ОРИГИНАЛЬНЫЕ ИССЛЕДОВАНИЯ

doi : 10.52485/19986173_2022_3_1
УДК 616.33-002-053.2 (571.55)

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СИНДРОМ ДИСПЕПСИИ У ДЕТЕЙ ЗАБАЙКАЛЬСКОГО КРАЯ

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Цель. *Изучить причины и распространенность симптомов синдрома диспепсии (СД) у детей.*
Материалы и методы. *В исследовании приняли участие 550 детей жителей Забайкальского края в возрасте 8-15 лет с СД. Исследование проведено в 2 этапа. Сначала были обследованы все больные с СД. Затем более подробно обследованы пациенты с функциональной диспепсией (ФД). Диагностика ФД основывалась на Римских критериях IV пересмотра. Эндоскопия верхних отделов желудочно-кишечного тракта выполнена 156 детям. Антитела к Helicobacter pylori (HP) IgM исследованы ИФА-методом в сыворотке крови.*
Результаты. *У девочек СД была более распространена, чем у мальчиков. СД чаще встречалась в возрастной группе 12-15 лет. Органические причины СД выявлены у 144 больных (26,2% случаев). ФД была у 406 (73,8% случаев). Этнических различий в распространенности HP-инфекции выявлено не было. У пациентов с более длительным течением симптомов HP выявлялся чаще. Инфицирование HP чаще возникало у пациентов с ранним искусственным вскармливанием, наследственной предрасположенностью к гастриту и/или язвенной болезни. Одной из возможных причин развития ФД была инфекция HP. У пациентов с семейным анамнезом гастрита или язвенной болезни HP-инфекция встречалась в 72,9% случаев.*
Заключение*. В Забайкальском крае функциональные причины СД распространены больше, чем органические. Возможными причинами ФД были аллергия, раннее искусственное вскармливание и наследственная отягощенность по гастриту и/или язвенной болезни. Антитела к HP обнаружены у 57% больных. Наиболее распространенным симптомом у больных, инфицированных HP, было чувство жжения в эпигастрии, вызывающее беспокойство.*
Ключевые слова: *синдром диспепсии, функциональная диспепсия, дети, Римские критерии IV, Helicobacter pylori.*

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SYNDROME OF DYSPEPSIA IN CHILDREN OF THE TRANSBAIKAL TERRITORY

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Objective. *To study the causes and prevalence of symptoms of the syndrome of dyspepsia (SD) in children.*
Materials and Methods. *The study involved 550 children of the Transbaikal Territory aged 8-15 years with SD. The study was conducted in 2 stages. First, all patients with SD were examined. Then, patients with functional dyspepsia (FD) had a complete examination. Diagnostics of FD was based on the Rome IV criteria. Upper gastrointestinal endoscopy was made in 156 children. Helicobacter pylori (HP) IgM antibodies were detected by ELISA test in the serum.*
Results*. The organic causes of SD were found in 144 patients (26.2% cases). FD was found in 406 (73.8%) cases. SD occurred more often in girls than in boys. SD was more widespread in the age group of 12-15. There were no ethnic differences in the prevalence of HP infection. The patients with longer duration of symptoms had HP infection more often. HP infection more often occurred in patients with early bottle feeding and family gastritis or ulcer history. One of the possible causes was HP infection. Patients with family history of gastritis or ulcer had HP infection in 72.9% cases.*
Conclusion. *In the Transbaikal Territory functional causes of SD were more widespread than organic ones. Probable causes of the FD were considered to be allergy, early bottle feeding and family gastritis / ulcer history. Antibodies to HP were found in 57% patients. The most widespread symptom in patients, infected with HP, was bothersome epigastric burning.*
Key words: *syndrome of dyspepsia, functional dyspepsia, bothersome epigastric burning, children, Rome IV criteria, Helicobacter pylori.*

Relevance. The Rome IV criteria of functional gastrointestinal disorders (FGIDs) have changed some previous Rome III recommendations. The Rome III criteria emphasize that there should be "no evidence" for organic disease, which may have prompted a focus on testing [1]. In the Rome IV criteria, the phrase "no evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject's symptoms" has been removed from the diagnostic criteria. Instead, it includes the statement that "after appropriate medical evaluation, the symptoms cannot be attributed to another medical condition" [2]. This change permits selective or no testing to support a positive diagnosis of FGIDs. It has been also pointed out that FGIDs can coexist with other medical conditions.

