

# Gastro-oesophageal reflux and Gastro-oesophageal reflux disease in infants and children: an exploration of symptom-based questionnaires

## Abstract

In Pediatric patients, Gastro-oesophageal reflux (GER) and Gastro-oesophageal reflux disease (GERD) are common and constitute disorders with a large workload for pediatricians. Clinical symptoms and signs are variable and nonspecific, particularly in neonates and infants. Indeed, many symptoms/signs may be secondary to other diagnoses, such as cow's milk allergy, malformation, metabolic, renal, and neurologic disorders. Thus, this may lead to underdiagnosis, overdiagnosis, and unneeded treatment. Therefore, standardizing information regarding clinical information could help define the diagnosis, observe the therapeutic response, and allow the participation of parents and caregivers in the diagnosis-treatment process. For clinical practice, valid and reliable assessment tools can complement clinical assessment to guide decision-making. Parent-reported assessment tools can be used to compare symptoms between populations and longitudinally to measure change over time or in response to interventions. Few non-invasive Questionnaires are available to measure GER/GERD in infants and children. The primary purpose of this Mini review is to describe the main Symptom-Based Questionnaires.

**Keywords:** gastroesophageal reflux, reflux, infant questionnaire, I-GERQ-R, symptom index, symptom questionnaire, GIGER

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**Abbreviations:** GER, gastro-oesophageal reflux; GERD, gastro-oesophageal reflux disease; I-GERQ, the infant gastroesophageal reflux questionnaire; I-GERQ-R, infant gastroesophageal reflux questionnaire-revised; GSQ-I, GERD symptom questionnaires for infants; GSQ-YC, GERD symptom questionnaires for young children, GIGER, gastrointestinal and gastroesophageal reflux scale

## Introduction

### Gastro-oesophageal reflux and Gastro-oesophageal reflux disease in infants and children: an exploration of symptom-based questionnaires

#### Concerns

Gastro-oesophageal reflux (GER) and Gastro-oesophageal reflux disease (GERD) are regularly seen in Pediatric clinics, particularly among neonates and infants. So, for very prevalent problems, practical solutions must be appropriate.

Indeed, GER and GERD constitute disorders with a large workload for pediatricians. Thus, this may lead to underdiagnosis, overdiagnosis, and unneeded treatment. Therefore, standardizing information regarding clinical information could help define the diagnosis, observe the therapeutic response, and allow the participation of parents and caregivers in the diagnosis-treatment process. So, measuring symptoms using Questionnaires could be a better option than empirical therapy.

#### Definitions

GER is a physiological process in healthy infants and children,

- 1 GER has a peak incidence in infants between the third and fourth months of age<sup>1-4</sup>
- 2 In a systematic review, the pooled prevalence of GERD from cross-sectional studies was 26.9%<sup>5</sup>
- 3 Regurgitation decreases from six months onwards, and almost all of them resolve between 12 and 18 months of age<sup>6-10</sup>
- 4 Regurgitation is the most observable symptom by parents/caregivers, as it can occur four or more times daily in 25% of infants. As well, in 50%, 30% respectively in infants <3 and <6 months respectively<sup>1,11,12</sup>
- 5 Around 25% of parents schedule a pediatric appointment to evaluate reflux symptoms<sup>1,13-15</sup>
- 6 In population studies, 70% of children from birth to age five present as primary complaints for ≥1 visit and 25% for ≥3 visits for GERD complaints<sup>16</sup>
- 7 Symptoms related to GER/GERD are among the main concerns of parents during routine visits and a reason for intervention to reduce symptoms<sup>17</sup>
- 8 In clinical practice, it is not easy to differentiate between GER and GERD, and special investigations are only sometimes available.

defined as the passage of gastric contents into the esophagus that occurs during two particular situations:

1. The transient relaxation of the Lower Esophageal Sphincter, and
2. The abdominal pressure and consequent inadequate adaptation of the sphincter tone. GER worsens after feeding and when the infant is in a recumbent position.<sup>12,18-21</sup>

In contrast, in GERD, the gastric contents reflux into the esophagus and oropharynx with symptoms resulting in complications.<sup>4,22-27</sup>

## The clinical symptoms/signs

GER presents at 15 to 21 days of life when oral intake increases.<sup>1,2</sup> The regurgitation episodes become less frequent when changing from a supine posture to a more upright posture and introducing a complementary diet with the transition to more solid foods.<sup>4,12,27</sup> Despite these episodes, children with GERD eat well and thrive without other symptoms. They may often be named as “the happy spitters.”

