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The role of endoscopy in dyspeptic syndrome in children and adolescents

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ABSTRACT – **Background** – Dyspepsia is pain or discomfort in the epigastric region, and can be subdivided into organic and functional. The diagnosis of functional dyspepsia is based on the criteria defined by the Rome committee. In the pediatric population, functional dyspepsia is more common than organic dyspepsia, in addition to being part of a set of diseases called defined gastrointestinal disorders, defined by the Rome IV criteria. The most efficient diagnostic method of functional dyspepsia in the pediatric population is still uncertain since endoscopy is an important test to rule out organic changes, but it is invasive to be performed on a large scale. **Objective** – To evaluate the role of endoscopy in the diagnosis of functional dyspepsia in pediatric patients, aiming at preventing invasive procedures and reaching high specificity in the result, which is important to determine the best diagnostic guideline for these patients. **Methods –** Narrative literature review study performed by searching for articles in the PubMed/Medline and LILACS database using the PRISMA method. **Results** – A total of 102 articles were found in PubMed, 15 of which were selected for the study. In the LILACS database, nine articles were found and one was selected. Thus, 16 articles were selected for the study. The most appropriate indications for endoscopy, how to differentiate organic from functional dyspepsia without endoscopy, the main endoscopic findings of the studies, the differences between Rome III and Rome IV criteria, and the prevalence and factors possibly associated with functional dyspepsia were approached through the selected articles. **Conclusion** – The main indication for endoscopy is the presence of alarm symptoms in pediatric patients with dyspepsia and the Rome clinical criteria are efficient for the diagnosis of functional dyspepsia. However, there is still no standardized diagnostic guideline to be followed in this age group.

Keywords – Dyspepsia; children; diagnosis; endoscopy.

INTRODUCTION

Dyspepsia is defined as pain or discomfort located in the epigastric region, but it can include several other symptoms such as postprandial fullness, early satisfaction, anorexia, nausea and vomiting, swelling in the upper abdomen, burning and regurgitation. Thus, dyspepsia is a heterogeneous set of symptoms present in the upper abdomen[1]. It can be differentiated into two categories, organic and functional. Organic dyspepsia occurs when there is structural or metabolic alteration justifying the symptoms, while in functional dyspepsia, none of these changes are found by clinical evaluation and subsidiary exams such as endoscopy[2,3].

In the pediatric population, functional dyspepsia is within a set of symptoms called functional gastrointestinal disorders that are common in children of all ages and gather disorders unexplained by structural or biochemical changes[4,5]. This group of symptoms includes disorders of the brain-gut interaction, with gastrointestinal symptoms related to disorders of motility, visceral hypersensitivity, alteration of mucosal and immune function, alteration of the intestinal microbiota and altered central nervous system CNS. processing[6]. According to the Rome IV criteria, functional gastrointestinal disorders include the following pathological groups: functional nausea and vomiting disorders, functional abdominal pain disorders and functional defecation disorders[5].

The group of functional nausea and vomiting disorders involves diseases of cyclic vomiting syndrome, functional nausea and vomiting, rumination syndrome and aerophagia. The group of functional abdominal pain disorders includes functional dyspepsia, irritable bowel syndrome, abdominal migraine and functional abdominal pain. Functional defecation disorders comprise functional constipation and fecal incontinence[5].

According to the Rome IV criteria, functional dyspepsia must include one or more of the following symptoms: postprandial fullness, early satiety, epigastric pain or epigastric burning not associated with defecation. The frequency should be at least four times a month and at least two months before diagnosis, and symptoms cannot be explained by another medical condition after evaluation[7].

As for the epidemiology of functional dyspepsia, in a meta-analysis conducted by Korterink, et al. 2015.[8], was analyzed the period from 1957 to 2014 in relation to recurrent abdominal pain in the pediatric population, and in 196,472 children included in the 58 studies, was found an overall prevalence of 13.5% of this symptom. The prevalence of irritable bowel syndrome was 8.8%; of functional dyspepsia was 4.5%; and of functional abdominal pain was 3.5%.

The predisposition to this disorder is associated with several factors, such as sex, since it is more common in girls[9]. There is also an association between victims of psychological stress and the development of functional abdominal pain disorders[10-13]. Exposure to traumatic life events such as physical, sexual and emotional abuse also predisposes to the development of functional abdominal pain

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disorders[14]. Children born to mothers with gestational diabetes and pregnancy-induced hypertension were also more prone to the disorder[15].