The Rome IV criteria provide symptom-based guidelines by which child and adolescent FGIDs can be diagnosed. Previous Rome III criteria were based mostly on a medical consensus, as research in child/adolescent FGIDs was still largely lacking. An expanded evidence base from the last 10 years provides the basis for many of the recommendations of the child/adolescent committee for the Rome IV [3]. For disorders still lacking scientific data, the committee used clinical experience and consensus among the committee members.

The Rome IV FGIDs for children and adolescents are as follows:

H1. Functional nausea and vomiting disorders:
H1a. Cyclic vomiting syndrome;
H1b. Functional nausea and functional vomiting;
H1c. Rumination syndrome;
H1d. Aerophagia.
H2. Functional abdominal pain disorders:
H2a. Functional dyspepsia;
H2b. Irritable bowel syndrome;
H2c. Abdominal migraine;
H2d. Functional abdominal pain not otherwise specified.
H3. Functional defecation disorders:
H3a. Functional constipation;
H3b. Non-retentive fecal incontinence.

The pathology of the gastro-duodenal zone consists of two main groups of diseases: functional and organic. In both groups there are clinical symptoms of dyspepsia (uninvestigated dyspepsia). The multifactorial causes of dyspepsia are proved. HP is considered as one of the main causes of gasrtointestinal diseases [4, 5]. One of the most controversial issues is the role of HP in the development of syndrome of dyspepsia (SD). It should be noted that most studies do not confirm the relationship between HP and dyspepsia [6, 7]. At the same time, according to the other scientists, eradication of the bacteria significantly reduces dyspeptic symptoms [8].

Objective. To study the causes and the prevalence of symptoms of SD in children.

Materials and Methods. The Transbaikal Territory is located in the eastern part of Siberia. Its administrative center is Chita. It borders with Mongolia and China. Time zone is GMT +9. The area of the territory is 431,892 km². The population is 1 043 467 inhabitants. The population density is about 2.42 people / km².

The study involved 550 residents of the Transbaikal Territory with SD. The patients were examined in the Chita Regional Children's Hospital. The study was conducted in 2 stages. First, all the patients with SD had a routine medical examination. Then, patients with functional dyspepsia (FD) underwent a more detailed examination. Anamnestic and clinical signs were examined. Diagnostics of FD was made by the Rome IV criteria [2]. Upper gastrointestinal endoscopy was made in 156 children. Organic diseases were found in 144 (92.3%) patients during endoscopy.

Inclusion criteria were as follows: age range 8-15 years, epigastric pain syndrome or postprandial distress syndrome present for at least last 3 months with the onset of at least 6 months before diagnosing.

Exclusion criteria were as follows: bleeding, family cancer history, palpable abdominal mass or lymphadenopathy, anemia, leukocytosis, increased erythrocyte sedimentation rate.

HP IgM antibodies were examined by ELISA test in the serum. For the ELISA we used the following equipment: shaker-thermostat Elmi ST-3 (made in Latvia), automatic washer Atlantis 4 (the UK), Immunoassay Analyzer Awareness Technology (the USA). Informed consent was taken in all patients. Statistical processing was carried out using the program Statistica-10 (the USA). Statistical significance was evaluated by χ^2 Pearson criterion. Differences were considered statistically significant at $p < 0.05$.

Results.

1. Syndrome of dyspepsia

SD may be caused by organic and functional disorders. At first, we studied all patients with SD. According to the opinion of the authors of the Roman IV Foundation [2], from an etiological viewpoint, patients with dyspeptic symptoms can be subdivided into 2 main categories:

1. Those with an organic, systemic, or metabolic cause for the symptoms that can be identified by traditional diagnostic procedures where, if the disease improves or is eliminated, symptoms also improve or resolve (eg, peptic ulcer disease, malignancy, pancreaticobiliary disease, endocrine disorders, or medication use) and is described by the term "secondary dyspepsia". HP-associated dyspepsia is diagnosed in a subset of dyspepsia patients whose symptoms are treated by HP eradication.
2. Those in whom no identifiable explanation for the symptoms can be identified by traditional diagnostic procedures that are exemplified under the umbrella term "functional dyspepsia" [9].

In our study the organic causes of SD (figure 1) were found in 144 patients (26.2%). FD was found in 406 (73.8%) cases.

