LUMEN ET VIRTUS
ISSN: 2177-2789

GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN INFANTS: FROM DEFINITIONS TO TREATMENT: A SYSTEMATIC REVIEW

https://doi.org/10.56238/levv16n47-002

Submitted on: 02/03/2025 **Publication date:** 02/04/2025

Maria Eugênia Alves Martins de Araújo Tristão[1], Isadora Alves Gianecchini[2], Matheus Teixeira Garcia[3], Jessica Reis Lopes[4], Nelson Antonio da Silva Neto Segundo[5], Pedro Jorge Melro Cansanção Filho[6], Mariana Maria Batista[7], Simony Paixão Queroz[8], Déborah Danyelle Lopes da Silva[9] and Mariana Farias Savioli[10]

ABSTRACT

Objective: The objective of this literature review was to compile the current knowledge on the definition, epidemiology, pathophysiology, risk factors, clinical manifestations, complications, and treatments associated with gastroesophageal reflux disease (GERD) in infants and children. Methodology: Searches were carried out through searches in the PubMed Central (PMC) and Virtual Health Library (VHL) databases. Three main descriptors were used combined with the Boolean term "AND": Gastroesophageal Reflux, Pediatrics and Treatment. The search strategy used in the PMC database was: Gastroesophageal Reflux AND Pediatrics AND Treatment, while in the VHL it was: Gastroesophageal Reflux AND Pediatrics. After this initial search, 78 articles were found, which were submitted to the selection criteria. After screening, 9 articles were selected to compose this review. Results: The data revealed that GERD is a prevalent condition in infants, especially in preterm infants and children with neurological or congenital conditions. Its manifestations vary, and regurgitation, vomiting, refusal to feed and irritability are the most frequent symptoms in the first years of life. Complications include esophagitis, breathing difficulties, growth retardation, and, in severe cases, apnea and aspiration pneumonia. Diagnosis is often

[1] Advisor: Physician from the University of Franca (UNIFRAN), Pediatrician specialized in pediatric palliative care, pediatric and neonatal ICU and pediatric nutrition. Professor and preceptor of the discipline of Pediatrics in the Medicine course at the University of Franca
E-mail: mariaeugênia _059@hotmail.com
[2] Medical student at the University of Franca - UNIFRAN
E-mail: Isa Gianecchini.80@gmail.com
[3] Medical student at the University of Franca – UNIFRAN
E-mail: matheuss.ggarcia1@gmail.com
[4] Physician and resident in surgery at the João de Barros Barreto University Hospital
E-mail: Jessica123reis2017@gmail.com
[5] Doctor from the University Center of João Pessoa and resident in Family and Community Medicine from UFPE
Email: nelsonnsegundo@gmail.com
[6] Medical Student at Cesmac University Center
E-mail: pjfilho@gmail.com
[7] Graduated from the Federal University of Goiás - UFG
E-mail: marianamariabatista@gmail.com
[8] Medical student at Universidade Nove de Julho Osasco – Uninove
E-mail: simony-paixao@hotmail.com
[9] Doctor from Centro Universitário Facisa - Unifacisa
E-mail: deborahdanyelle13@gmail.com
[10] Graduated in Medicine from the University of Santo Amaro – UNISA
E-mail: fariasmari2501@gmail.com

clinical, with additional tools used only in cases of diagnostic doubt or suspected complications. Management includes non-pharmacological and pharmacological measures and, in more severe cases, surgical treatment. Conclusion: It is concluded that the characterization of GERD in infants and children is essential to ensure effective symptomatic control and prevent long-term complications. Treatment should be individualized, based on the severity of symptoms and associated conditions, including non-pharmacological, pharmacological, and, when necessary, surgical approaches.

Keywords: Gastroesophageal reflux disease. Paediatrics. Pathophysiology. Complications. Treatment.

INTRODUCTION

Gastroesophageal reflux (GER) is characterized by the retrograde passage of gastric contents to the esophagus, which can reach the oral cavity. It is a common condition in infants, especially due to the immaturity of the gastrointestinal tract. However, when GER exceeds the limits of normality, leading to persistent bothersome symptoms and/or complications, it is called gastroesophageal reflux disease (GERD) (Boza et al., 2019; Gulati et al., 2019). Differentiating between physiological GER and pathological GERD is essential to avoid misdiagnosis and inappropriate treatment.

