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ANALYSIS OF FACTORS AND STRUCTURE OF CONGENITAL MALFORMAYIONS OF THE GASTROINTESTINAL TRACT IN CHILDREN

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Summary

Congenital malformations of the gastrointestinal tract (CMGIT) rank fourth in the structure of congenital malformations in newborns.

The aim *is to analyze the factors and structure of congenital malformations of the gastrointestinal tract in children.*

Methods. *A retrospective cohort epidemiological study of CMGIT in Chernivtsi region was conducted with a detailed analysis of probable factors for the development of defects in 96 children with CMGIT. The comparison group consisted of 96 children without CMGIT. The main unit of information storage was the «Questionnaire of the examined child», on which all data were recorded and combined with a single code that was automatically generated for each child and processed by generally accepted methods of variational statistics in medicine. Ethics committee approval was received for this study. The research design and all the methods used in this study were reviewed and approved by the bioethics commission of the Bukovinian State Medical University (protocol No. 4, dated 12//2024).*

Results. *Among all CM, the share of CMGIT was 9.9%. The first ranking place in the structure of CMGI belongs to anal atresia (13.5%), the second – to esophageal atresia (12.5%), the third – pylorospasm (11.5%). The least common were pancreatic defects (3.1%), Hirschsprung's disease and eventration of intestinal loops (4.1%). Every fourth child had a combination of CMGIT with malformations of other organs. If a child had CMGIT, the pregnancy proceeded with toxicosis of the first and second trimesters, (35.4% and 29.2%, respectively). Anemia of the first half of pregnancy, the threat of abortion, and fetoplacental insufficiency occurred more often in mothers who gave birth to children with CMGIT. 23.8% of women during pregnancy with a child with CMGIT had a respiratory tract infection or exacerbation of chronic pathology of other organs and systems. Examination for the presence of infection with intracellular pathogens during pregnancy revealed specific IgG in 15.6% of cases of birth of children with CMGIT. Signs of morphofunctional immaturity and asphyxia during childbirth were more often observed in children with CMGIT (18.8% and 15.6%, respectively). Mothers of children with CMGIT more often took medications during pregnancy.*

Conclusion. *Congenital malformations of the gastrointestinal tract are highly prevalent, often combined with other malformations. In the structure of congenital malformations of the gastrointestinal tract, atresia of the anus and esophagus prevail. The identified probable factors of congenital malformations of the gastrointestinal tract include toxicosis of pregnancy, fetoplacental insufficiency, anemia and infections in the mother, use of medications during pregnancy, bad habits, intrauterine infections, morphofunctional immaturity of the fetus, premature birth.*

Key words: *Children. Congenital Malformations of the Gastrointestinal Tract, Structure and Probable Factors of the Defects.*

Introduction

Congenital malformations (CM) are considered a significant cause of perinatal pathology, infant mortality and disability. According to data from domestic researchers, WHO experts and EUROCAT (European Registration of Congenital Anomalies), the frequency of fetal CM in different countries of the world ranges from 22.7 to 50.0‰ [1-4]. According to data [5, 6], about 10 thousand children with congenital pathology are born in Ukraine annually. The medical significance of the problem is deepened by its social component, since out of 20,000 children who become disabled every year, about 5,000 have congenital malformations [7, 8].

CM are persistent disorders of structure, function or metabolism that arise in utero as a result of developmental disorders of the embryo, fetus or sometimes after birth as a result of impaired further organ formation and have a multifactorial etiology. The terms «congenital malformations», «dysplastic diseases», «dysontogenies», «teratoses» proposed by individual researchers have not been widely used.

Congenital defects are caused by a combination of negative external conditions (the influence of exogenous teratogenic factors) and endogenous factors (hereditary pathology, impaired maturation of germ cells, parental age).

Hereditary congenital malformations arise as a result of mutations in chromosomes or genes. Their share is more than 30% of all developmental defects [9, 10]. Mutations occur in the germ cells of the child's parents or their more distant ancestors. In the first case, we are talking about acquired mutations, in the second – about inherited permanent changes.

