



Cross-sectional Study

Co-occurrence of childhood functional constipation and gastroesophageal reflux disease (GERD)[☆]Shokoufeh Ahmadipour^{a,b}, Aysan Salami-Khaneshan^a, Fatemeh Farahmand^c, Parastoo Baharvand^{d,*}^a Department of Pediatric, Faculty of Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran^b Hepatitis Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran^c Pediatric Gastroenterology and Hepatology Research Center, Tehran University of Medical Sciences, Tehran, Iran^d Department of Community Medicine, Lorestan University of Medical Sciences, Khorramabad, Iran

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ABSTRACT

Objective: Functional constipation (FC) and Gastroesophageal Reflux Disease (GERD) are common gastrointestinal disorders in children. The aim of this study is to investigate the correlation between functional constipation and GERD in children.**Methods:** In this cross-sectional study, a total of 82 children aged <16 years who referred to the pediatric gastroenterology clinic of (XXX) and were diagnosed with functional constipation according to ROME III criteria, and gastroesophageal reflux disease according to clinical history and DeMeester Score. Questionnaire was used to obtain the data regarding age, sex, cause of the visit, presence or absence of any symptom was noted, clinical examinations and difficulty in defecation.**Results:** Of the 82 children with FC and GERD, 45 were boys and 37 were girls. Among children with FC and GERD, FC was reported in 50 (61%) cases prior to the onset of GERD, whereas 32 (39%) of the children had reflux before FC. The mean age of participants presented with FC was 5.66 ± 3.52 and that of GERD was 5.24 ± 2.83 . The difference in mean age was not statistically significant. Of the children with gastroesophageal reflux disease, there were 13 (40.6%) males and 19 females while 32 (64%) males and 18 females had FC and the gender-based difference was statistically significant between the 2 groups.**Conclusion:** The prevalence of functional constipation in children was higher than gastroesophageal reflux disease. Gastroesophageal reflux disease and functional constipation should be simultaneously considered for therapeutic interventions and patients with functional digestive diseases should be monitored and followed-up.

1. Introduction

Functional constipation (FC) and Gastroesophageal Reflux Disease (GERD) are common gastrointestinal disorders in children that can lead to complications, if left untreated. FC is characterized by delay or a disorder of fecal excretion that lasts for two weeks or longer and does not include the anatomical and/or physiological abnormalities [1]. Children with constipation typically have less appetite and have low fiber intake. GERD is defined as upward movement of gastric content into the esophagus [2], that is reported in 1.8–7.2% of children [3,4]. It can be associated with clinical symptoms such as regurgitation, dysphagia,

heartburn, and abdominal pain. Excessive crying, restlessness, irritability, impaired weight gain and apnea are among the most common symptoms in infants [5,6]. However, the clinical symptoms in patients are not limited to upper digestive tract symptoms and can include lower digestive system disorders, upper respiratory tract infections and sleep disorders [7–9]. Children presenting such signs usually need longer-acting antacids to for treatment of symptoms [10].

Functional disorders of gastrointestinal tract are characterized by recurrency and chronic symptoms without any structural or biochemical anomalies of the gut [11]. According to ROME III criteria [12], infants regurgitation, functional infant constipation (G7), and functional

Abbreviations: FC, Functional constipation; GERD, Gastroesophageal Reflux Disease.

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children's constipation (H3A) are categorized as functional gastrointestinal disease [13]. Overlap and association between the functional GI diseases have been reported in the studies [14]. A Chinese study reported that overlap of GERD and functional bowel disorder is 26.28% [15] whereas dyspepsia and GERD overlap has been reported as 4% and GERD and FC is 60% [16,17]. In this study we evaluated pediatric patients with GERD and FC, overlap of these disorders, clinical presentations and demographic factors associated with the overlap.

2. Materials and methods

In this cross-sectional study, all the children between 4 and 16 years of the age who were referred to the pediatric gastroenterology clinic of (XXX) from May 2016 to April 2019 were studied. Children suspected to be presented with FC and GERD based on initial complaints and symptoms were included in our study. FC was assessed using ROME III criteria (two of the following conditions are met: <3 defecation per week for 3 months, straining, lumpy or hard stool, feeling of incomplete emptying of bowel and anorectal obstruction) whereas, GERD was determined based on signs and symptoms and DeMeester score based on 24-h esophageal pH monitoring [18]. Briefly, 10 cm dual sensory pH probe ((Orion II; MMS B-V., Enschede, the Netherlands) was placed approximately 87% of esophageal length, assisted by chest radiography. The electrodes were calibrated using pH 7 and pH 1 buffer solution prior to the insertion. The results obtained was read computer software provided by the manufacturer. PH < 4.0 indicated a reflux episode. Reflux episode >50 lasting longer than 5 min and reflux index >5.4% was diagnosed of abnormal reflux [17]. All the children suspected of FC and GERD during the period were included in the study. A questionnaire that included demographic data, symptoms of reflux disease and functional constipation and diagnosis was completed by all the participants.

Exclusion criteria include intellectual disability, cerebral palsy, endocrine and electrolyte imbalances, neurological and spinal cord disorders, and the presence of food allergies in the patient or family.

Parent-report form for children (4 years of age and older), the Questionnaire on Pediatric Gastrointestinal Symptoms, Rome III version (QPGS-RIII) and children and adolescents' (10 years of age and older) self-report form was customized in four stages. The validity analysis such as the content, construct, and language were carried out in the first three stages, while the reliability analysis was carried out in the fourth stage.