In pediatric and neonatal settings, especially in neonatal intensive care units (NICU), GERD presents specific diagnostic and therapeutic challenges. Premature infants or infants with congenital conditions are particularly vulnerable to reflux events due to the functional and anatomical immaturity of the gastroesophageal system. The gastroesophageal junction (GIJ), which is made up of the lower esophageal sphincter (LES) and other supporting structures, plays a crucial role in preventing reflux. However, in premature infants, inadequate development of this junction may predispose to GER and GERD (Gulati et al., 2019; DAVIS et al; 2024)).

The epidemiology of gastroesophageal reflux disease (GERD) presents challenges due to variation in definitions, diagnostic criteria, and clinical practices, especially in the pediatric and neonatal setting. GERD is a common condition that significantly affects infants and children, and is particularly prevalent among those hospitalized in neonatal intensive care units (NICUs). These patients, often premature or with underlying conditions, are more vulnerable to reflux due to the functional and structural immaturity of the gastrointestinal tract (Gulati et al., 2019; Boza et al., 2019; SHAQRAN et al; 2023).

The exact incidence of GERD in NICU infants is not established, precisely because of the inconsistencies in diagnostic practices and the lack of consensus on the definition criteria. However, studies suggest that the condition is relatively frequent due to factors such as frequent feeding, supine position, and immaturity of the lower esophageal sphincter (LES). The variability of definitions contributes to the difficulty of estimating their true prevalence (Gulati et al., 2019; (DAVIS et al; 2024, SHAQRAN et al; 2023)).

In infants in general, GERD is more frequently seen in preterm infants. Babies with prematurity have both anatomical and functional immaturity of the gastroesophageal junction, which makes them more susceptible to reflux. In addition, the prevalence of GERD is especially high in infants with underlying neurological conditions, such as hypoxic-ischemic encephalopathy and intraventricular hemorrhage, which can impact protective mechanisms against reflux and aggravate symptoms (Gulati et al., 2019; Boza et al., 2019).

Regarding the NICU, GERD is also associated with significant morbidity. For example, in infants with bronchopulmonary dysplasia, a condition that affects about 30% of extremely low birth weight infants, elevated respiratory effort, associated with increased intra-abdominal pressure, may predispose to reflux events. These associations are relevant because, in severe cases, GERD can prolong the length of neonatal hospital stay and complicate health care (Gulati et al., 2019).

Epidemiological studies indicate that the coexistence of GERD and other conditions, such as cow's milk allergy (ALV), varies widely, affecting between 16% to 56% of infants with persistent gastrointestinal symptoms. This intersection reflects the complexity of differential diagnosis and the need for judicious approaches to managing these conditions (Salvatore et al., 2021).

In addition to the prevalence, the economic burden of GERD is also noteworthy. In hospitalized infants, especially in the NICU, the diagnosis of GERD is associated with significantly elevated hospital costs, with an estimated increase of $70,000 per diagnosed patient. The widespread use of acid-suppressing therapies in neonates without a definitive diagnosis adds costs and raises concerns about potential long-term adverse effects (Gulati et al., 2019).

Therefore, the epidemiology of GERD reflects the interaction of multiple factors, including physiological immaturity, the presence of underlying conditions, and variable clinical practices. Understanding its prevalence and associated factors is critical for the development of more effective diagnosis, management, and prevention strategies, especially in high-risk populations, such as premature infants and those hospitalized in the NICU (Gulati et al., 2019; Salvatore et al., 2021; Boza et al., 2019).

METHODOLOGY

This study is characterized as a literature review aimed at understanding the main aspects related to gastroesophageal reflux disease (GERD) in infants and children, analyzing its definition, epidemiology, pathophysiology, risk factors, clinical manifestations, complications and therapeutic strategies. The objective was to organize and synthesize information that can contribute to a better understanding of the condition, helping in the diagnosis and clinical management.

To develop this research, a guiding question was formulated based on the PVO (population, variable and objective) strategy: "What are the relevant aspects about the pathophysiology, risk factors, clinical manifestations and treatment options of GERD in pediatric patients?".