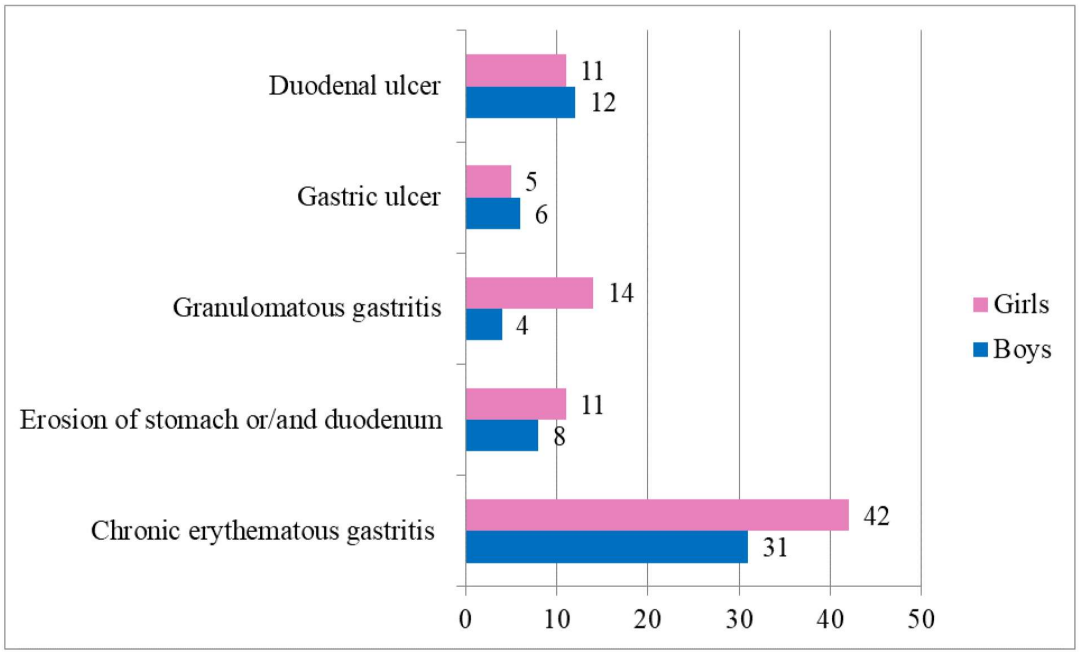

Figure 1. Organic causes of syndrome of dyspepsia.

Antibodies to HP were found in 313 (57%) patients. Antibodies to HP among Caucasoid population were found in 56.8% (289 children out of 524) and among the Mongoloids – in 57.9% (15 children out of 26). There were no ethnic differences of the HP prevalence ($p>0.05$).

In our study SD was more widespread in girls than in boys (figure 2). All cases, either functional or organic, prevailed in girls. We assume that this is due to the more mobile and changeable nervous system of girls than boys, because these disorders are commonly associated with dysfunction of the brain-gut axis interaction [2].

