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**PATHOMORPHOSIS OF DISEASES OF THE DIGESTIVE SYSTEM ALLERGIC
AND NON-ALLERGIC GENESIS IN CHILDREN OF UKRAINE IN THE DYNAMICS
OF 25 YEARS OF OBSERVATION**

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The purpose of the study was a retrospective 25-year analysis of the incidence and prevalence of the digestive system diseases of allergic and non-allergic genesis in children of Ukraine to determine the possibility of environmental factors' influence on their development. We have used methods of system approach, epidemiological, correlation and cluster analysis of medical statistics data of the Ministry of Health of Ukraine. A retrospective study from 1993 to 2017 have revealed that among children of Ukraine (aged 0–17 years included) there was a tendency of increasing the prevalence of diseases of the digestive system by 13.6 %, as well as their incidence – by 12.1 %, especially it is related to the children, affected by the Chernobyl accident. Over 25 years there have been significant changes in their structure, which requires careful attention to the above contingent of children.

Key words: children, prevalence, disability, diseases of the digestive system, ecology.

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**ПАТОМОРФОЗ ХВОРОБ ОРГАНІВ ТРАВЛЕННЯ АЛЕРГІЧНОГО ТА НЕАЛЕРГІЧНОГО
ГЕНЕЗУ У ДІТЕЙ УКРАЇНИ В ДИНАМІЦІ 25-РІЧНОГО СПОСТЕРЕЖЕННЯ**

Метою дослідження став 25-річний аналіз захворюваності та поширеності хвороб органів травлення алергічного та неалергічного генезу у дітей України для визначення можливості впливу на їх розвиток екологічних факторів. Було використано методи системного підходу, епідеміологічного, кореляційного, кластерного аналізу даних медичної статистики Міністерства охорони здоров'я України. Проведене дослідження з 1993 року по 2017 рік дозволило виявити, що у дітей України 0–17 років включно спостерігається збільшення на 13,6 % показника поширеності хвороб органів травлення, а також – на 12,1 % захворюваності із суттєвою перевагою виявлення даної патології у дітей, які постраждали від наслідків аварії на Чорнобильській АЕС. З 1994 до 1997 р.р. показник інвалідності внаслідок цієї патології збільшився більш ніж удвічі. Хвороби органів травлення є однією з найпоширеніших захворювань у дітей України. За 25 років відбулися суттєві зміни у їх структурі, що потребує ретельної уваги до вищезгаданого контингенту дітей.

Ключові слова: діти, поширеність, інвалідність, захворюваність, хвороби органів травлення, екологія.

The study is a fragment of the research project "Peculiarities of clinical progression and treatment of bronchial asthma in children with supraworld body weight and obesity", state registration No. 0120U100804.

Digestive diseases in Ukraine (hereinafter – DD) are the third of the five leading causes of death [8]. These diseases lead to significant changes in quality of life and are often disabling [6, 12]. Given the onset of most digestive tract diseases in childhood, it is necessary from the moment of birth to deal with their prevention and detection [1].

Thus, now only chronic inflammatory bowel diseases, especially such as Crohn's disease, are diagnosed in children more frequently than ever before [6, 7, 8]. In the practice of pediatric gastroenterology, allergy problems are becoming more common, and the picture of the disease has changed significantly.

The prevalence of food allergy due to the lack of uniform standardized approaches to its diagnosis and the variety of clinical manifestations in children is unknown and makes approximately 2 % to 10 %, and one in three children has a severe recurrent course [14]. The range of eosinophilic gastrointestinal disorders has expanded, which now includes: eosinophilic esophagitis, eosinophilic gastritis/gastroenteritis, eosinophilic colitis [6].

It should be noted that the epidemic of COVID-19 not only leads to the development of inflammatory changes in the intestine, but also significantly aggravates the course of diseases of the digestive system in children, especially liver damage [9].

Numerous longitudinal studies of the world's leading scientists show that inflammatory bowel disease in children has now become common, from an early age [10, 13, 15]. Chronic hepatitis and diseases of the pancreas that are so difficult to treat remain an urgent problem of pediatric gastroenterology [9]. The

American Academy of Pediatrics, concerned about the rise in childhood obesity, strongly recommends that tests for non-alcoholic fatty liver disease be included in their examination protocols to prevent cirrhosis [12]. A significant number of gastrointestinal disorders of various kinds (inflammatory, infectious, allergic, genetic and other etiologies) can cause significant changes in the oral cavity [11].