Several pathophysiological mechanisms are proposed to explain the occurrence of functional abdominal pain disorders, and they are the same for functional dyspepsia, since it falls within the functional abdominal pain disorder group. Among the diverse mechanisms, the main ones are the brain-gut axis and visceral hypersensitivity[16,17].

As these functional disorders do not have biochemical or structural changes in exams, the means of diagnosing children and adolescents have become based on the Rome criteria. Thus, the importance that these criteria are accurate, clear and not ambiguous[18].

Endoscopy is an important exam in the diagnosis of functional dyspepsia, as it is used to rule out organic changes. However, since this is an invasive exam to be performed in the pediatric population and there is no well-established standard regarding compliance, diagnosis becomes more difficult in children and adolescents.

The purpose of this study is to research how the diagnosis of functional dyspepsia should be performed in pediatric patients and evaluate the role of endoscopy in this diagnosis, considering this is an invasive exam that may cause risks if used as a diagnostic standard in cases of abdominal pain and discomfort; and what is the best standard to be followed in order to reduce invasive procedures and have high specificity in the result.

METHODS

A literature review was performed through national and international articles published in the PubMed/Medlin and LILACS database using the PRISMA method and searched at three different times.

The fundamental elements of the research question were represented by the acronym population, intervention, comparison, outcome PICO. with the details of the criteria established below:

- Population: pediatric and adolescent patients, aged 0 to 18 years, without restrictions on other demographic data.
- Intervention: studies reporting pediatric patients with symptoms of functional dyspepsia, addressing the conduct and diagnostic methods and/or discussing the indications and contraindications for upper gastrointestinal endoscopy in these patients, and/or the effectiveness of the Rome criteria.
- Comparison: comparison of pediatric patients who did not undergo upper digestive endoscopy for the diagnosis of functional dyspepsia with the endoscopy results of those who had undergone the examination. Comparison of Rome III and Rome IV criteria for diagnosis.
- Outcome: definition of the best diagnostic approach in these patients, preferably clinical, avoiding upper digestive endoscopy in all cases.

RESULTS

In the first step of the study, the descriptors "functional dyspepsia", "child", "diagnosis" were used in PubMed database. In the second step, the descriptors "dyspepsia", "child", "diagnosis", "endoscopy" were used interspersed by the Boolean operator "AND". Then, four PubMed filters were applied: publication period in the previous 10 years publication date from 10 years., studies in humans humans., English and Portuguese languages English, Portuguese. and age range from birth to 18 years Child: birth -18 years.

The articles found were analyzed by title and abstract, and those that met the objectives were included in the study. The eligibility criteria of the studies correspond to the studies that resulted after the application of the filters and that met the PICO criteria.

In the first step of the study, seven articles were found and all were included in the study.

In the result of the second search, 95 articles were found, of which 72 were excluded by the four PubMed filters, 70 of which had been published more than ten years earlier, one study was performed in animals, one study included people of all ages. Thus, 23 articles remained for analysis. Their titles and abstracts were assessed, and 15 articles were excluded because they did not refer specifically to the topic in question. Thus, eight articles resulting from the second research were studied.

In the third stage of the research, the LILACS database was used, with the descriptors "dyspepsia", "child", "diagnosis", "endoscopy", interspersed by the Boolean operator "AND". Nine articles were found, of which 7 were excluded after reading the title and abstract, as they did not refer to the topic in question, one article was excluded due to its previous selection in the second PubMed search, one article was selected, which answered the established eligibility criteria.

The articles found at each stage of the research were grouped in the diagram preferred reporting items for Systematic reviews and meta-analyses PRISMA. shown in FIGURE 1.

