

Findings of upper gastrointestinal endoscopy in children with short stature

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Abstract

Introduction: The study of short stature of digestive origin in children shows no pre-established laboratory patterns. However, endoscopy of the digestive tract may be a useful tool for this purpose. **Objective:** To report a series of cases of children with a diagnosis of short stature who underwent upper digestive tract endoscopy as part of their study. **Case report:** 15 children between the ages of 2 and 16 years were included; 53.3 % were girls. 26.7 % presented with malnutrition according to their body mass index and height-for-age, 66.7 % had short stature, and 33.3 % moderate short stature. Abdominal pain was reported in 53.3 % of the cases, and no weight gain in 46.7 %. Other symptoms were lack of appetite in 26.7 %, vomiting in 13.3 %, among others. Between 40 % and 93.4 % of the children presented macro and/or microscopic esophagitis, gastritis, and duodenitis. The most important microscopic findings were chronic duodenitis with giardiasis, duodenal ulcers, duodenal nodular lymphoid hyperplasia, *Helicobacter pylori*, and chronic eosinophilic duodenitis. **Conclusions:** Although endoscopy of the digestive tract is a method barely used and not well described in the study of children with short stature, this case report describes organicity in 80 % of the children analyzed.

Keywords

Growth failure, Children, Endoscopy.

INTRODUCTION

Short stature in children is determined after performing a nutritional assessment and observing that they do not gain height according to their growth and development stage (1). Short stature is a frequent condition and occurs when caloric intake is insufficient to maintain growth (2). It has multiple causes and they can be psychosocial, organic and non-organic, being the latter found in only a few cases, and its main warning sign is the difficulty to have or maintain an ideal healthy weight (2).

In most cases, short stature is reversible by means of nutritional intervention; otherwise, its persistence can turn it into an underlying organic disease that requires performing laboratory, imaging and other tests, such as upper gastrointestinal endoscopy (also known as esophagogastroduodenoscopy - EGD), to determine its etiology (2). From the digestive point of view, short stature can be secondary to gastroesophageal reflux disease, celiac disease and other chronic disorders (3, 4).

The World Health Organization (WHO) classification (5), which includes children with > -2 standard devia-

tions (SD) of height-for-age (HA), was considered in this case series report. Provided that in this definition weight/height and body mass index (BMI) can be normal, short stature may be related to long-term chronic processes and organic diseases.

There is no a standard regarding the specific complementary tests that should be performed in these cases; however, paraclinical testing by a multidisciplinary team is fundamental in the initial management of children with short stature, and EGD is a useful tool to rule out digestive etiologies as it allows the macro- and microscopic identification of an organic alteration as the cause of short stature (2, 3, 6).

The objective of this paper is to report a series of cases of children aged between 2 and 16 years with a diagnosis of short stature according to the WHO definition, and who underwent an upper gastrointestinal endoscopy in a pediatric endoscopy unit (PEU) in Cali, Colombia, as part of their assessment studies.

CASES REPORT

General characteristics

A total of 15 children aged 7.1 ± 4.9 years (range = 2-16 years) were included: 46.7 % were preschoolers (2-5 years), 40.0 %, schoolchildren (6-12 years), and 13.3 %, adolescents (13-16 years); 53.3 % were female and attended a PEU in Cali, Colombia. The following mean \pm SD and range values were found: weight = 16.4 ± 9.3 kg (range = 7.8-39.9 kg), height = 100.6 ± 24.6 cm (range = 74-148 cm), BMI according to the WHO = -0.8 ± 1.2 SD (range = -3.1 and +1.4 SD) and HA = -3.9 ± 1.3 SD (range = -6.4 and -2.0 SD); According to the WHO definition of BMI, 26.7% of the children were undernourished, and severe and moderate short stature was observed in 66.7% and 33.3%

of the cases, respectively, according to the HA definition of the WHO.

Symptomatology

Symptoms such as abdominal pain, absence of weight gain, lack of appetite, vomiting, and diarrhea and abdominal distension were reported in 53.3 %, 46.7 %, 26.7 %, 13.3 %, 6.7 % and 6.7% of the cases, respectively (Table 1).