The impact on the development of DD caused by ecology, lifestyle and nutrition of families, the quality of food and water is indisputable. Significant changes have been noted in the incidence of DD in children of Ukraine after the Chernobyl accident (hereinafter – Chernobyl) [1, 15].

The purpose of the study was a retrospective 25-year analysis of changes in the incidence and prevalence, the structure of the digestive system's diseases of allergic and non-allergic origin in children of Ukraine.

Materials and methods. We assessed the dynamics of the incidence and prevalence of the digestive system diseases in children from different regions of Ukraine, including those contaminated by the Chernobyl accident in 1986. Methods of statistical assessment and epidemiological analysis of state medical statistics from 1993 to 2020 were used [8]. A separate observation group consisted of children with gastroenterological pathology and those affected by the Chernobyl accident.

Statistical assessment methods were used, in particular U-criterion of Mann-Whitney sign ranking to compare the incidence of DD in children from the same regions of Ukraine in 1993 and 2017. Cluster analysis of the incidence of DD in children of the Ukrainian regions was performed using the K-means method by comparing the incidence of DD in children in the regions and in the city of Kiev to the level of this index in Ukraine and taking into account the presence of radiological control territories (hereinafter RCT) which appeared as a consequence of the Chernobyl accident.

To determine the linear dependence and correlation, as well as the degree of relationship between the population-weighted effective doses in millisieverts (hereinafter referred to as mSv) of the total body exposure of different regions' residents of the country in the time period from 1997 to 2011 and the incidence of DD in children from different regions Spearman's correlation ranking coefficient was used [3]. Statistical processing of the study results was carried out using the software product STATISTICA 6 and Excel-2010 [2].

Results of the study and their discussion. Among all registered diseases in Ukrainian children, diseases of the digestive system take 2nd place after respiratory diseases, and in the structure of morbidity, they take 4th place out of 17, which indicates their special role in influencing the health of the child population. In children permanently residing in areas with RCT and children affected by the Chernobyl accident, DD in the structure of morbidity is in a higher 3rd place. In general, in 2017, according to state medical statistics, the incidence of children aged 0–17 years inclusive of DD was 345.619 newly diagnosed cases, which corresponds to 45.38 per 1.000 of the corresponding child population (hereinafter, per 1.000 children).

Of these, in children in the first year of life in 2017, 20124 cases of DD were detected for the first time, or 56.63 cases per 1000 children. And in 2021, in children in the first year of life, 13.962 cases of DD or 56.02 per 1000 children (4.46 % of all newly registered diseases at this age) were detected for the first time, which indicates an increase in the number of DD already at an early age due to insufficient duration of breastfeeding and the significant number of nutritional supplements in baby food. In 2021 alone, 162 children under the age of one year with diseases of the oral cavity, glands and jaws were hospitalized in pediatric healthcare institutions (a total of 7969 children aged 0–17 years). More frequently gastroenterological pathology in all age groups occurred in girls (53 % versus 47 %) than in boys.

The prevalence of DD in 2017 among the children of Ukraine was 850997 or 111.74 cases per 1000 children. The proportion of the DD prevalence in the structure of registered childhood diseases is 6.39 % (in 1993–7.64 %), and the incidence rate is 3.9 % (4.11 %). In children affected by the Chernobyl accident, in 2017, 25.663 cases of DD were detected for the first time, or 66.69 cases per 1.000 of the corresponding child population, which is by 1.47 times higher than the mean incidence rate of DD in children in Ukraine. The prevalence of DD in children affected by the Chernobyl accident was 79.212 or 204.25 cases per 1.000 children, which is by 1.83 times higher than the nationwide index of the DD prevalence. Peptic ulcer of the stomach and duodenum in such children was first registered in 83 people or 0.21 per 1000 children, which is relatively more than in 1994, when the incidence rate was 0.12 per 1000 children affected by the Chernobyl accident. This may indirectly indicate a possible negative impact of the Chernobyl accident consequences in combination with other factors on the state of the gastric and intestinal mucosa, since in general, the incidence of gastric and duodenal ulcers in Ukrainian children has almost halved during this time, although in hospitals in 2021 989 children were hospitalized, 40 of them – with a perforated ulcer.