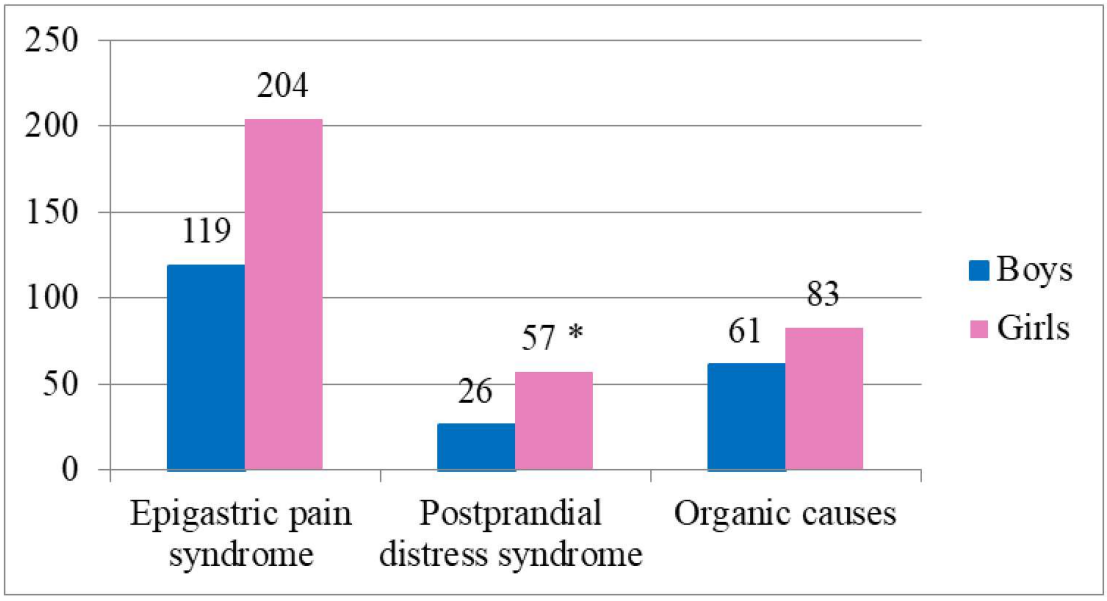

Figure 2. Syndrome of dyspepsia rate depending on the sex.
Note: * statistical significance was evaluated by χ^2 Pearson criterion ($p < 0.05$).

There were no differences of HP infection incidence in FD, but they were among the organic causes (figure 3)**.**

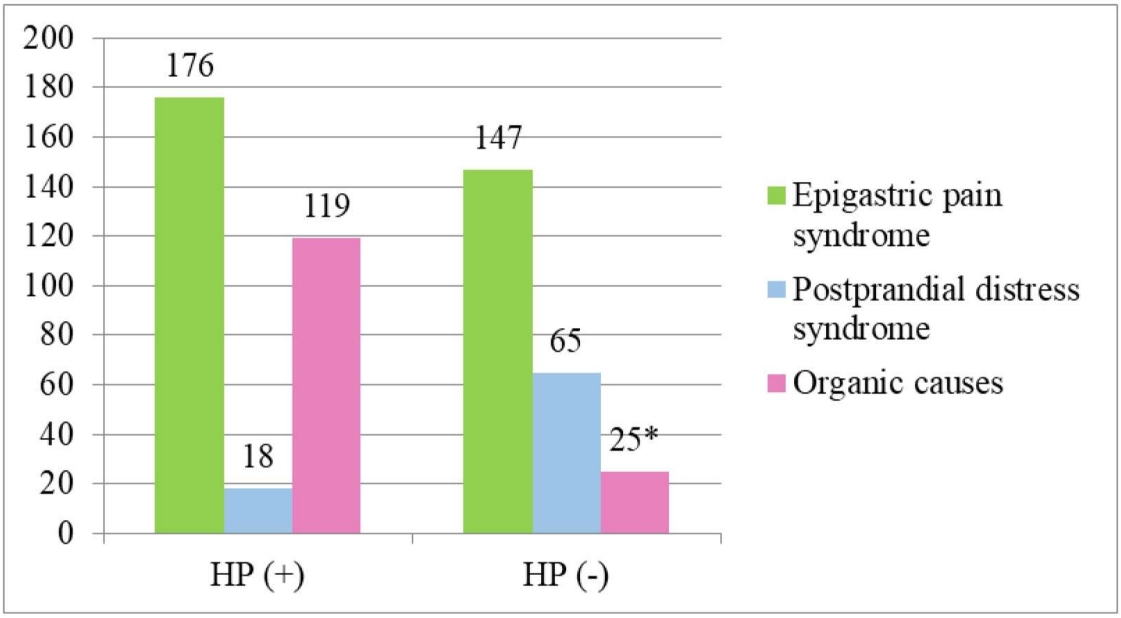

Figure 3. Helicobacter pylori infection prevalence in children with syndrome of dyspepsia.
Note: * statistical significance was evaluated by χ^2 Pearson criterion ($p < 0.05$).

SD was more widespread at the age of 12-15 (figure 4).