Macro- and microscopic findings

The most frequent findings reported in the EGDs and the biopsy reports were esophagitis, gastritis and duodenitis, ranging from 40.0 % and 93.4 % (Table 2).

Other important findings such as chronic duodenitis with giardiasis (Figure 1), duodenal ulcers (Figure 2), duodenal nodular lymphoid hyperplasia, *Helicobacter pylori*, and chronic eosinophilic duodenitis were also identified (Table 3).

Giardiasis, *H. pylori* and short stature

In order to analyze the association between the presence of *Giardia lamblia* and *H. pylori* and short stature (Tables 4 and 5) we searched for original articles published between January 1, 2000 and October 31, 2019 in the PubMed database using the following search terms in Spanish, English and Portuguese, respectively: “malnutrición” and “niños”; “malnutrition” and “children”; and “desnutrição” and “crianças”. Only original articles reporting research results were considered. Prevalence of giardiasis, short stature and the possible association between giardiasis and short stature were mainly considered. Duplicate publications, as defined by having similar authors, sample sizes, and country, were not included.

Table 1. Symptomatology dependent on microscopic findings in 15 children with low stature from a pediatric endoscopy unit in Cali, Colombia

| | Esophagus (n, %) | | p | Stomach (n, %) | | p | Duodenum (n, %) | | p |
|------------------------|------------------|----------|-------|----------------|----------|-------|-----------------|----------|-------|
| | Normal | Inflamed | | Normal | Inflamed | | Normal | Inflamed | |
| Abdominal pain | 4 (26.7) | 4 (26.7) | 0.659 | 4 (26.7) | 4 (26.7) | 0.659 | 4 (26.7) | 4 (26.7) | 0.659 |
| Absence of weight gain | 1 (6.7) | 6 (40.0) | 0.040 | 5 (33.3) | 2 (13.3) | 0.195 | 3 (20.0) | 4 (26.7) | 0.599 |
| Lack of appetite | 0 (0.0) | 4 (26.7) | 0.050 | 2 (13.3) | 2 (13.3) | 0.701 | 1 (6.7) | 3 (20.0) | 0.299 |
| Vomiting | 0 (0.0) | 2 (13.3) | 0.241 | 1 (6.7) | 1 (6.7) | 0.759 | 1 (6.7) | 1 (6.7) | 0.759 |
| Diarrhea | 1 (6.7) | 0 (0.0) | 0.500 | 0 (0.0) | 1 (6.7) | 0.500 | 1 (6.7) | 0 (0.0) | 0.500 |
| Abdominal distension | 1 (6.7) | 0 (0.0) | 0.500 | 0 (0.0) | 1 (6.7) | 0.500 | 1 (6.7) | 0 (0.0) | 0.500 |

Table 2. Macro- and microscopic findings in 15 children with short stature from a pediatric endoscopy unit in Cali, Colombia

| Findings | Macroscopic | Microscopic | p |
|------------------------------------|-------------|-------------|-------|
| | n (%) | n (%) | |
| Esophagitis | 14 (93.4) | 11 (73.4) | 0.165 |
| Gastritis | 13 (86.7) | 7 (46.7) | 0.025 |
| Duodenitis | 12 (80.0) | 6 (40.0) | 0.030 |
| Esophagitis, gastritis, duodenitis | 9 (60.0) | 3 (20.0) | 0.030 |