Compared to the index of 1994, the incidence of DD in these children increased by 11.13 % during the monitoring period. The proportion of the DD prevalence in the structure of registered diseases of childhood in this contingent of children was 8.9 %, and the incidence was 5.7 %, which is higher than the national indices and also indicates the possible influence of the radiation factor, along with others, on the development of DD.

In 1993, 530656 cases of DD were detected for the first time, which amounted to 40.5 per 1000 children, which was by 12.05 % less compared to the data of 2017 ($p > 0.05$). The prevalence of DD in children then was 1209033 or 113.37 cases per 1000 children aged 0 to 17 years, which is by 13.56 % less than in 2017 ($p > 0.05$).

As it can be seen in fig. 1, the largest number of DD cases in 2017 was detected in children aged 7 to 14 years inclusive – 52.3 % (in 1994–57.5 %) of the total number of cases, which indicates that the school period is a risk zone for the emergence of gastroenterological pathology in children due to the excessively “broad” diet of their nutrition in educational institutions in the absence of first courses and the use of fast food products, a more intense effect on the child's digestive tract of food additives, dyes and xenobiotics in general. According to the international study HBSC (Health Behavior in School-aged Children – “Healthy Behavior in School-aged Children”), performed in our country under the auspices of UNICEF, now school-age children consume dairy and sour-milk products only 1–4 times a week, instead of WHO recommended 2.5 times a day.

Interestingly, over 25 years of observation, the dominance of this age period in terms of the gastroenterological pathology occurrence, unfortunately, has not changed much. A possible role in the development of DD in adolescents is played by overweight and obesity, which during the monitoring period began to be detected by 1.8 times more frequently and mainly in older children.

Over the period of 25-year monitoring, a moderate decrease in the proportion of the DD incidence detection in children aged 7–14 years inclusive (from 57.5 % to 52.3 % of the total number of detected cases) against the background of an increase by 1.8 times is observed in dynamics proportion of newly

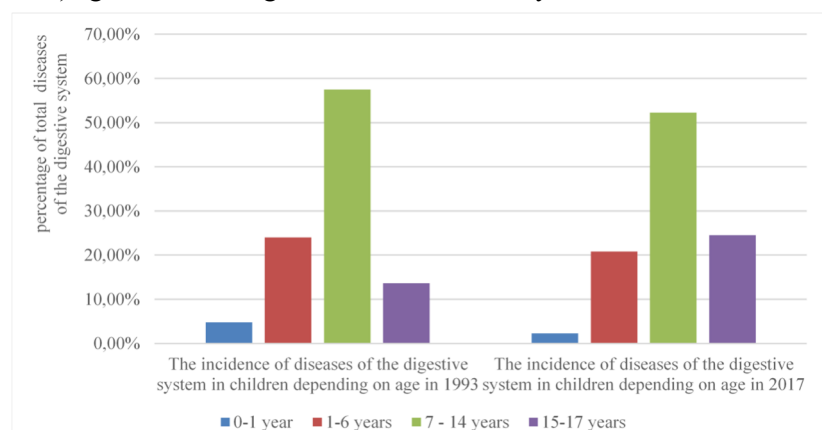


Fig. 1. Comparative characteristics of changes in the incidence of the digestive system diseases among children depending on age (in 1993 and 2017).

diagnosed DD cases in adolescents out of the total number of detected cases. In children aged 0–1 years and 1–6 years inclusive, during the observation period, there was a decrease in the number of diagnosed DD by 2.5 % and 3.2 %, respectively (Fig. 1).

In the age aspect, the smallest number of newly diagnosed cases of DD was observed in infancy – 2.3 % (in 1993–4.8 %) of the total number of detected DD cases,

however, the incidence and prevalence of DD in this age cohort were approaching the maximum rates of DD prevalence observed in adolescents, which may have reflected the influence of artificial feeding, which dominates in the second half of life, which stimulated premature activity of enzymes and, accordingly, an excessive load on the functionally immature stomach and pancreas.

In general, functional disorders of the gastrointestinal tract (colic, constipation, regurgitation, diarrhea), so widespread among children of the first 6 years of life, negatively affect their health in general, as well as their quality of life. In the future, they will become risk factors and the basis for the formation of functional, allergic and organic diseases, as indirectly evidenced by an almost two-fold increase over 25 years of monitoring the incidence of DD in children aged 15–17 years inclusive.