The presentation of GERD signs and symptoms is broad and unspecific, differs by age, and broadly may be classified as Esophageal or Nonesophageal symptoms and signs. Esophageal conditions commonly include regurgitation and vomiting. Nevertheless, feeding difficulties and intolerances such as poor appetite, feeding refusal, poor food intake, poor weight gain, gagging, back arching during feedings, irritability, presumably painful swallowing, dysphagia, abdominal or substernal/retrosternal pain, Failure To Thrive may occur.<sup>13,28</sup>

In addition, Nonesophageal symptoms and signs include chronic cough, wheezing, stridor, hoarseness, recurrent otitis media, aspiration, laryngitis, and choking. Also, many behavioral problems (excessive crying, irritability, grimacing), sleep disturbances, opisthotonos, torticollis, and dental erosions may be present. Apparent life-threatening events can be present as GERD symptoms.<sup>4,17,24,27,28</sup>

## Diagnosis

As described, the clinical symptoms and signs of GER and GERD are variable and nonspecific, especially in infants and young children. Indeed, this plethora of symptoms/signs may be secondary to food allergy, renal, and neurologic disorders.<sup>29,30</sup> It is essential to obtain information about the age of onset of symptoms, dietary history, characteristics of regurgitation (time, frequency, intensity, relationship with food), growth, dietary and pharmacological treatments performed, and family history. Subsequently, the alarm signs (Table 1) should be ruled out as a first step in managing infant regurgitation and indicating referral.<sup>12,31</sup> Therefore, the diagnosis is primarily clinical.<sup>4,10,12,32–34</sup> For most patients, history and physical examination without warning signs are essential for diagnosis and sufficient to initiate treatment.<sup>22</sup> However, investigations may be necessary when the diagnosis is not evident or in the face of complications.

**Table 1** Warning signals/symptoms in infants with regurgitation or vomiting (Red flags)

The onset of regurgitation/vomiting <2 weeks of life or >6 months or increasing/persisting >12–18 months of age
Vomiting (Persistent, Forceful, Bilious, Nocturnal, or Severe)
Diarrhea (Chronic, bloody); Abdominal distension, Hepatosplenomegaly
Hematemesis, Hematochezia
Dysphagia, Excessive irritability/pain, Failure to thrive/weight loss,
Fever, Lethargy, Dysuria, Recurrent pneumonia
Abnormal physical examination (abdominal, neurological, respiratory)
Neurological abnormalities: Bulging fontanel, excessive increase of head circumference or micro/macrocephaly, Seizures
Abnormal muscle tone, Abnormal psychomotor development
Documented or suspected genetic/metabolic syndrome
<b>Compiled from:</b> <sup>12</sup> Rosen et al, <i>JPGN</i> . 2018;66:516–554; <sup>31</sup> <b>Quitadamo &amp; Staiano (2022)</b>

## Investigation

The instrumental investigation depends on the clinical situation 35, and the main used to distinguish GERD from other disorders are:

- Upper Gastrointestinal Radiography. The objective is to describe anatomic abnormalities (malrotation, hiatal hernia, intestinal obstruction), esophageal peristalsis, and the level of reflux.<sup>36,37</sup>
- Ultrasound is non-invasive, allows real-time GER detection by imaging the gastroesophageal junction, and detects secondary GER (pyloric stenosis, gastric outlet obstruction).
- Esophageal pH Monitoring. It is a quantitative measure of esophageal acid exposure. It may correlate with symptoms and select infants and children with respiratory symptoms in whom GER aggravates.
- The Combined Multiple Intraluminal Impedance and pH Monitoring. This test detects acid, weakly acid, and nonacid reflux episodes.<sup>38–40</sup>
- Endoscopy and Biopsy. Infrequently used to evaluate infants and young children. The histopathological results are not sensitive or specific for diagnosing reflux esophagitis.
- Nuclear Scintigraphy. Gastric emptying studies do not confirm the diagnosis of GERD.

## Symptom-based questionnaires

Questionnaires are based on symptoms and complement clinical assessment. Also, assist in the final treatment decision. Few Questionnaires are available for the Pediatricians.