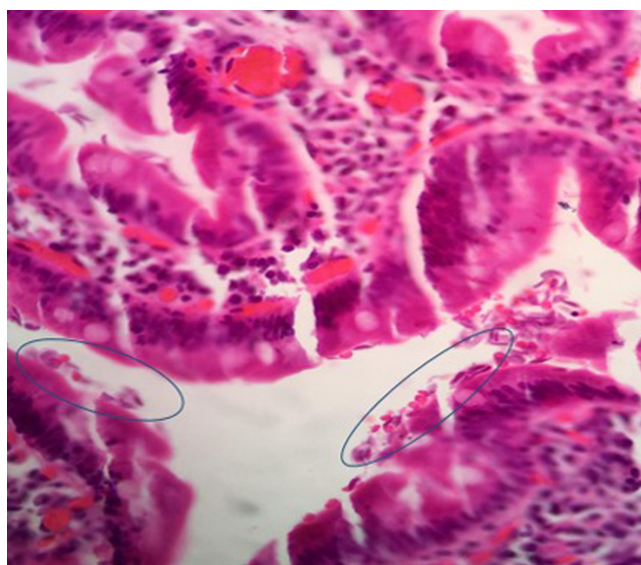


Figure 1. A 2-year-old girl with chronic duodenitis and giardiasis. Courtesy of Ramiro Pineda. Clínica Materno Infantil Los Farallones. Cali, Colombia.

DISCUSSION

Although the use of EGD is indicated for the study of children with short stature (6), it remains a poorly used method for this purpose and it has not been well described in the literature, as reported by Larson et al. (28), who found that this procedure is more useful in children with short stature than imaging or paraclinical tests and reported the presence of organic etiologies in 16.7 % of the children; however, in said study upper GI endoscopy was only indicated in 10 % of these patients.

In our study, 12 out of 15 children (80.0 %) had at least one esophageal, stomach or duodenal alteration, which differs from the findings reported in the study by Larson et al. (28), where non-organic etiologies for failure to thrive were determined for most of the children referred to a tertiary care pediatric gastroenterology clinic due to having short stature,

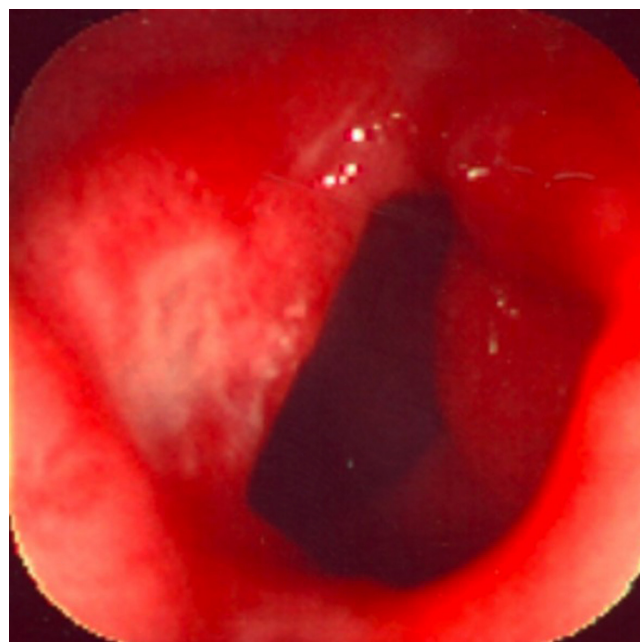


Figure 2. A 3-year-old girl with duodenal ulcers.

despite the fact that in 66.3% of these children a diagnostic test was required to evaluate short stature. Additionally, in our study, 40.0 % of the patients had duodenitis according to the histopathology report, which is a similar figure to that described by El Mouzan et al. (29), who, in a study conducted in 116 children with short stature and in which a duodenal biopsy was performed, reported abnormal findings in 44.0 % (n=65): villous atrophy in half of them and unspecific chronic duodenitis in the other half.

Two of our patients presented with severe short stature, along with chronic duodenitis and giardiasis. Studies are controversial regarding the possible association between giardiasis and short stature (Table 4) (7, 20). *Giardia lamblia* causes a decreased intake of the nutrients required by the body due to its interrelation with intestinal absorption surfaces and nutrient consumption by the organism, as a consequence of physical obstruction in the intestinal lumen and the production of proteolytic substances, among others (30). Parasitic infections are believed to contribute to malnutrition through the subtle reduction of digestion and nutrient absorption, chronic inflammation and nutrient loss (31). *Giardia* is known to cause acute diarrhea, as well as fats, vitamins and D-xylose malabsorption, and lactose intolerance, especially in children (32). In addition, it has been well documented that *Giardia* trophozoites disrupt the normal villous architecture by causing a shortening of the villi and the inflammation of the foci in the crypts and lamina propria, resulting in malabsorption (31). All these