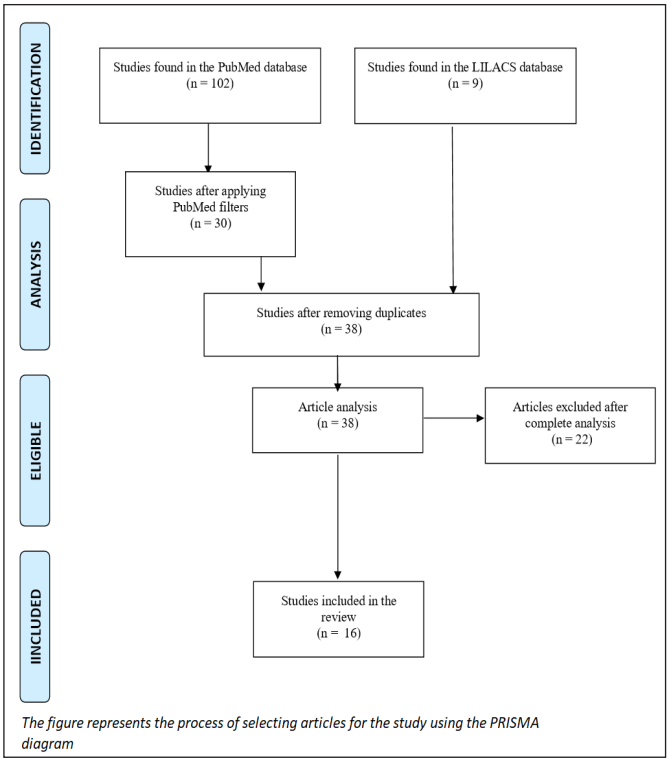

FIGURE 1. PRISMA (Preferred Reporting Itens for Systematic Reviews and Meta-Analyses).

By adding the first, second and third search, there were 16 articles selected for the review, as shown in TABLE 1. The study selection and analysis process was conducted by an independent reviewer and a senior reviewer.

TABLE 1. Total articles selected for the review.

Reference	Type of study	Sample number	Objective	Conclusion
Guariso G, et al. 2010.[19]	Observational retrospective study	2304	Check if endoscopic indications for children with dyspepsia were adequate	Endoscopy is appropriately indicated only in cases of family history of peptic ulcer and/or *H. pylori*, when it interferes with daily activities, when age is more than 10 years, and the longer the duration and the more severe the symptoms.
Canan O, et al. 2011.[22]	Prospective experimental study	161 10–17 years	Define a symptomatic score that indicates organic dyspepsia, before endoscopy.	It was not possible to determine a cutoff value in the score that differentiated organic from functional dyspepsia.
Tam YH, et al. 2011.[20]	Prospective experimental study	80 7–15 years	To evaluate the efficiency of the Rome III criteria as a guideline to differentiate organic from functional dyspepsia, and identify predictors for positive endoscopic findings.	The Rome III criteria are effective in screening for functional dyspepsia in children and to differentiate from those with organic dyspepsia.
Carvalho MA, et al. 2012.[24]	Cross-sectional case control study	185 4–17 years	To investigate the histopathology of lesions in the gastric mucosa, associated with infection by *H. pylori* in patients with dyspepsia without peptic ulcer.	There is a higher prevalence of *H. pylori* infection in participants with dyspepsia who had significant inflammation in the mucosa.
Ganesh M, et al. 2014.[21]	Review	-	To review the characteristics of functional dyspepsia, endoscopic findings, diagnostic method, types of treatment.	Functional dyspepsia must be diagnosed by the Rome III criteria.
Hyams JS, et al. 2016.[5]	Review	-	To review the changes between Rome III and Rome IV criteria, regarding the definitions of disorders and their respective treatments.	The Roma IV committee does not believe that endoscopy is necessary to make a diagnosis of functional dyspepsia.
Koppen IJ, et al. 2017.[18]	Review	-	To report the news contained in the Rome IV criteria in comparison to the previous ones.	The Rome IV criteria are well formulated and help a lot in the diagnosis of functional gastrointestinal disorders in children.
Wauters L, et al. 2017.[26]	Cohort retrospective study	72 4–18 years	Association between dyspeptic symptoms and duodenal eosinophilia in endoscopy.	Functional dyspepsia is strongly related to duodenal eosinophilia.
Saps M, et al. 2019.[29]	Cross-sectional	4394 8–18 years	To determine the prevalence of functional gastrointestinal disorders in school children in Colombia and its associated factors.	These disorders are more common in children in private schools than in public schools and are associated with stress.
Rajindrajith S, et a.l 2018.[7]	Review	-	Study on functional abdominal pain disorders.	Endoscopy should be considered when alarm symptoms are present.
Chumpitazi BP, et al. 2018.[30]	Retrospective and prospective	129 4–18 years	To determine the frequency, demographics and clinical characteristics associated with disaccharidase deficiency in children with dyspepsia.	Half of children with functional dyspepsia had disaccharidase deficiency. There may be a race/ethnicity relationship.
Friesen C, et al. 2018.[31]	Cross-sectional retrospective	235 8–17 years	To evaluate the relationship between headaches and functional dyspepsia and headaches with mucosal mast cells and eosinophils.	Headaches are related to the presence of functional dyspepsia and to increased duodenal mast cell density and variety of somatic symptoms.
Saps M, et al. 2018.[28]	Observational	3767 8–18 years	Compare the prevalence of functional gastrointestinal disorders in children using the Rome III criteria and then, using the Rome IV criteria.	Using the Rome IV criteria resulted in a decrease in the prevalence of these disorders, and the new diagnoses of these criteria were present in a small percentage of children.
Trivić I, et al. 2018.[23]	Observational	294 1–18 years	Detect the symptoms of patients with functional gastrointestinal disorders, the characteristics and results of the diagnostic investigation.	Early diagnosis increases the chance of symptom resolution, and these disorders affect quality of life.
Adeniyi OF, et al. 2019.[25]	Prospective descriptive	113 Children under 19 years	Describe endoscopic findings in children with recurrent abdominal pain.	Upper gastrointestinal endoscopy is valuable in investigating recurrent abdominal pain in children, as it offers an accurate diagnosis of the causes.
Toporovski MS, et al. 1998.[27]		106 4–16 years	Compare clinical, endoscopic and colonization data of *H. pylori* in children and teenagers with peptic disease.	Prevalence of peptic disease in females. All with digestive bleeding associated with ulcerative lesions were colonized by *H. pylori*.