### Questionnaires

- The Infant Gastroesophageal Reflux Questionnaire (I-GERQ)<sup>13, 14</sup>

(Orenstein et al, 1996; Orenstein 1993)

The I-GERQ was planned and validated for diagnosis of GERD in children ages 1–14 months. It may help distinguish GER from GERD infants. However, it is too long (138-item).

- Infant Gastroesophageal Reflux Questionnaire-Revised I-GERQ (I-GERQ-R)<sup>41</sup>

(Kleinman et al. 2006)<sup>41</sup>

The Questionnaire was based on the I-GERQ,<sup>13</sup> with acceptable Internal Consistency, Test-Retest Reliability, and Group Validity. It is suitable for determining the severity of symptoms, the relationship between reflux and symptoms, evaluating treatment, and identifying differences between cases and controls.<sup>42</sup> When assessed by parents/caregivers and the Pediatrician, the scores are associated with severity Table 2 summarises the Questionnaire.

- GERD Symptom Questionnaires for Infants (GSQ-I) and young children (GSQ-YC)

(Deal et al. (2005)<sup>43</sup>

The GSQ-I is suitable for infants between 1- 11 months, and the GSQ-YC is for children between 1-4 years old. Both questionnaires are easy to use, differentiate GERD from control infants and young children, and assess response to treatment. Tables 3 and 4 summarise both Questionnaires.

- The Infant Gastroesophageal Reflux Questionnaire (I-GERQ) modified by Salvatore et al. (2005)<sup>44</sup>

It is an original Orenstein questionnaire, adding 18 items to cover the broad spectrum of clinical presentations of GERD. The number of total items is 35. Table 5 summarises the Questionnaire.

- v. Gastrointestinal and gastroesophageal Reflux (GIGER) Scale<sup>45</sup> (Pados et al. 2021)<sup>45</sup> gastrointestinal and GER symptoms as a parent report. The tool has good Internal Consistency and Reliability. The total score was higher in infants with a GER diagnosis and was correlated with the I-GERQ-R). Table 6 summarises the Questionnaire.
- The Questionnaire was developed with a dual intention: assess

**Table 2** Infant Gastroesophageal Reflux Questionnaire-Revised (I-GERQ-R)

Parent-report measure of symptoms. Evaluate the impact on infants <18 months. The recall period is one week. Response options vary from 2 to 5 categories.	
12 Items	Score calculation
Including the frequency, amount, and discomfort (3 items) Refusal or stopping feeding (2 items) Crying and fussing (3 items) Hiccups (1 item) Arching back (1 item)	I-GERQ-R scores vary by question type  Like Yes/No questions,  Rate the severity of symptoms  or Never to Always.  The total score is the sum of all responses (ranging from 0 to 42)
Stopping breathing or color change (2 items)	Higher scores indicate a more significant symptom burden.  Score reductions of 3 points characterize a minimally significant difference.  Between 5 and 6 points are considered clinically expressive.
<b>GER</b> was defined as score $\geq 1$ to the first question with I-GERQ-R score < 16. <b>GERD</b> as score $\geq 1$ on the first item (presence of regurgitations) to the first question with a score $\geq 16$ .	

<sup>41</sup>Kleinman L, Rothman M, Strauss R, et al. The infant gastroesophageal reflux questionnaire revised: development and validation as an evaluative instrument. *Clin Gastroenterol Hepatol.* 2006;4(5):588–596.

**Table 3** GERD Symptom Questionnaire-Infants (GSQ-I)

The GSQ-I was designed to assess symptoms' frequency and usual severity in the previous seven days. Parents/caretakers were asked to indicate the frequency of each symptom by providing a whole number of zero or greater.	
6 Items	Score calculation
Arching back Choking/gagging Episodes of hiccups Irritability/fussiness Refusal to feed Vomiting/regurgitation	The ISS was defined as the frequency and the severity of that symptom  (from 1 "not at all severe" to 7 "most severe")  If a symptom frequency was zero, respondents were instructed to skip the severity assessment for that symptom.  The CSS was calculated as the sum of the ISSs.

<sup>43</sup>Deal et al. Age-specific questionnaires distinguish GERD symptom frequency and severity in infants and young children: development and initial validation. *J Pediatr Gastroenterol Nutr.* 2005;41(2):178–185.