The searches were carried out in two main databases: PubMed Central (PMC) and Virtual Health Library (VHL). The descriptors used were combined with the Boolean operator "AND", namely: Gastroesophageal Reflux, Pediatrics, Pathophysiology, Risk Factors and Treatment. The search strategy used in the PMC was: *((Gastroesophageal Reflux) AND (Pediatrics)) AND (Pathophysiology) AND (Risk Factors)* and, in the VHL, it was: *(((Gastroesophageal Reflux) AND (Pediatrics)) AND (Treatment))*.

The following inclusion criteria were considered: articles published in English, Portuguese and Spanish; available in full; published between 2018 and 2024; and that directly addressed the proposed theme. Review, observational, and experimental studies were accepted. The exclusion criteria included duplicate articles, available only in abstract format, that did not directly address the topics studied or that did not meet the previously established criteria.

Initially, 78 articles were found, 60 in the PubMed database and 18 in the Virtual Health Library. After applying the inclusion and exclusion criteria, a total of 9 articles were selected to compose the survey and provide the information that supported this analysis.

DISCUSSION

The pathophysiology of gastroesophageal reflux disease (GERD) is complex and multifactorial, involving changes in the functional and anatomical integrity of the gastroesophageal junction (GEJ), as well as a dynamic interaction between esophageal, gastric, and behavioral factors. Understanding the underlying mechanisms is essential for accurate diagnosis and the application of targeted therapeutic interventions, especially in vulnerable populations such as infants and preterm infants (Gulati et al., 2019; Boza et al., 2019; Rybak et al., 2020).

The SGJ is composed of several anatomical structures, including the lower esophageal sphincter (LES), diaphragmatic crural fibers, intra-abdominal esophagus, and stomach fibers. These structures, together, form a crucial barrier to prevent the backflow of gastric contents into the esophagus. The effective functioning of this barrier is maintained by the tonic activity of the LES, which transiently relaxes to allow the passage of the food bolus, but which may also be one of the main mechanisms of gastroesophageal reflux when transient relaxations occur with excessive frequency (Gulati et al., 2019).

The weakness of the LES or its malfunction are key factors in the appearance of reflux. Neonates, especially premature infants, are more predisposed to GERD due to the immaturity of this barrier, which compromises its functionality. Other structural conditions,

such as hiatal hernia, can also exacerbate reflux episodes, contributing to prolonged exposure of the esophagus to gastric acid content (Gulati et al., 2019; Rybak et al., 2020).

Several esophageal and laryngeal reflexes are activated in response to reflux, such as anterograde peristalsis and upper esophageal sphincter (EES) closure. These protective mechanisms prevent the refluxed gastric contents from reaching the pharynx and upper airways, minimizing damage and preventing respiratory complications. However, in infants and neonates with immature or dysfunctional mechanisms, these reflexes may be insufficient, aggravating the condition (Gulati et al., 2019).

Esophageal and gastric motor function also play a central role in the pathophysiology of GERD. Impaired gastrointestinal motility, caused by neuropathies or myopathies as in pediatric intestinal pseudoobstruction syndrome (PIPO), can lead to problems such as accelerated or delayed bowel transit, ineffective anterograde peristalsis, and delayed gastric emptying (Rybak et al., 2020). Reduced number or functionality of Cajal interstitial cells (CHF), which are responsible for coordinating the electrical activity of the gastrointestinal tract, is associated with dysmotility in conditions such as gastroschisis and intestinal atresia (Rybak et al., 2020). In addition, events such as duodenogastric reflux, in which bile and other contents of the small intestine reach the stomach and esophagus, are related to the destruction of the esophageal mucosa and the worsening of GERD symptoms, due to prolonged exposure to irritants (Rybak et al., 2020).

Gastric hypersecretion is a relevant factor in the pathophysiology of GERD, especially in patients with extensive bowel resection, such as in short bowel syndrome (SBS). In such cases, transient hypergastrinemia can result in excess gastric acid, making gastric emptying difficult and contributing to severe reflux events. Treatment of acid hypersecretion, through proton pump inhibitors (PPIs) or H2 receptor antagonists, is effective in improving nutrient absorption and reducing symptoms (Rybak et al., 2020).

On the other hand, external factors such as the baby's positioning, feeding methods, and the presence of nasogastric tubes can also negatively influence the anti-reflux barrier. The supine position, recommended to prevent sudden infant death syndrome (SIDS), is associated with a higher frequency of reflux episodes, while the prone position, while reducing events, is contraindicated due to the elevated risk of SIDS (Gulati et al., 2019; Boza et al., 2019).