Table 3. Clinical-pathological correlation in 15 children with short stature from a pediatric endoscopy unit in Cali, Colombia

| Sex | Age (years) | Nutritional diagnosis | Symptoms | Microscopic findings |
|--------|-------------|------------------------|--|---|
| Female | 2 | Severe short stature | Lack of appetite | Chronic duodenitis Giardiasis |
| Female | 2 | Severe short stature | Lack of appetite Absence of weight gain | Chronic duodenitis Giardiasis |
| Male | 3 | Moderate short stature | Vomiting | Acute prepyloric ulcer |
| Female | 2 | Severe short stature | Abdominal pain | <i>H. pylori</i> Duodenal nodular lymphoid hyperplasia |
| Female | 2 | Moderate short stature | Absence weight gain | Duodenal nodular lymphoid hyperplasia |
| Male | 16 | Severe short stature | Absence weight gain | Chronic eosinophilic duodenitis |

Table 4. Giardiasis and short stature

| Author | Year | Country | n | Age (years) | G. lamblia (%) | Growth failure (%) | Association |
|----------------------|------|---------------|--------|-------------|----------------|---------------------|-------------|
| Ihejirika (7) | 2019 | Nigeria | 300 | 5-13 | 2.7 | 26.0 | No |
| Lehto (8) | 2019 | Malawi | 840 | 0-2 | 5.1-10.6 | z-score -0.12 | Yes |
| Rivero (9) | 2018 | Argentina | 303 | 0-15 | 33.3 | 38.9 | Yes |
| Yentur (10) | 2015 | Turkey | 100 | 0-6 | 42.5 | 16.0 | Yes |
| Heimer (11) | 2015 | Rwanda | 622 | 6-18 | 28.0-43.9 | z-score -1.8 y -0.6 | Yes |
| Centeno-Lima (12) | 2013 | Guinea-Bissau | 109 | 0-5 | 29.0 | 28.4 | No |
| Al-Mekhlafi (13) | 2013 | Malaysia | 374 | 7-12 | 22.2 | 24.8 | No |
| Verhagen (14) | 2013 | Venezuela | 390 | 4-16 | 20.0 | 13-84 | Yes |
| Zonta (15) | 2010 | Argentina | 178 | 1-14 | 20.0 | 44.9 | Yes |
| Maia (16) | 2009 | Brazil | 451 | 0-10 | 21.5 | 17.5 | No |
| Silva (17) | 2009 | Brazil | 405 | 0-6 | 26.3 | 7.9 | No |
| Nematian (18) | 2008 | Iran | 19 209 | 8.5 ± 1.5 | 11.5 | 2.8-3.8 | Yes |
| Muniz-Junqueira (19) | 2002 | Brazil | 124 | 1-6 | 30.4 | 16.0 | Yes |
| Berkman (20) | 2002 | Peru | 239 | 0-2 | 14.1 | 42.0 | Yes |

mechanisms contribute to the development of malnutrition in individuals infected with *Giardia lamblia* (33).

The results of studies evaluating the effect of *H. pylori* infection on children's growth differ a lot, as some report the presence of this association, while others, its absence (**Table 5**) (21, 27). The mechanism through which *H. pylori* causes failure to thrive has not yet been researched, since it is not clear whether the inflammation induced by

H. pylori directly affects child growth, or if the latter is a consequence of *H. pylori* infection indirect effects such as infection-induced anorexia, changes in intestinal permeability, malabsorption or diarrheal disease (34). Currently, environmental enteric dysfunction (DEA), generalized altered structure and function of the small intestine, subclinical state of intestinal inflammation, bowel incontinence, increased permeability, dysbiosis, bacterial translocation,