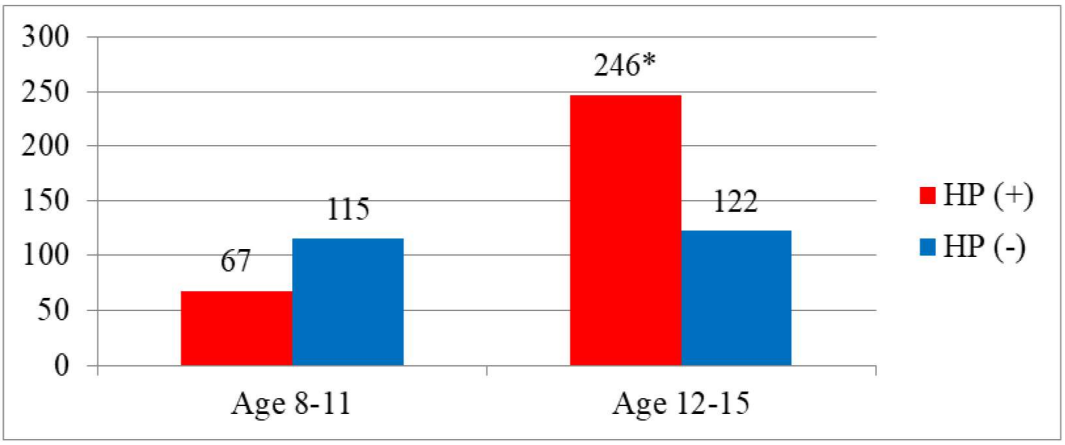

Figure 4. The prevalence of Helicobacter pylori infection in children with the syndrome of dyspepsia depending on the age.
Note: * statistical significance was evaluated by χ^2 Pearson criterion ($p < 0.05$).

Thus, the organic causes of SD were found in 26.2% cases. FD was found in 73.8% cases. SD was more widespread in girls than in boys. SD was more widespread in the age group of 12-15. There were no ethnic differences in the prevalence of HP infection.

2. Functional dyspepsia.

Then we studied patients with FD only. FD is designated as H2a in the Rome IV FGIDs classification. FD is a medical condition that significantly has an impact on the usual activities of a patient and is characterized by one or more of the following symptoms: postprandial fullness, early satiation, epigastric pain, and epigastric burning that remain unexplained after a routine clinical evaluation.

According to the Rome IV, diagnostic criteria for FD must include one or more of the following bothersome symptoms occurring for at least 4 days per month:

1. Postprandial fullness;
2. Early satiation;
3. Epigastric pain or burning not associated with defecation;
4. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition.

Criteria fulfilled for at least 2 months before diagnosis.

Within FD, the following subtypes are now adopted [10]:

1. Postprandial distress syndrome including bothersome postprandial fullness or early satiation that prevents finishing a regular meal. Supportive features include upper abdominal bloating, postprandial nausea, or excessive belching.
2. Epigastric pain syndrome, which includes all of the following: bothersome (severe enough to interfere with normal activities) pain or burning localized to the epigastrium. The pain is not generalized or localized to other abdominal or chest regions and is not relieved by defecation or passage of flatus. Supportive criteria can include burning quality of the pain but without a retrosternal component and the pain is commonly induced or relieved by ingestion of a meal but may occur while fasting.

In our study the patients with longer duration of symptoms had more often HP infection (Table 1).

Table 1

The prevalence of Helicobacter pylori infection in children with Functional Dyspepsia depending on duration of symptoms with the onset at least 6 months before diagnosis

Sign	Variants of FD			
	Epigastric pain syndrome		Postprandial distress syndrome	
	Patients n=323	HP (+)	Patients n=83	HP (+)
1. 3-6 months n=163	141	63 (44.7%)	22	6 (27.3%)
2. 6-12 months n=97	92	59* (64.1%)	5	3* (60.0%)
3. More than 12 months n=146	90	75* (83.3%)	56	34* (60.7%)
Total n=406	323	197 (61.0%)	83	43 (51.8%)

Note: * statistical significance was evaluated by χ^2 Pearson criterion.

Then we divided all the patients with different variants of FD according to their main symptoms. HP (+) patients with bothersome epigastric burning occurred in 77%, patients without HP - in 23% cases (table 2).

Table 2

The prevalence of symptoms in children with Functional Dyspepsia depending on Helicobacter pylori infection

Sign	n	Variants of FD			
		Epigastric pain syndrome n=323		Postprandial distress syndrome n=83	
		Bothersome epigastric pain n=221	Bothersome epigastric burning n=102	Bothersome postprandial fullness n=43	Bothersome early satiation n=40
HP (+)	280	145 (66%)	79* (77%)	31 (72%)	25 (63%)
HP (-)	126	76 (34%)	23 (23%)	12 (28%)	15 (37%)

Note: * statistical significance was evaluated by χ^2 Pearson criterion ($p < 0.05$).

HP infection was more often found in patients who had early bottle feeding and family gastritis or ulcer history. Patients with family history of gastritis or ulcer had HP infection in 72.9% cases (table 3).