**Table 4** GERD Symptom Questionnaire -Young Children (GSQ-YC)

The GSQ-I was designed to assess symptoms' frequency and usual severity in the previous seven days. Parents/caretakers were asked to indicate the frequency of each symptom by providing a whole number of zero or greater.	
7 Items	Score calculation
Abdominal pain Burping or belching Choking when eating Difficulty swallowing Refusal to eat Vomiting or Regurgitation	The ISS was defined as the frequency and the severity of that symptom  (from 1 "not at all severe" to 7 "most severe")  If a symptom frequency was zero, respondents were instructed to skip the severity assessment for that symptom.  The CSS was calculated as the sum of the ISSs.

<sup>43</sup>Deal et al. Age-specific questionnaires distinguish GERD symptom frequency and severity in infants and young children: development and initial validation. *J Pediatr Gastroenterol Nutr.* 2005;41(2):178–185.

**Table 5** Orenstein's Questionnaire modified by Salvatore et al. (2005)<sup>44</sup>

It is a questionnaire with the addition of items to cover the broad spectrum of clinical presentations of GERD.	
The Questionnaire was filled in by the parents, who read and marked it without assistance	
<b>35 Items</b>	The validation was based on test-retest (intra-observer) consistency of each question, resubmitting the questionnaire to the same responder parent one week later.
<b>18 questions were added to the original Orenstein questionnaire:</b>	
01 about projectile regurgitation	
01 about difficulties in burping	
01 about noisy respiration	
03 about pneumonia, bronchitis or chronic cough	
02 about frequency and duration of hiccups	
05 about bowel habits	
04 about family history of reflux disease and allergy	
01 about parental suspicion of Reflux disease in their infant	

<sup>44</sup>Salvatore S, Hauser B, Vandemaele K, Novario R, Vandenplas Y. Gastroesophageal Reflux disease in infants: how much is predictable with questionnaires, pH-metry, Endoscopy and histology? *J Pediatr Gastroenterol Nutr.* 2005;40:210–215.

**Table 6** Gastrointestinal and Gastroesophageal Reflux (GIGER) Scale<sup>45</sup>

Is a parent-report scale for children < 2 years old	
Both Gastrointestinal and GER symptoms are evaluated.	
It can be used for both clinical care and measuring response to treatment.	
<b>36 Items</b>	<b>Score calculation</b>
<b>Subscale 1</b> (15 items)	Gastrointestinal and GER symptoms
<b>Subscale 2</b> (13 items)	Compelling Gastrointestinal and GER symptoms
<b>Subscale 3</b> (8 items)	Difficulties with self-regulation

<sup>45</sup>Pados BF, Repsha C, Hill RR. The Gastrointestinal and Gastroesophageal Reflux (GIGER) Scale for Infants and Toddlers. *Glob Pediatr Health.* 2021 Jul 14;8:2333794X211033130.

## Concluding remarks

Diagnostic procedures, such as pH-meter, Esophageal impedance monitoring, and Endoscopy, are invasive, uncomfortable, and not always accessible. Therefore, given the plethora of signs and symptoms that GERD can present, applying a Questionnaire could standardize these different findings into a score that would be used for diagnosis and follow-up. However, the Questionnaire could be easily administered and repeatedly applied at each visit to measure infant symptoms/signs and their changes over time. The GER/GERD Symptom Questionnaires, including primary and tertiary care, must be applied, and the sum of the clinical evaluation and the answers to the Questionnaire would help the Pediatrician make a better treatment decision. In conclusion, Questionnaires are a great support, and the choice of which one to use must be based on the specific interest of the Paediatrician, such as only assisting in the initial diagnosis, the evolution of symptoms, treatment, or clinical research.

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## Author contributions

Nilton Carlos Machado and Mary de Assis Carvalho contributed to the conception of the work and drafted the final manuscript. Juliana Tedesco Dias, Maria Paula Gasparini da Silva Lippelt, Gabriela Nascimento Hercos, and Thabata Koester Weber revised the manuscript critically.

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## Conflicts of interest

The authors declare no conflict of interest.