Obviously, this is due to an increase in the index of accumulation of chronic pathology from 3.0 in children aged 7–14 years inclusive to 3.35 in children aged 15–17 years inclusive.

An alarming fact is the growth we have established over the past 25 years in the structure of incidence and prevalence of DD in children in the proportion of pancreatic diseases (+122 %), cholelithiasis (+120 %) and functional diseases of the stomach (+181.9 %), irritable intestines (hereinafter – IBS) (+28.9 %), dyspepsia (+63.8 %), Crohn's disease (+53.9 %), gastroesophageal reflux disease (hereinafter – GERD) (+46.15 %), celiac disease (+42.9 %) (fig. 2).

While the share of incidence of gastritis and duodenitis (–4.34 %), gastric and duodenal ulcer (–45 %), ulcerative colitis (–50 %), cholecystitis and cholangitis (–54 %), chronic hepatitis (–88.5 %). An alarming fact is the identification of 41 cases of cirrhosis in children due to fatty and congenital liver lesions.

Obviously, this phenomenon is based on many factors: hereditary, environmental, socio-economic and, especially, the growing irrational nature of nutrition and the decline in the preventive focus of health systems.

It should be noted that 25 years ago we did not have the ability to diagnose many of these digestive tract diseases and there were no protocols for their treatment, especially celiac disease, GERD and IBS.

Of course, the above dynamics regarding the decrease in the incidence of these pathological conditions in children also reflects the success of Ukrainian pediatrics in the application of modern medical and rehabilitation technologies in the treatment of diseases of the liver, stomach and intestines. There is a modern trend towards a decrease in the share of organic gastroenterological pathology in children and an increase in functional and allergic diseases of the digestive tract (Fig. 2).

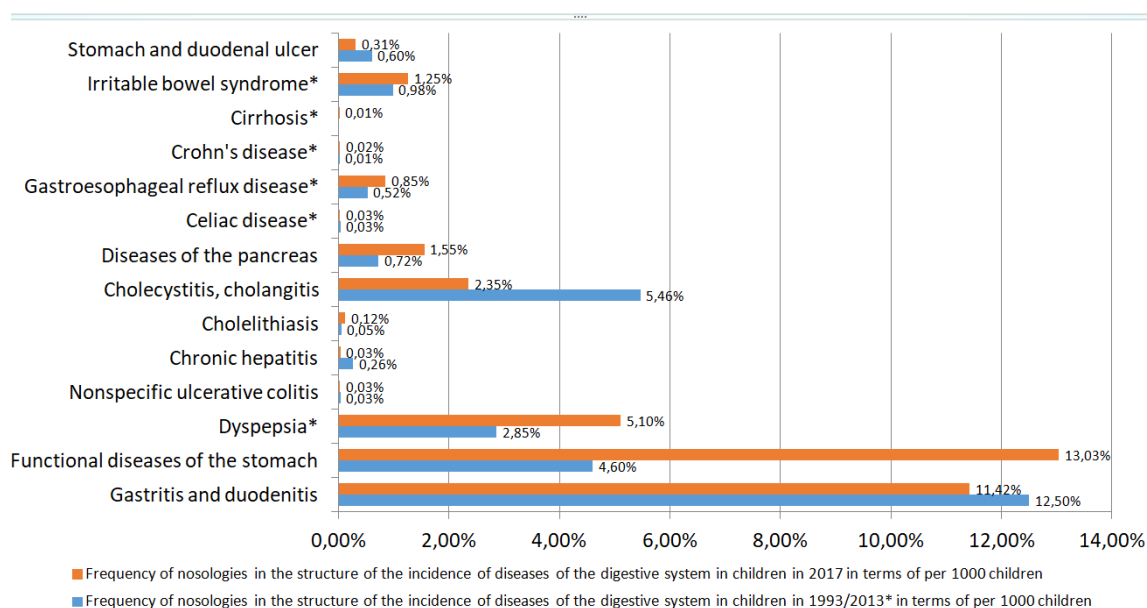


Fig. 2. Comparison of the frequency of nosologies in the structure of the incidence of diseases of the digestive system among children in 1993/2013 and in 2017 in terms of per 1000 children

* – the comparison was made with the indices of 2013 due to the absence of these nosologies in the state statistics in 1993

Thus, now in the structure of children's gastroenterological diseases, the first place certainly belongs to diseases of the upper parts of the digestive system, which account for 49.1 %. These primarily include such common acid-dependent diseases as: gastroesophageal reflux disease (hereinafter referred to as GERD) and functional dyspepsia. In childhood, GERD is often etiologically associated with cow's milk protein allergy or secondary to it. In 2021 alone, 988 children with GERD were hospitalized in pediatric hospitals, 12 of them under the age of one year.