The pathophysiological mechanisms of GERD often result in a series of clinical manifestations ranging from irritability and persistent crying to erosive esophagitis and respiratory complications such as apnea and pulmonary aspiration. Frequent contact of the acidic content with the esophageal mucosa can lead to chronic inflammation and significant

damage, resulting in more severe symptoms such as pain when swallowing and refusal to feed (Boza et al., 2019; Gulati et al., 2019). In addition, respiratory changes resulting from aspiration of gastric contents can predispose to respiratory infections, such as pneumonia and laryngitis, aggravating morbidity in infants and neonates with GERD (Boza et al., 2019).

The risk factors for the development of gastroesophageal reflux disease (GERD) are diverse and are often associated with congenital, neurological and metabolic conditions, as well as factors related to feeding methods and body positioning. These factors play a critical role in the predisposition of infants and infants in the neonatal intensive care unit (NICU) to GERD, highlighting the need for careful diagnosis and appropriate interventions (Gulati et al., 2019; Boza et al., 2019).

Prematurity is one of the main risk factors for GERD. Preterm infants have anatomical and functional immaturity of the gastroesophageal junction (SGJ), which results in an insufficient anti-reflux barrier. This immaturity increases the frequency of transient relaxations of the lower esophageal sphincter (LES), facilitating the reflux of gastric contents into the esophagus (Gulati et al., 2019). In addition, conditions such as bronchopulmonary dysplasia, which affects about 30% of babies with extremely low birth weight, also contribute to reflux. This complication of prematurity leads to greater respiratory effort and increased intra-abdominal pressure, aggravating the risk of reflux events (Gulati et al., 2019).

Neurological diseases, such as hypoxic-ischemic encephalopathy and intraventricular hemorrhage, are significant risk factors for GERD. These conditions compromise the neuromuscular mechanisms that control LES and esophageal motility. The prevalence of GERD in infants with underlying neurological conditions can reach up to 50%, highlighting the relevance of careful evaluation in patients with neurological impairment (Gulati et al., 2019; Boza et al., 2019).

Congenital abnormalities of the gastrointestinal tract, such as esophageal atresia, diaphragmatic hernia, pyloric stenosis, and intestinal malrotation, are associated with a higher risk of GERD. These conditions can alter the anatomy and functionality of JEG, predisposing patients to reflux (Boza et al., 2019).

In addition, genetic syndromes, such as Down syndrome, and inherited diseases, such as cystic fibrosis, affect both esophageal motility and respiratory function, increasing the incidence of GERD in these groups (Boza et al., 2019).

Feeding methods play a crucial role in GERD risk. Infants who use nasogastric tubes may have insufficient closure of the LES due to the presence of the device, facilitating reflux. However, some studies indicate that tube-fed infants may have fewer reflux events

compared to those exclusively orally fed, highlighting the complexity of this risk factor (Gulati et al., 2019). The volume and composition of meals also affect the frequency and severity of reflux episodes. Large volumes of feeding and high-fat diets may exacerbate transient LES relaxations, increasing reflux episodes (Boza et al., 2019).

The baby's position during and after feedings directly influences the risk of reflux. The supine position, often recommended to reduce the risk of sudden infant death syndrome (SIDS), is associated with a higher frequency of reflux. On the other hand, prone position is effective in reducing reflux events, but is contraindicated in infants under one year of age due to the risk of SIDS (Gulati et al., 2019; Boza et al., 2019).

Metabolic conditions, such as lactose intolerance and cow's milk protein (ALV) allergy, are also related to GERD. The concomitant presence of ALV and GERD ranges between 16% and 56% in infants with persistent gastrointestinal symptoms, indicating a significant intersection between these conditions (Salvatore et al., 2021). A family history of reflux-related diseases, such as Barrett's esophagus and esophageal adenocarcinoma, may also increase reflux predisposition, indicating a possible genetic component (Boza et al., 2019).

The risk factors for GERD are multifaceted and often interrelated, ranging from congenital conditions and prematurity to environmental and behavioral factors. Early identification and appropriate management of these risk factors are essential to minimize complications associated with GERD and improve patients' quality of life (Gulati et al., 2019; Boza et al., 2019; Salvatore et al., 2021).