DISCUSSION

As each selected article was analyzed, the most relevant issues related to the topic in question were observed, as shown below:

Indications for endoscopy

In the study by Guariso G, et al. 2010.[19], 2,304 children were evaluated and the most appropriate indications for esophagogastroduodenoscopy for children with functional dyspepsia were addressed. The conclusion was that indications for endoscopy are appropriate when the child has a family history of peptic ulcer and/or *H. pylori*, when dyspepsia interferes with daily activities, when patients are older than 10 years, the longer the duration more than 6 months. of symptoms and the more severe they are. The recommendation for endoscopy was considered less appropriate in cases of patients with worsening symptoms at mealtime, with a family history of irritable bowel syndrome and in cases of association with other symptoms such as lipothymia, tachycardia, sweating and flushing. In addition, it was considered inappropriate for cases of family history of lactose intolerance. According to the study, the examination should not be indicated for any case of functional dyspepsia or any symptom, restricting it only to more necessary cases. In the study by Tam YH, et al. 2011.[20], is also reinforced that indications for endoscopy should be restricted to the cases mentioned above. In the study by Rajindrajith S, et al. 2018.[7], it was emphasized that endoscopy should be considered when alarm symptoms are present, and these would be involuntary weight loss, growth retardation, significant vomiting, chronic and significant diarrhea, loss of gastrointestinal blood, persistent sensitivity located in the upper or lower right quadrant, unexplained fever, family history of inflammatory bowel disease. In addition, this study showed the importance of performing a careful clinical evaluation, with adequate anamnesis and physical examination to assist in the diagnosis. For Ganesh M, et al. 2014.[21], endoscopy is not a mandatory exam for the diagnosis of functional dyspepsia and should be based on the Rome criteria with attention to alarm symptoms.

Differentiate between organic and functional dyspepsia without endoscopy

In the study by Canan O, et al. 2011.[22], the objective was to determine the possibility of a score by asking questions in relation to symptoms, in order to establish a cutoff value to determine if the child has organic or functional dyspepsia without the need for endoscopy. However, it was not possible to determine a cutoff value that differentiated the types of dyspepsia. The objective of the study conducted by Tam YH, et al. 2011.[20] was to evaluate if the Rome III criteria could be used as a guideline to differentiate organic from functional dyspepsia, and the conclusion reached was that these criteria are efficient for the diagnosis. It also highlighted the importance of alarm symptoms and infection by *H. pylori* as probable indicators of the organic disease. Likewise, in the study by Trivić I, et al. 2018.[23] was reaffirmed the importance of these symptoms and the history and physical examination, as well as tests such as CRP, urine and celiac disease were used as diagnostic conduct in this last study.