Therefore, allergic lesions of the mucous membrane of the digestive organs are observed in 48–67 % of children with food allergies and are clinically manifested in the form of functional syndromes (regurgitation, vomiting, flatulence, intestinal colic, diarrhea, constipation), but the lack of timely diagnosis leads to the establishment of alternative diagnoses (esophagitis, functional dyspepsia, enterocolitis) and the appointment of inadequate therapy.

Unfortunately, today in Ukraine there are no unified recommendations for the management of children with this pathology, which in practice leads from their complete disregard to overdiagnosis of non-allergic gastroenterological pathology, long-term pharmacotherapy and often unreasonable diet.

It should be noted that during 25 years of observation in Chernivtsi, Luhansk, Kharkiv, Zhytomyr and Zaporizhzhya, Kherson regions and Kyiv, there was the largest increase in the incidence of DD in children, by 118.4–45.4 %, respectively, compared to the incidence of DD in children. in 1993. While in Cherkasy, Chernihiv, Volyn and Poltava regions, the incidence of DD in children was decreasing, which may be due to an improvement in the quality of life and nutrition of children, as well as a decrease in time of radionuclides and pollutants' influence due to a decrease in the ecotoxic load on the environment.

At the same time, relatively low rates of morbidity in children with DD were observed in: Lugansk, Zaporizhzhya, Odesa and Kherson regions.

As it can be seen from fig. 3, the morbidity rate of DD in the children's population from the regions with RCA slightly decreased over 25 years by 2.4 %, on the contrary, in children affected by the Chernobyl accident, it increased by 11.1 %. The incidence rate of DD in children from regions without TRK also increased by 11.7 %.

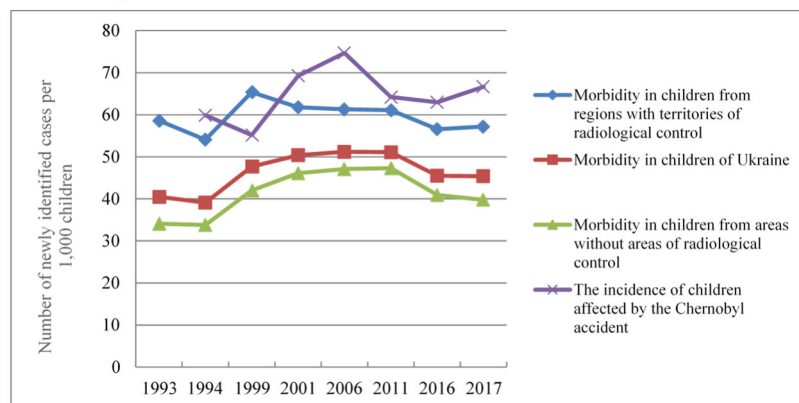


Fig. 3. Comparative dynamics of the morbidity incidence rates among children of Ukraine per 1.000 of the corresponding child population with diseases of the digestive system, children affected by the Chernobyl accident, children from radiological control areas, children from areas without radiological control (1993–2017)

(by 11.7 %) than that of children from territories with RCA and significantly exceeded the nationwide incidence rate by 46.9 % ($p < 0.01$). But the incidence rate of DD in children from regions without RCA was more than by 1.6 times higher or by 67.6 %.

The morbidity rates of children with CPD from regions without RCA have always been lower than the national indices ($p > 0.05$). It is obvious that the children affected by the Chernobyl accident did not significantly differ in their indices from the morbidity rates of children from the territories with radiological control areas ($p > 0.05$), which indicates their similarity in terms of the influence degree on the body of the prevailing environmental conditions. Also, the incidence rates of DD in this contingent over the course of all 25 years significantly exceeded the national level of the incidence rate in children with DD and the corresponding index in children from conditionally “clean” regions ($p < 0.01$).