CLINICAL MANIFESTATIONS OF GASTROESOPHAGEAL REFLUX DISEASE (GERD)

The clinical manifestations of gastroesophageal reflux disease (GERD) vary widely in infants and children, depending on the severity and associated complications. Although many cases of gastroesophageal reflux (GERD) are physiological and do not result in serious consequences, GERD is characterized by persistent and/or bothersome symptoms that can impact nutrition, growth, respiratory system, and even neurological development (Boza et al., 2019; Gulati et al., 2019).

The main gastrointestinal symptoms include frequent vomiting or regurgitation, which is common in infants with GERD. Although physiological GER is often benign, GERD can lead to complications such as esophagitis, a painful inflammation of the esophagus caused by frequent contact with gastric acid. Esophagitis can result in pain when swallowing, refusal to feed, and significant irritability. These symptoms, in addition to making it difficult to

eat, can lead to delayed growth, due to inadequate nutrient intake and impaired absorption (Boza et al., 2019).

Another common effect of GERD in infants is inadequate weight gain. Infants who suffer from persistent regurgitation may not reach the expected developmental milestones, requiring nutritional interventions, such as the introduction of enteral feeding by tubes (Boza et al., 2019).

The clinical manifestations of GERD often affect the respiratory system, due to the aspiration of gastric contents into the airways. This can result in aspiration pneumonia, a serious condition that requires immediate medical intervention. In addition, babies with GERD may have chronic symptoms, such as persistent cough, wheezing, stridor (high-pitched sound during breathing), and laryngitis. These respiratory complications are especially prevalent in infants with a history of asthma or other preexisting respiratory conditions (Boza et al., 2019; Gulati et al., 2019).

Another critical aspect is apnea, which is characterized by temporary pauses in breathing and is often associated with GERD in infants. Chronic aspiration and recurrent lung damage can lead to the development of chronic respiratory diseases such as bronchospasm, further increasing the morbidity associated with GERD (Boza et al., 2019).

Irritability is one of the most common symptoms in infants with GERD, due to the pain and discomfort caused by frequent exposure to gastric acid in the esophagus. This irritability often manifests as persistent crying, difficulty sleeping, and fussy behavior, significantly impacting the quality of life of babies and their caregivers. In addition, food refusal caused by pain when swallowing or esophagitis further aggravates the clinical picture (Boza et al., 2019; Gulati et al., 2019).

Repeated episodes of acid reflux and aspiration can also have neurological consequences. Oxygen desaturation associated with apneas and aspiration episodes increases the risk of cerebral hypoxia, which can affect the neurological development of infants. These effects make proper management of GERD critical to minimize the risks of long-term complications (Gulati et al., 2019).

Clinical manifestations of GERD may also include ENT symptoms, such as otalgia (ear pain) and recurrent otitis. These conditions are associated with inflammation and infection of the middle ear, caused by the migration of gastric contents into the upper airways. These symptoms significantly affect the well-being of infants and can interfere with hearing and speech development if not treated properly (Boza et al., 2019).

In many cases, GERD symptoms may be nonspecific, overlapping with those of other conditions, such as cow's milk protein (ALV) allergy, metabolic and neurological

disorders. The coexistence of ALV and GERD, observed in about 16% to 56% of infants with persistent gastrointestinal symptoms, underscores the importance of a detailed clinical evaluation to avoid misdiagnosis and unnecessary treatments (Salvatore et al., 2021).

The clinical manifestations of GERD are diverse and often interrelated, encompassing gastrointestinal, respiratory, behavioral, and neurological symptoms. The significant impact of GERD on the quality of life of infants and their families requires a careful diagnostic approach and appropriate therapeutic management to prevent long-term complications. Early identification and effective treatment are essential to improve health outcomes in these patients (Boza et al., 2019; Gulati et al., 2019; Salvatore et al., 2021).

COMPLICATIONS ASSOCIATED WITH GASTROESOPHAGEAL REFLUX DISEASE (GERD)

Gastroesophageal reflux disease (GERD), when not treated properly, can result in several complications that impact multiple systems in the body, significantly compromising the health and well-being of patients. Complications range in severity, ranging from local inflammation in the gastrointestinal tract to long-term respiratory and neurological problems. Identifying and managing these complications is essential to prevent adverse outcomes (Boza et al., 2019; Gulati et al., 2019).