The main endoscopic findings

In the article by Carvalho MA, et al. 2012.[24], the histopathology of mucosal lesions in children with dyspepsia without peptic ulcer was studied. Dyspeptic patients with *H. pylori* infection had significant inflammation in the mucosa with high colonization density in the antrum and body of the stomach. In the study by Adeniyi OF, et al. 2019.[25], were described the endoscopic findings of children with recurrent abdominal pain. Half of participants who had dyspepsia and underwent endoscopy, had alarm symptoms. In addition, the main endoscopic finding of patients with dyspepsia was gastritis. In the study by Wauters L, et al. 2017.[26], they sought a relationship between dyspeptic symptoms in children and findings of duodenal eosinophilia in endoscopy, since it was considered that only these symptoms are not enough to differentiate organic dyspepsia from functional. It was confirmed that duodenal eosinophilia is common in children with dyspepsia. In the study by Toporovski 1998.[27] the endoscopic examination performed in patients was normal in 30% of children with peptic disease and in 13% of adolescents. According to the study, a biopsy would be necessary for the diagnosis of peptic disease even when the macroscopy is normal.

Differences between Rome III and Rome IV criteria

According to the study by Hyams JS, et al. 2016.[5], some concepts were differentiated between the committees. According to Rome IV criteria, functional gastrointestinal disorders were grouped, namely functional nausea and vomiting, functional abdominal pain and functional defecation disorders. It was analyzed if the endoscopy for functional dyspepsia would be necessary, considering that according to Rome IV criteria, there is no need to perform this exam for the diagnosis. The possibility of the examination in cases of history of peptic ulcer in the family, children older than 10 years, cases of severe intensity of symptoms, and duration longer than six months was also highlighted. Likewise, in the study by Koppen IJ, et al. 2017.[18] the Rome IV criteria became more specific for the diagnosis of functional disorders, whereas in the study by Saps M, et al. 2018.[28], they sought the prevalence of disorders when comparing the different criteria of Rome III and Rome IV.

The differences between the prevalence of functional disorders using the Rome III and Rome IV criteria, are that there was a lower prevalence of gastrointestinal functional disorders overall, when using the Rome IV criteria 21.2%. compared to the criteria of Rome III 23.7%.. However, there were differences regarding the categories of each disorder, regarding the category of functional dyspepsia, a higher prevalence was seen when using the Rome IV criteria 3%. while Rome III was 1%. This can be explained by the fact that the Rome IV committee used a subclassification for functional dyspepsia, one of them is the postprandial stress syndrome, which no longer required the presence of abdominal pain to be included in the disorder, which increased the prevalence. Thus, the study concludes that the new changes made to classify each disorder allowed for greater specificity in this diagnosis, since some subcategories were added according to the need to further differentiate the symptoms of each disorder.

Prevalence and associated factors

In the study by Saps M, et al. 2019.[29], it was found that functional disorders were more present in children and adolescents in private schools than in public schools, and had a greater relationship with parents' history of divorce, thereby indicating that stress is an important factor in the development of pathophysiological changes in the gastrointestinal tract. Thus, stress, anxiety and depressive symptoms are associated with these functional disorders. Meanwhile, in the study by Chumpitazi BP, et al. 2018.[30], half of

children with functional dyspepsia who underwent esophagogastroduodenoscopy had disaccharidase deficiency, and there may be a relationship between the deficiency of this enzyme and the presence of functional dyspepsia. Furthermore, in the study by Friesen C, et al. 2018.[31], there was a possible relationship between a higher prevalence of headache in the group of patients with functional dyspepsia compared to the group without functional dyspepsia. In the study by Toporovski 1998.[27] the group of children was compared with those of adolescents in relation to clinical and endoscopic data for peptic disease. It was seen that females had a higher prevalence of peptic disease in both groups, in addition to the fact that the abdominal pain pattern in these two groups was of long duration 7.2 months in children and 8.1 months in adolescents., with strong intensity and annoying, with interruption of activities. The occurrence of nausea and vomiting accompanied the symptoms in both age groups, in most patients with ulcer disease and the location of epigastric pain in children was in the lower portion or in the mesogastrium, while in adolescents the more accurate epigastric pain predominated.