Table 5. *H. pylori* and short stature

| Author | Year | Country | n | Age (years) | <i>H. pylori</i> (%) | Growth failure | Association |
|---------------|------|---------------|------|-------------|----------------------|---|-------------|
| Chiu (21) | 2017 | Taiwan | 53 | 4-18 | 29.2 | 32.0 % | No |
| Kocaoglu (22) | 2016 | Turkey | 200 | 7-18 | 59.5 | *0.49 ± 3.85 | Yes |
| Soylu (23) | 2008 | Turkey | 108 | 6.9-17.3 | 52.8 | 12.3% | No |
| Fialho (24) | 2007 | Brazil | 353 | 0.6-14 | 55.8 | **6.62 (IC 95 % 1.71-25.55. <i>p</i> = 0.006) | Yes |
| Süoglu (25) | 2007 | Turkey | 70 | 4-16 | 50.0 | ***-0.768 ± 1.252 | Yes |
| Chimonas (26) | 2006 | United States | 650 | 7-11 | 87.1 | 39.0 % ± 26.4 % | No |
| Richter (27) | 2001 | Germany | 3315 | 5-7 | 6.2 | ***-0.253 ± 1.088 | Yes |

*Growth velocity. **Odds ratio (OR). ***Mean ± SD. CI: Confidence interval.

systemic inflammation and nutrient malabsorption (35) resulting from chronic pathogen exposure, which in turns involves healing and growth delay (36) cannot be ruled out as possible causes of short stature in children. Although pathogenesis between these two conditions is not yet fully defined, nutritional recommendations based on WASH (water, sanitation and hygiene) interventions are proposed (36). Some of these interventions include reducing exposure to stools and animal contact through programs such as improved water, sanitation and hygiene access; breast-feeding and improved dietary diversity; probiotics and pre-biotics; nutritional supplements, including zinc, polyunsaturated fatty acids and amino acids; anti-inflammatory agents such as 5-aminosalicylic acid; and antibiotics in acute malnutrition and infection cases (35).

In addition, “omics” technologies (genomics, epigenomics, transcriptomics, proteomics, and metabolomics) and stable isotope techniques (e.g. Carbon-13 breath tests) aimed at evaluating gut microbiota in children are thought to improve the ability to successfully identify, manage, and prevent this disorder in the future (35).

In the present study, eosinophilic duodenitis was found in 1 patient, being inability to gain weight the main symptom, a finding that has also being described by other authors (37, 38); likewise, it seems these patients respond adequately to montelukast therapy (39). Other digestive symptoms in children with eosinophilic duodenitis are abdominal pain and diarrhea (37, 38). In addition, in these patients, histopathological changes in the duodenum include micro erosion and fibrosis (40), however in these children, biomarkers are not diagnostic tests usually considered (41).

In our study, only one child presented with prepyloric ulcer. The occurrence of peptic ulcer disease in children is rare: between 0.6 % and 12.8 % gastric or duodenal ulcers cases are reported in this population (42, 43); however, its morbidity may include severe complications such as perforation, bleeding, stricture and intestinal obstruction. Weight-for-length/height growth alterations in children with acid peptic disease is associated, to a greater or lesser extent, with the presence of symptoms, which in early ages can be irritable bowel syndrome, poor feeding, regurgitation, vomiting or digestive bleeding; and in older children, abdominal pain, flatulence, abdominal distension, nausea, and sleep disorders, among others (44).

In addition, duodenal nodular lymphoid hyperplasia was observed in two patients, one of them with gastric *H. pylori* infection, an association that was reported by Blanco et al. (45). Although the amount of lymphoid tissue found in the mucosa of the digestive tract can be greater in children than in adults, the presence of duodenal nodular lymphoid hyperplasia is a rare endoscopic finding with an uncertain clinical significance, and unclear clinical anthropometric repercussions. Lymphoid hyperplasia has been described in children with food allergy, hypogammaglobulinemia (46), *G. lamblia* infestation (47), and in patients with end-stage renal failure and with peptic disease secondary to *H. pylori* infection (45).

In conclusion, despite that upper GI endoscopy is a method poorly used in children with short stature, and its usefulness in this population has not been well described, in this case series an organic etiology was determined for short stature in 80.0 % of children who underwent this procedure.

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