Data was collected using a questionnaire by the project implementer. The questionnaire was designed in three sections. First part included characteristics of the child such as age, sex, and cause of the visit. In the second part GERD symptoms, specific to the age groups (infants and older children), the presence or absence of any symptom was noted. The third part of the questionnaire included biographies, clinical examinations and subsequent results in pediatric patients with difficulty of defecation. Written consent was obtained from all the parents for the participation in the study.

Data were analyzed by SPSS version 16 through chi-square test and fisher's exact test. The frequency of FC and GERD as first manifestation was unevenly compared among children with disease. $P < 0.05$ was considered as a significant difference.

Entire course of the study was approved by ethical committee of (XXX).

Unique identifying number is: researchregistry7384.

The methods have been stated in accordance with STROCSS 2021 guidelines [19].

3. Results

3.1. Patients' characteristics

From 253 patients included in the study, 82 (32.4%) patients presented with both FC and GERD, 45 (54.9%) were male and 37 (45.1%)

were female. Constipation was first presented in 50 (61%) cases, and GERD in 32 (39%).

3.2. Correlation of FC and GERD with age and gender

The mean age of participants with FC was 5.66 ± 3.52 and those with GERD was 5.24 ± 2.83 . The difference in mean age was not statistically significant ($p = 0.755$).

13 (40.6%) males and 19 females had GERD while 32 (64%) males and 18 females were presented FC. This difference was statistically significant between the two groups ($p = 0.040$) (Table 1).

3.3. Clinical presentation

The most commonly reported symptoms of GERD were regurgitation, hiccups, restlessness during sleep, retrosternal burning and pain, pulmonary infections and abdominal pain.

4. Discussion

GERD is associated with various complications and morbidities where, investigating the underlying problems associated with the disease, as well as treating or preventing them, is important in reducing the burden of the disease, particularly in children [20].

Constipation is one of the most important lower GI problems associated with GERD. On the other hand, various studies on the etiology of constipation in children have shown that constipation can be the consequence of various pre-existing conditions/disease, where in order to treat constipation effectively, understanding the cause is significant [21–23].

Establishing a correlation between GERD and FC is important to determine the precise treatment and prevent unconventional therapies for constipation. So far, limited studies have been conducted in this regard [24]. The pH sampling (using pH probe) was recorded at every 6 s. GR was defined as a condition with pH of <4 during at least 12 s.

Of all the children included in the study, 32.7% children had both, FC and GERD, where in 61% cases FC was prior to the onset of GERD, 39% of the cases presented GERD before acquiring FC. In a review article, Karimi et al. study reported 63.3% of children under 1 years of the age with GERD, diagnosed with sonography [25]. Difference of age and diagnostic modalities could be the cause of possible discrepancies in the studies [26].

Our study also revealed that the prevalence of FC (56.5%) in children with GERD is more than otherwise condition. This association can be due to already established condition in GERD children such as intestinal movements, increased intra-abdominal pressure, and reduced stomach emptying.

However, Baran et al. findings report that pathologic acid reflux in the lower and/or laryngopharyngeal portion of the esophagus was 39.5% in FC and in 42.5% in GERD patients, determined by 24-h pH analysis [27]. In a study by Borowitz and colleagues, 34 children with chronic upper gastrointestinal symptoms including nausea, vomiting, GERD and abdominal pain were unresponsive to conventional treatment. However, treating constipation in these patients resulted in the rapid elimination of the upper GI symptoms in all the children [3].

Limitations of our study included small sample size, absence of control group, limited demographic and diet-related data and lack of therapeutic information. DeMeester score is likely to be associated with

Table 1
Comparison of children with FC and GERD in terms of gender and age.

Groups	Count	Sex(male/female)	Age
FC Initially	50(61%)	32/18	5.66 ± 3.52
GERD initially	32(39%)	13/19	5.24 ± 2.83
Difference		$P = 0.040$	$P = 0.755$

false negative outcomes for which other methods such as Multichannel intraluminal impedance pH may provide sensitive outcomes [28].

Future studies in this area can aid the development of diagnostic and therapeutic programs for the patients with GERD or FC. Evaluation of GERD in FC patients and vice versa can help long-term elimination of both the disorders and reduce the usage of unnecessary medications, particularly in children.

5. Conclusion

It is suggested that similar studies with greater number of patients including confounding variables and therapeutic approaches in this area can lead to more accurate results. GERD must be assessed in children with FC. In this cohort study, it was found that a significant correlation exists between the co-occurrence of GERD and FC.

Availability of data and material

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Ethical approval

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Sources of funding

No funding was secured for this study.

Author contribution

Dr. Dr. Fatemeh Farahmand: conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Shokoufeh Ahmadipour: Designed the data collection instruments, collected data, carried out the initial analyses, and reviewed and revised the manuscript. Dr. Azam Mohsenzadeh: Coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

Registration of research studies

1. Name of the registry: N/a
2. Unique Identifying number or registration ID
3. Hyperlink to the registration (must be publicly accessible):

Guarantor

Shokoufeh Ahmadipour.

Consent

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors deny any conflict of interest in any terms or by any

means during the study. All the fees provided by research center fund and deployed accordingly.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103302>.

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