Table 3

Probable causes of Functional Dyspepsia

Causes	n (%)
Allergy	231 (56.9%)
Giardiasis	94 (23.2%)
Viral gastroenteritis	126 (31.0%)
Parasites	132 (32.5%)
Early bottle feeding	247 (60.8%)
Family gastritis or ulcer history	296 (72.9%)
HP (+)	280 (69.0%)

Note: some children had a combination of causes, what's why the total percentage was more than 100.

Thus**,** the patients with longer duration of FD symptoms had HP infection more often. HP infection more often occurred in patients with early bottle feeding and family gastritis or ulcer history. One of the possible causes of FD was HP infection.

Discussion.

FD is a worldwide problem with a pooled prevalence of 13.5%. There are certain predisposing factors and pathophysiological mechanisms including stressful events, child maltreatment, visceral hypersensitivity, altered gastrointestinal motility and change in intestinal microbiota. It is possible that the environmental risk factors intricately interact with genes through epigenetic mechanisms to contribute to the pathophysiology. The diagnosis mainly depends on clinical evaluation. Commonly used pharmacological interventions do not play a major role in relieving symptoms. Centrally directed, nonpharmacological interventions such as hypnotherapy and cognitive behavioral therapy have shown both short and long term efficacy in relieving pain in children with FD. However, these interventions are time consuming and need specially trained staff and are, therefore, not currently available at primary level care. Clinicians and researchers should join hands in searching for more pragmatic and effective therapeutic methods to improve overall care of children with FD [11, 12]. Children with a FGID have a lower quality of life than healthy ones [13].

Prevalence of HP infection in children with the SD in the Transbaikal Territory was not significantly different from other regions of Russia [14, 15]. According to the 7th statement of the Kyoto consensus (2015), HP may be a cause of dyspepsia symptoms in patients. According to the 8th statement of the Consensus, Helicobacter pylori-associated dyspepsia should be considered as a special form of the disease [5].

We found that allergy might be one of the frequent causes of FD. Our results corresponded to those of the Australian study, where duodenal eosinophil infiltration in children with FD had been reported [16].

There are no adequately sized, double blind, placebo-controlled pediatric studies of FD treatment [10]. That’s why there exist difficulties treating children. Following an appropriate diet is one of the main factors in managing functional dyspepsia [17]. Foods aggravating symptoms (e.g., caffeine containing, spicy, fatty) and nonsteroidal anti-inflammatory agents were avoided. Psychological factors that could contribute to the severity of the problem were addressed. Acid blockade with proton pump inhibitors was offered for pain predominant symptoms. Nausea, bloating, and early satiety were more difficult to treat, and prokinetics such as domperidone were offered where available. In case of HP (+) triple eradication therapy (proton pump inhibitor + amoxicillin + metronidazole) was administered for 14 days. Clarithromycin-containing regimens should be restricted to those infected with clarithromycin-susceptible strains [18]. In the Transbaikal Territory clarithromycin susceptibility profiles hadn’t been properly investigated, therefore we didn’t use clarithromycin-based regimes. Longitudinal studies are needed to detect whether FD persists in adults.

Conclusion. According to the data obtained**,** functional causes of the syndrome of dyspepsia were more widespread than organic ones in the Transbaikal Territory. Probable causes of the functional dyspepsia were considered to be allergy, early bottle feeding and family gastritis/ulcer history. Antibodies to Helicobacter Pylori were found in 57% patients. The most widespread symptom in patients, infected with Helicobacter Pylori, was bothersome epigastric burning.

References:

1. Baaleman D.F., Velasco-Benítez C.A., Méndez-Guzmán L.M., Benninga M.A., Saps M. Functional gastrointestinal disorders in children: agreement between Rome III and Rome IV diagnoses. Eur J. Pediatr. 2021. 180(7). 2297-2303. doi: 10.1007/s00431-021-04013-2**.**
2. Drossman D.A. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology. 2016. 150. 1262-1279 doi: 10.1053/j.gastro.2016.02.032.