## References

1. Nelson SP, Chen EH, Syniar GM, et al. Prevalence of symptoms of gastroesophageal reflux during infancy. A pediatric practice-based survey. Pediatric Practice Research Group. *Arch Pediatr Adolesc Med.* 1997;151(6):569–572.
2. Dranove JE. New technologies for the diagnosis of gastroesophageal reflux disease. *Pediatr Rev.* 2008;29(9):317–320.
3. Ferguson TD. Gastroesophageal reflux: Regurgitation in the infant population. *Crit Care Nurs Clin North Am.* 2018;30(1):167–177.
4. Leung AK, Hon KL. Gastroesophageal reflux in children: an updated review. *Drugs Context.* 2019;8:212591.
5. Singendonk M, Goudswaard E, Langendam M, et al. Prevalence of Gastroesophageal Reflux Disease Symptoms in Infants and Children: A Systematic Review. *J Pediatr Gastroenterol Nutr.* 2019;68(6):811–817.
6. Nelson SP, Chen EH, Syniar GM, et al. Prevalence of symptoms of gastroesophageal reflux during childhood: a pediatric practice-based survey. Pediatric Practice Research Group. *Arch Pediatr Adolesc Med.* 2000;154(2):150–154.
7. Hegar B, Dewanti NR, Kadim M, et al. Natural evolution of regurgitation in healthy infants. *Acta Paediatr.* 2009;98(7):1189–1193.