Among the most frequent digestive complications is esophagitis, which is an inflammation of the esophageal mucosa due to prolonged exposure to gastric acid. Esophagitis can progress to erosive or ulcerated forms, resulting in pain when swallowing (odynophagia), refusal to feed, irritability, and even hematemesis (vomiting blood). Repetitive damage to the esophageal mucosa also increases the risk of esophageal stenosis, which is the narrowing of the esophagus caused by scarring, leading to swallowing difficulties (Boza et al., 2019; Gulati et al., 2019).

GERD is also associated with a condition called Barrett's esophagus, in which an intestinal metaplasia of the esophageal mucosa occurs. This change is considered premalignant, increasing the risk of esophageal adenocarcinoma over time. Although Barrett's esophagus is most often reported in adults, its association with severe and prolonged episodes of GERD is also a long-term pediatric concern (Boza et al., 2019).

The impact of GERD on the respiratory system is particularly significant. Aspiration of gastric contents into the airways can cause aspiration pneumonia, a serious and recurrent condition that often requires hospitalization. Chronic aspiration can result in bronchoaspiration, leading to the development of persistent lung inflammation, bronchospasm, and chronic respiratory diseases (Boza et al., 2019; Gulati et al., 2019).

Other respiratory manifestations include chronic cough, stridor (sharp noise when breathing), laryngitis (inflammation of the larynx), and wheezing. These symptoms result from the contact of gastric acid with the upper airways and larynx. In infants, recurrent episodes of apnea may occur, increasing the risk of hypoxia and sudden infant death (Gulati et al., 2019).

Neurological complications are mainly related to oxygen desaturation due to apnea and aspiration associated with GERD. Recurrent cerebral hypoxia can have a significant impact on neurological development, increasing the risk of delayed motor and cognitive development. This is especially concerning in premature infants, who are already vulnerable to neurological injury due to the immaturity of the central nervous system (Gulati et al., 2019).

GERD often interferes with patients' nutrition and growth, due to refusal to feed and nutrient malabsorption. Persistent regurgitation and frequent vomiting contribute to malnutrition and make it difficult to gain weight. Infants with untreated GERD may experience growth retardation, requiring additional nutritional support, such as enteral or parenteral feeding (Boza et al., 2019).

The gastric hypersecretion seen in some conditions associated with GERD can also lead to inactivation of pancreatic enzymes, impairing the digestion of fats and carbohydrates. This situation further aggravates malnutrition, especially in children with underlying conditions such as short bowel syndrome (SBS) (Rybak et al., 2020).

Complications related to the ENT tract include recurrent otitis media and otalgia (earache). These conditions can be a consequence of inflammation caused by acid reflux in the upper airways, affecting the Eustachian tube and increasing the risk of middle ear infections. These manifestations are particularly prevalent in infants and can interfere with the development of hearing and speech (Boza et al., 2019).

In addition to the physical implications, complications from GERD also have a significant impact on the psychological well-being of caregivers and families. Constantly managing an infant with irritability, refusal to feed, and recurrent respiratory symptoms can be stressful, increasing the emotional burden and risk of exhaustion for caregivers (Boza et al., 2019).

The complications of GERD are broad and often interconnected, encompassing gastrointestinal, respiratory, neurological, and ENT problems. Early identification and appropriate management of complications are crucial to minimize adverse outcomes and improve patients' quality of life. Evidence-based approaches and individualized

interventions are essential to prevent long-term complications and optimize clinical outcomes (Boza et al., 2019; Gulati et al., 2019; Rybak et al., 2020).

DIAGNOSIS OF GASTROESOPHAGEAL REFLUX DISEASE (GERD)

The diagnosis of gastroesophageal reflux disease (GERD) in infants and children presents important challenges due to the absence of a diagnostic gold standard and the similarity of symptoms to other pediatric conditions. Diagnosis is usually based on a clinical approach, supplemented by additional tools only in cases of doubt or suspicion of complications. This detailed assessment is essential for effective management of GERD, especially in more vulnerable patients (Ayerbe et al., 2019; Gulati et al., 2019).