Thus, over 25 years, the expected convergence of the studied indices did not occur, since in 1993 the incidence rate of DD in children affected by the Chernobyl accident was by 1.5 times higher than the national index, and the incidence rate of DD in children from regions without RCA was almost by 1.5 times higher. By 1.8 times, which is noted even now. Indirectly, this may indicate the continuing influence of the consequences of the largest environmental catastrophe on the occurrence and course of the DD in children affected by it, and those children who permanently lived in areas with radiological control territories.

As mentioned above, among the children of Ukraine there is a high prevalence of DD, which determines the number of children who have developed a disability due to this pathology.

Thus, in 2020, for the first time in Ukraine, 2.187 children with disabilities due to DD were registered, which amounted to 2.9 cases per 10,000 children. For the first time, disability was established for 218 children with DD, which corresponds to 0.3 cases per 1000 children. In the structure of pathologies that led to disability, celiac disease stood out, which was the cause of disability in 20 % of children with gastroenterological pathology (418 cases or 0.6 per 10 thousand population). In 1993, celiac disease accounted for only 10.1 % of the causes of disability. It should be noted that the highest rates of children's disability due to DD were observed precisely in the regions that were characterized by the presence of territories of radiological control: Sumy – 5.7 per 10 thousand children, Ivano–Frankivsk – 4.0, Volyn – 3.9, Cherkasy – 3.8, Rivne – 3.5, Kyiv – 3.2 per 1000 children.

In 1993, the disability rate due to DD was 0.83 per 1.000 children, which is by 3.5 times less than the disability rate in 2017. The proportion of disability due to DD, among other causes, increased from 0.57 % to 1.3 % over 25 years of observation, which is obviously a consequence of the increase in the prevalence of DD in Ukrainian children.

According to the results of the correlation analysis, we found that the Spearman correlation coefficient (ρ) was 0.066, and the relationship between the prevalence of of the digestive system diseases in children aged 0–14 inclusive in 2011 and the population-weighted effective dose (in mSv) of total exposure of the whole body in residents of different regions of Ukraine for the period 1997–2011 was insignificant and statistically unreliable ($p > 0.05$).

In 2017, the incidence rate of DD in children from regions with RCA exceeded the national index by 26.0 %, and the incidence rate of DD in children from other regions – by 43.7 %. During the entire observation period, the morbidity rate of DD in children from areas with RCA significantly exceeded the national incidence rate of DD in children from territories without areas of radiological control.

In its turn, the incidence rate of DD in children affected by the Chernobyl accident was higher

The highest levels of morbidity in children with DD were observed in Rivne, Ivano–Frankivsk, Zhytomyr regions, which are characterized by the presence of areas of radiological control after the Chernobyl disaster. Among other regions, only the Chernivtsi region was a clear leader in the incidence of DD in children [2, 4]

The low morbidity rates among children with DD from Lugansk, Zaporizhzhya, Odesa and Kherson regions can, among other things, be explained by their low detection rate due to a decrease in alertness and a shortage of specialized specialists in the field. It is noteworthy that there are no regions with RCA among the regions with a low incidence of DD in children.

At the same time, isolated and eosinophilic esophagitis are not included into the state medical statistics and account for a little less than 1.5 % in the structure of gastropathology. Although with gastritis, a combined lesion of the esophagus is determined in 15 % of children, with gastroduodenitis – in 38.1 %, and with duodenal ulcer, esophagitis occurs in almost all children. It is worth agreeing with the opinion of Yu.V. Karpushenko (2019) that in the pathogenesis of the gastroduodenal zone and allergic diseases are similar mechanisms of dysfunction in the nervous, endocrine and immune systems [5, 7].

Conclusion

Diseases of the digestive system were and are one of the most common pathological conditions in children in Ukraine, especially in people affected by the consequences of the Chernobyl accident. Over 25 years of monitoring observations in the period from 1993 to 2017 in Ukraine, there was an increase by 13.6 % in the prevalence of the digestive system diseases in children and by 12.5 % of the incidence.

During the observation period, there have been significant changes in their structure, which requires careful attention to the above contingent of children and the development of a complex of therapeutic and rehabilitation measures. In particular, there is a trend towards greater significance of functional gastrointestinal diseases and the role of the allergic factor in the genesis of the digestive system pathology, which is important to take into account in the practice of doctors of various specialties.

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