8. Jadcherla SR, Chan CY, Moore R, et al. Impact of feeding strategies on the frequency and clearance of acid and nonacid gastroesophageal reflux events in dysphagic neonates. *JPEN J Parenter Enteral Nutr.* 2012;36(4):449–455.
9. Hegar B, Satari DH, Sjarif DR, et al. Regurgitation and gastroesophageal reflux disease in six to nine months old Indonesian infants. *Pediatr Gastroenterol Hepatol Nutr.* 2013;16(4):240–247.
10. Czinn SJ, Blanchard S. Gastroesophageal reflux disease in neonates and infants: when and how to treat. *Paediatr Drugs.* 2013;15(1):19–27.
11. Dhillon A, Ewer A. Diagnosis and management of gastro-oesophageal reflux in preterm infants in neonatal intensive care units. *Acta Paediatr.* 2004;93(1):88–93.
12. Rosen R, Vandenplas Y, Singendonk M, et al. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). *J Pediatr Gastroenterol Nutr.* 2018;66(3):516–554.
13. Orenstein SR, Shalaby TM, Cohn JF. Reflux symptoms in 100 normal infants: diagnostic validity of the infant gastroesophageal reflux questionnaire. *Clin Pediatr (Phila).* 1996;35(12):607–614.
14. Orenstein SR, Cohn JF, Shalaby TM, et al. Reliability and validity of an infant gastroesophageal reflux questionnaire. *Clin Pediatr.* 1993;32(8):472–484.
15. Hegar B, Boediarso A, Firmansyah A, et al. Investigation of Regurgitation and other symptoms of gastroesophageal reflux in Indonesian infants. *World J Gastroenterol.* 2004;10(12):1795–1797.
16. Chitkara DK, Talley NJ, Weaver AL, et al. Incidence of presentation of common functional gastrointestinal disorders in children from birth to 5 years: a cohort study. *Clin Gastroenterol Hepatol.* 2007;5(2):186–191.
17. Lightdale JR, Gremse DA, Heitlinger LA, et al. Gastroesophageal reflux: management guidance for the Pediatrician. *Pediatrics.* 2013;131(5):e1684–e1695.
18. Salvatore S, Hauser B, Vandenplas Y. The natural course of gastro-oesophageal reflux. *Acta Paediatr.* 2004;93(8):1063–1069.
19. Chawla S, Seth D, Mahajan P, et al. Gastroesophageal reflux disorder: a review for primary care providers. *Clin Pediatr.* 2006;45(1):7–13.
20. Michail S. Gastroesophageal reflux. *Pediatr Rev.* 2007;28(3):101–110.
21. Ciciora SL, Woodley FW. Optimizing the use of medications and other therapies in infant gastroesophageal reflux. *Paediatr Drugs.* 2018;20(6):523–537.
22. Cezard JP. Managing gastro-oesophageal reflux disease in children. *Digestion.* 2004;69(Suppl 1):3–8.
23. Omari T. Gastro-oesophageal reflux disease in infants and children: new insights, developments, and old chestnuts. *J Pediatr Gastroenterol Nutr.* 2005;41(Suppl 1):S21–S23.
24. Gupta SK, Hassall E, Chiu YL, et al. Presenting symptoms of non-erosive and erosive esophagitis in pediatric patients. *Dig Dis Sci.* 2006;51(5):858–863.
25. Shin MS. Esophageal pH and combined impedance-pH monitoring in children. *Pediatr Gastroenterol Hepatol Nutr.* 2014;17(1):13–22.
26. Esposito C, Roberti A, Turra F, et al. Management of gastroesophageal reflux disease in pediatric patients: a literature review. *Pediatric Health Med Ther.* 2015;6:1–8.
27. Rybak A, Pesce M, Thapar N, et al. Gastroesophageal reflux in children. *Int J Mol Sci.* 2017;18(8):1671.
28. Mousa H, Hassan M. Gastroesophageal reflux disease. *Pediatr Clin North Am.* 2017;64(3):487–505.
29. Vandenplas Y, Rudolph CD, Di Lorenzo C, et al. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). *J Pediatr Gastroenterol Nutr.* 2009;49(4):498–547.
30. Martigne L, Delaage PH, Thomas-Delecourt F, et al. Prevalence and management of gastroesophageal reflux disease in children and adolescents: a nationwide cross-sectional observational study. *Eur J Pediatr.* 2012;171(12):1767–1773.
31. Quitadamo P, Staiano A. Symptoms of GER. In: Vandenplas, Y. (eds) *Gastroesophageal Reflux in Children.* Springer, Cham. 2022:29–38.
32. Sullivan JS, Sundaram SS. Gastroesophageal reflux. *Pediatr Rev.* 2012;33(6):243–253.
33. Rosen R. Gastroesophageal reflux in infants: more than just a phenomenon. *JAMA Pediatr.* 2014;168(1):83–89.
34. Randel A. AAP releases guidelines for the management of gastroesophageal reflux in children. *Am Fam Physician.* 2014;89(5):395–397.
35. Wenzl TG. Role of diagnostic tests in GERD. *J Pediatr Gastroenterol Nutr.* 2011;53(Suppl 2):S4–S6.
36. Simanovsky N, Buonomo C, Nurko S. The infant with chronic vomiting: the value of the upper GI series. *Pediatr Radiol.* 2002;32(8):549–550.
37. Aksglaede K, Pedersen JB, Lange A, et al. Gastroesophageal reflux demonstrated by radiography in infants less than one year of age. Comparison with pH monitoring. *Acta Radiol.* 2003;44(2):136–138.
38. Størdal K, Johannesdóttir GB, Bentsen BS, et al. Gastroesophageal reflux disease in children: association between symptoms and pH monitoring. *Scand J Gastroenterol.* 2005;40(6):636–640.
39. Woodley FW, Mousa H. Acid gastroesophageal reflux reports in infants: a comparison of esophageal pH monitoring and multichannel intraluminal impedance measurements. *Dig Dis Sci.* 2006;51(11):1910–1916.
40. Vandenplas Y, Salvatore S, Devreker T, et al. Gastro-oesophageal reflux disease: oesophageal impedance versus pH monitoring. *Acta Paediatr.* 2007;96(7):956–962.
41. Kleinman L, Rothman M, Strauss R, et al. The infant gastroesophageal reflux questionnaire revised: development and validation as an evaluative instrument. *Clin Gastroenterol Hepatol.* 2006;4(5):588–596.
42. Van Howe RS, Storms MR. Gastroesophageal reflux symptoms in infants in a rural population: longitudinal data over the first six months. *BMC Pediatr.* 2010;10:7.
43. Deal L, Gold BD, Gremse DA, et al. Age-specific questionnaires distinguish GERD symptom frequency and severity in infants and young children: development and initial validation. *J Pediatr Gastroenterol Nutr.* 2005;41(2):178–185.
44. Salvatore S, Hauser B, Vandemaële K, et al. Gastroesophageal Reflux disease in infants: how much is predictable with questionnaires, pH-metry, Endoscopy, and histology? *J Pediatr Gastroenterol Nutr.* 2005;40(2):210–215.
45. Pados BF, Repsha C, Hill RR. The Gastrointestinal and Gastroesophageal Reflux (GIGER) Scale for Infants and Toddlers. *Glob Pediatr Health.* 2021;8:2333794X2111033130.