov/23864772/)]. [PubMed Central: [PMC3710411](https://pubmed.ncbi.nlm.nih.gov/PMC3710411/)].
- Leung AK, Robson WL, Cho H. Chest pain in children. *Can Fam Physician.* 1996;**42**:1156-60.