CONCLUSION

After evaluating the articles selected for the review, the conclusion was the lack of a standard form of diagnostic investigation of functional dyspepsia in the pediatric population, even though functional dyspepsia is more common than organic dyspepsia. For the diagnosis, conducts are preferably clinical, based on Rome criteria, which proved to be efficient for the diagnosis, and Rome IV criteria are the most updated.

As endoscopy is an invasive process to be performed in all patients with functional dyspepsia, its indication should be restricted to cases of patients with alarm symptoms following the symptoms of dyspepsia, such as persistent vomiting, involuntary weight loss, symptoms at night, growth retardation, chronic and significant diarrhea, gastrointestinal blood loss, persistent tenderness located in the upper or lower right quadrant, unexplained fever and family history of inflammatory bowel disease. In addition, it is also important to request endoscopy in cases of patients with a history of peptic ulcer in the family and/or the presence of *H. pylori* infection, when they are older than 10 years, symptoms have been present for more than six months and are severe enough to interfere with daily activities and sleep quality.

Therefore, a good anamnesis and a well-detailed physical examination are very important and decisive to perform more invasive tests such as endoscopy. As seen in the discussion, the presence of dyspeptic symptoms after the ingestion of milk or dairy products is important to be investigated in the anamnesis, as it can be diagnosed clinically and therefore would not require an upper digestive endoscopy.

In addition, there may be other signs and symptoms not specifically related to functional dyspepsia, but that can lead to this diagnosis, such as the presence of headache in these patients and the frequent presence of stress factors in their lives.

It is also important to highlight the efficiency of the early diagnosis of functional dyspepsia to reduce the impacts on the quality of life of these patients.

The data collection for this review was limited by the small number of publications on the use of endoscopy for pediatric patients with functional dyspepsia. More studies from a single center were found, and no standard follow-up was found for the diagnosis of these patients. Therefore, we recommend the development of further studies on the topic in question, in order to better determine a diagnostic approach and prevent late diagnoses and unnecessary invasive procedures.

Authors' contribution

Marciano NA: developed the study and Chehter EZ: guided the development of the study.

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RESUMO – **Contexto –** A dispepsia é a dor ou desconforto na região epigástrica, e pode ser subdividida em orgânica e funcional. O diagnóstico de dispepsia funcional é realizado com base nos critérios definidos pelo comitê de Roma. Na população pediátrica a dispepsia funcional é mais comum que a orgânica, além de que está dentro de um conjunto de doenças denominado distúrbios gastrointestinais funcionais, definidos pelos critérios de Roma IV. O método diagnóstico de dispepsia funcional mais eficiente na população pediátrica, ainda é incerto uma vez que a endoscopia é um exame importante para descartar alterações orgânicas, porém invasivo para ser realizado em alta escala, por isso a importância desse estudo, que visa definir a melhor conduta. **Objetivo –** Avaliar o papel da endoscopia no diagnóstico da dispepsia funcional em pacientes pediátricos, visando prevenir procedimentos invasivos e atingir alta especificidade no resultado, o que é importante para determinar a melhor diretriz diagnóstica para esses pacientes. **Métodos –** Estudo de revisão narrativa da literatura, realizada por meio de buscas de artigos na base de dados PubMed/Medline e LILACS, utilizando o método PRISMA. **Resultados –** No PubMed foram encontrados 102 artigos, sendo 15 selecionados para o estudo. Na base de dados LILACS foram encontrados nove artigos e selecionado um. Dessa forma, 16 artigos foram selecionados ao estudo, sendo abordado por meio deles quais são as indicações mais adequadas para a endoscopia, como diferenciar dispepsia orgânica de funcional sem endoscopia, quais os principais achados endoscópicos dos estudos, quais as diferenças entre os critérios de Roma III e Roma IV, qual a prevalência e os fatores possivelmente associados à dispepsia funcional. **Conclusão** – A principal indicação para endoscopia foi a presença de fatores de alarme nos pacientes pediátricos com dispepsia e os critérios clínicos de Roma mostraram-se eficientes para o diagnóstico de dispepsia funcional. Porém, ainda não existe uma diretriz diagnóstica padronizada a ser seguida nessa faixa etária.

Palavras-chave – Dispepsia; criança; diagnóstico; endoscopia.

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