Rosen et al. emphasize the growing role of technologies in the diagnosis of GERD, such as the multichannel impedance associated with pH-metry. This technique allows you to identify not only acid reflux episodes, but also non-acid reflux episodes, providing a more complete assessment of the relationship between symptoms and reflux events. This advancement is especially important to avoid overdiagnosis or misdiagnosis, which can lead to unnecessary treatments. The authors also highlight that, although non-invasive methods, such as the collection of a detailed clinical history and the evaluation of clinical questionnaires, are fundamental, more objective diagnostic tools have shown significant potential to improve diagnostic accuracy. (ROSEN et al; 2022)

History and physical examination are the initial pillars of diagnosis. Identifying symptoms such as frequent regurgitation, vomiting, food refusal, irritability, and alarm signs such as weight loss and apnea is essential to differentiate physiological reflux from GERD. Assessing the impact of these symptoms on the child's development and quality of life is also critical to guide the diagnosis (Ayerbe et al., 2019; Boza et al., 2019).

For patients with persistent symptoms or in doubtful cases, diagnostic methods such as esophageal pH-metry, upper GI endoscopy, and impedance studies are indicated. These tests help in the identification of acid and non-acid reflux events, as well as possible complications such as esophagitis. Endoscopy, in addition to direct visualization, allows the collection of biopsies to clarify inflammation or other structural changes (Ayerbe et al., 2019; Salvatore et al., 2021).

Although clinical diagnosis is sufficient for many cases, additional tools can be used in situations of diagnostic doubt or to evaluate complications, such as esophagitis or respiratory involvement. Among the diagnostic methods, the following stand out:

I. **Multichannel Esophageal Impedance and pH Testing:** These tests allow the detection of acid and non-acid reflux events, correlating them with the symptoms

presented. pH metry is especially useful for assessing esophageal acid exposure and identifying cases of refractory GERD (Boza et al., 2019; Gulati et al., 2019).

II. **Upper Gastrointestinal Endoscopy:** Endoscopy is indicated in patients with alarm signs such as hematemesis or suspected severe esophagitis. The exam allows direct visualization of the esophageal mucosa and biopsies can be performed, if necessary (Salvatore et al., 2021).

III. **Dietary Exclusion Test:** For cases in which cow's milk protein allergy (LLL) coexisting with GERD is suspected, it is recommended to exclude milk proteins from the mother's diet or the use of hydrolyzed formulas or amino acids. Clinical improvement during the diet and recurrence of symptoms after reintroduction of milk are suggestive of ALV (Salvatore et al., 2021).

IV. **Imaging:** Although little used as routine tools, contrast-enhanced studies of the upper GI tract may be indicated to exclude anatomical conditions, such as esophageal atresia or diaphragmatic hernia, that may contribute to symptoms (Gulati et al., 2019).

In many cases, GERD can coexist with other conditions, such as cow's milk protein (ALV) allergy or anatomical disorders. The use of elimination diets or contrast-enhanced tests may be necessary to rule out or confirm these hypotheses, avoiding misdiagnosis and unnecessary interventions (Ayerbe et al., 2019; Salvatore et al., 2021).

TREATMENT OF GASTROESOPHAGEAL REFLUX DISEASE (GERD)

The treatment of gastroesophageal reflux disease (GERD) in infants and children involves a multifactorial approach that encompasses non-pharmacological, pharmacological and, in more severe cases, surgical interventions. The choice of treatment is based on the severity of symptoms, the impact on quality of life, and the presence of associated complications. Proper management aims to alleviate symptoms, prevent complications, and improve the patient's overall well-being (Boza et al., 2019; Gulati et al., 2019; Rybak et al., 2020).

Initial interventions for GERD management include lifestyle changes and adjustments in feeding methods, which are considered the mainstay of treatment, especially in milder cases. Among the recommended measures are:

I. **Positioning:** Elevating the head of the crib can help reduce episodes of reflux during sleep. However, while prone status is effective in reducing reflux events, it is contraindicated in infants under one year of age due to the risk of sudden infant death syndrome (SIDS). The left lateral decubitus position can also be

used under supervision, especially in children over one year of age (Boza et al., 2019; Gulati et al., 2019).