3. Schmulson M.J., Drossman D.A. What Is New in Rome IV. J. Neurogastroenterol Motil. 2017. 23(2). 151–163. doi: 10.5056/jnm16214.
4. Malfertheiner P., Megraud F., O'Morain C.A., Gisbert J.P., Kuipers E.J., Axon A.T., Bazzoli F., Gasbarrini A., Atherton J., Graham D.Y., Hunt R., Moayyedi P., Rokkas T., Rugge M., Selgrad M., Suerbaum S., Sugano K., El-Omar E.M. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. Gut. 2017. 66(1). 6-30. doi: 10.1136/gutjnl-2016-312288.
5. Sugano K., Tack J., Kuipers E.J., Graham D.Y., El-Omar E.M., Miura S., Haruma K., Asaka M., Uemura N., Malfertheiner P. Kyoto global consensus report on Helicobacter pylori gastritis. Gut. 2015. 64. 1353-1367. doi: 10.1136/gutjnl-2015-309252.
6. Du L.J., Chen B.R., Kim J.J., Kim S., Shen J.H., Dai N. Helicobacter pylori eradication therapy for functional dyspepsia: Systematic review and meta-analysis. World J. Gastroenterol. 2016. 22(12). 3486-95. doi: 10.3748/wjg.v22.i12.3486.
7. Sýkora J., Huml M., Siala K., Pomahačová R., Jehlička P., Liška J., Kuntscherová J., Schwarz J. Paediatric Rome III Criteria-Related Abdominal Pain Is Associated With Helicobacter pylori and Not With Calprotectin. J. Pediatr Gastroenterol Nutr. 2016. 63(4). 417-22. doi: 10.1097/MPG.0000000000001172.
8. Ford A.C., Tsipotis E., Yuan Y., Leontiadis G.I., Moayyedi P. Efficacy of *Helicobacter pylori* eradication therapy for functional dyspepsia: updated systematic review and meta-analysis. Gut. 2022. 12:gutjnl-2021-326583. doi: 10.1136/gutjnl-2021-326583
9. Stanghellini V., Chan F.K.L, Hasler W.L., Malagelada J.R., Suzuki H., Tack J., Talley N.J. Gastroduodenal Disorders. Gastroenterology. 2016. 150. 1380–1392. doi.org/10.1053/j.gastro. 2016.02.011
10. Hyams J.S., Di Lorenzo C., Saps M., Shulman R.J., Staiano A., van Tilburg M. Functional disorders: children and adolescents. Gastroenterology. 2016. 150. 1456–1468.e2. doi: 10.1053/j.gastro. 2016.02.015.
11. Rajindrajith S., Zeevenhooven J., Devanarayana N.M., Perera B.J.C., Benninga M.A. Functional abdominal pain disorders in children. Expert Rev Gastroenterol Hepatol. 2018. 12(4). 369-390. doi: 10.1080/17474124.2018.1438188.
12. Korterink J., Devanarayana N.M., Rajindrajith S., Vlieger A., Benninga M.A. Childhood functional abdominal pain: mechanisms and management. Nat Rev Gastroenterol Hepatol. 2015. 12(3). 59-71. doi: 10.1038/nrgastro.2015.21.
13. Miller J., Khlevner J., Rodriguez L. Upper Gastrointestinal Functional and Motility Disorders in Children. Pediatr Clin North Am. 2021. 68(6). 1237-1253. doi: 10.1016/j.pcl.2021.07.009
14. Polivanova T.V., Vshivkov V.A. Helicobacter Pylori and familial factors. Journal of Gastroenterology and Hepatology. 2021. 36(S2). 186-187.
15. Vshivkov V.A., Polivanova T.V. The prevalence of CaGA Helicobacter Pylori in children of the Mongoloid population of Siberia. Helicobacter. Supplement. 2020. 25(S1). EP5.05. DOI: 10.1111/hel.12745.
16. Wauters L., Nightingale S., Talley N.J., Sulaiman B., Walker M.M. Functional dyspepsia is associated with duodenal eosinophilia in an Australian paediatric cohort. Aliment Pharmacol Ther. 2017. 45(10). 1358-1364. doi: 10.1111/apt.14045.
17. Chumpitazi B.P. Update on Dietary Management of Childhood Functional Abdominal Pain Disorders. Gastroenterol Clin North Am. 2018. 47(4). 715-726. doi: 10.1016/j.gtc.2018.07.001.
18. Jones N.L., Koletzko S., Goodman K., Bontems P., Cadranel S., Casswall T., Czinn S., Gold B.D., Guarner J., Elitsur Y., Homan M., Kalach N., Kori M., Madrazo A., Megraud F., Papadopoulou A., Rowland M. Joint ESPGHAN/NASPGHAN Guidelines for the Management of Helicobacter pylori in Children and Adolescents (Update 2016). J. Pediatr Gastroenterol Nutr. 2017. 64(6). 991-1003. DOI: 10.1097/MPG.0000000000001594