II. **Diet and Feeding:** Adjusting the volume and frequency of feedings is essential. Large volumes of food may exacerbate transient relaxations of the lower esophageal sphincter (LES) and, consequently, reflux episodes. Food thickeners, such as cornstarch or carob, can be used to increase the viscosity of gastric contents, reducing the risk of regurgitation. However, its use in preterm infants should be cautious due to the risk of necrotizing enterocolitis (Boza et al., 2019).

III. **Specific Diets:** In infants with suspected cow's milk protein (ALE) allergy, an elimination diet, replacing standard formulas with hydrolyzed or amino acid-based formulas, may be effective. The exclusion of cow's milk from the maternal diet is also recommended in cases of exclusive breastfeeding (Salvatore et al., 2021; Boza et al., 2019).

When non-pharmacological interventions are not sufficient to control symptoms, drug treatment is indicated. The most commonly used medications include:

I. **Proton Pump Inhibitors (PPIs):** Considered the most effective therapy today, PPIs, such as omeprazole and lansoprazole, reduce gastric acid production, relieving symptoms and promoting healing of esophagitis. They should be administered 30 minutes before meals and are generally well tolerated. However, its prolonged use can increase the risk of acute gastroenteritis, pneumonia, and respiratory infections (Boza et al., 2019).

II. **H2 Receptor Antagonists:** Medications such as ranitidine are an alternative to reduce gastric acidity, although they are less effective than PPIs. Its use can be considered in specific cases or combination with other treatments (Boza et al., 2019).

III. **Prokinetics:** Drugs such as domperidone are used to improve gastrointestinal motility and accelerate gastric emptying. However, adverse effects limit its use in pediatric patients, and evidence supporting its efficacy is limited (Boza et al., 2019; Gulati et al., 2019).

IV. **Mucosal Protective Agents:** Alginate and sucralfate are used to create a physical barrier in the esophagus, protecting the gastric mucosa from acid damage. However, they should not be used as monotherapy for GERD (Boza et al., 2019).

Surgery is reserved for severe cases of GERD, which do not respond to medical treatment or have life-threatening complications, such as severe esophagitis, esophageal

stricture, and reflux with a risk of pulmonary aspiration. **Nissen fundoplication**, which involves creating an anti-backflow valve around the LES, is the most common surgical procedure. Other interventions include gastrojejunostomy or laparoscopic fundoplication, which has lower postoperative morbidity (Boza et al., 2019; Gulati et al., 2019). For infants with GERD associated with morbid obesity or other conditions, such as short bowel syndrome (SBS), specific surgeries tailored to the patient's individual need may be considered, including bariatric procedures in selected cases (Rybak et al., 2020).

In neonates and infants hospitalized in the NICU, the management of GERD may be more challenging due to the coexistence of other medical conditions. In these cases, the use of jejunal feeding tubes may be necessary to prevent regurgitation, while continuous monitoring and specific tests, such as pH-metry or intraluminal multichannel impedance, may be used to guide interventions (Gulati et al., 2019; Boza et al., 2019).

The treatment of GERD requires an individualized approach, taking into account the severity of symptoms, the presence of associated conditions, and the response to previous interventions. While non-pharmacological measures remain the basis of management, the rational use of medications and the careful indication of surgery are essential to minimize complications and improve the quality of life of patients. Evidence-based approaches and multidisciplinary strategies play a crucial role in the effective management of the condition (Boza et al., 2019; Gulati et al., 2019; Rybak et al., 2020; Salvatore et al., 2021).

CONCLUSION

Gastroesophageal reflux disease (GERD) is a multifactorial condition with a high prevalence in infants and children, especially among vulnerable populations, such as premature infants and patients with neurological or congenital conditions. This article highlighted the importance of a comprehensive approach, highlighting the need to understand its pathophysiology, risk factors, clinical manifestations, complications, and therapeutic options.

GERD, when not properly managed, can lead to serious complications that impact both the digestive and respiratory systems, as well as affect neurological growth and development. Careful clinical diagnosis, combined with additional tools in suspected cases, allows for accurate identification of the disease and guides treatment, which must be individualized.

Management involves non-pharmacological measures, pharmacological interventions, and, in specific situations, surgical approaches, with the aim of controlling symptoms, preventing complications, and improving the quality of life of patients. Therefore,

early characterization and appropriate treatment of GERD are crucial to ensure the well-being and healthy development of affected children.

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