CM caused by teratogenic factors are much less common than those caused by heredity. According to generalized literature data, they can be the cause of almost 10% of CM [11]. The mechanism of malformations is not well understood. It is believed that the formation of CM occurs as a result of disruption of the processes of reproduction, migration and differentiation of cells, the death of individual cell masses, and disruption of tissue adhesion in the body of the embryo / fetus.

Congenital malformations of the gastrointestinal tract (CMGIT), according to various authors, occupy the fourth place in the structure of congenital malformations in newborns, their frequency varies in the regions of Ukraine within the range of 8.4-9.7 per 10,000 newborns [12-15]. This pathology occupies a significant place in the structure of neonatal mortality: 5.81% of children with gastrointestinal tract defects die within 24 hours, 19.7% within a week, 9.3% within the first month of life, which indicates the social significance and severity of this pathology [16-19]. The overall mortality among children with CMGIT, according to various sources, ranges from 16.3% to 60% [20-22].

The aim is to analyze the factors and structure of congenital malformations of the gastrointestinal tract in children.

Methods. A retrospective cohort epidemiological study of CMGIT in Chernivtsi region was conducted with a detailed analysis of probable factors for the development of defects in 96 children with CMGIT. The comparison group consisted of 96 children without CMGIT. The materials for the study were «Notification of the birth of a child and examination for congenital malformations (CM), chromosomal and hereditary pathology» (form No. 149-1/0), newborn histories, medical records, autopsy protocols and other archival materials, questionnaires filled out by parents of children with CMGIT.

In order to clarify the diagnosis of congenital developmental anomalies, the monitoring system used clinical examination, genealogical analysis, anthropometry, instrumental (ultrasound, radiography, neurosonography, electroencephalography) and cytogenetic research methods.

The main unit of information storage was the «Questionnaire of the examined child», which recorded passport data, dates of primary and repeated examinations.

Ethics committee approval was received for this study. The research design and all the methods used in this study were reviewed and approved by the bioethics commission of the Bukovinian State Medical University (protocol No. 4, dated 12//2024).

All data were combined with a single code that was automatically generated for each child and processed using generally accepted methods of variation statistics and Pearson correlation analysis in medicine using the computer program packages «Statistika» for Windows 8.0.0 (SPSS Inc., 1989-1997) and «Statistika» for Windows 5.1 (StatSoft Inc., 1984-1996).

Results. There is no generally accepted classification of CMGIT, so we used a scheme for distributing defects according to the localization of lesions (CM of the intestinal tube, CM associated with impaired intestinal rotation, CM of intestinal tube derivatives, CM of the gastrointestinal vascular system, CM of the gastrointestinal tract innervation, CM of the anterior abdominal wall).

During the 2018-2024 period, 969 cases of newborns with various CM were identified. Among them, gastrointestinal tract defects accounted for 96 cases (9.9%).

The structure of CMGIT is presented in Table 1. The first ranking place in the structure of CMGIT belongs to anal atresia (13.5%), the second – to esophageal atresia (12.5%), the third – to pylorospasm (11.5%). The least common were pancreatic defects (3.1%), Hirschsprung's disease and intestinal loop eventration (4.1%).

Gender differentiation of CMGIT was observed (Fig. 1). In boys, developmental defects occurred more often (65.6%).

It is worth noting that every fourth child had a combination of CMGIT with malformations of other organs (Fig. 2).

Table 1

Structure of congenital malformations of the gastrointestinal tract in children

Congenital malformation	n	%
Intestinal atresia	7	7,3
Hirschsprung's disease	4	4,1
Liver and gallbladder malformations	6	6,3
Anal atresia	13	13,5
Congenital intestinal obstruction	9	9,4
Esophageal atresia	12	12,5
Duodenal atresia	5	5,2
Peritoneal cysts	7	7,3
Eventration of intestinal loops	4	4,1
Pancreatic malformations	3	3,1
Pylorospasm	11	11,5
Megacolon	7	7,3
Pyloric stenosis	8	8,3
Gastroschisis	4	4,1

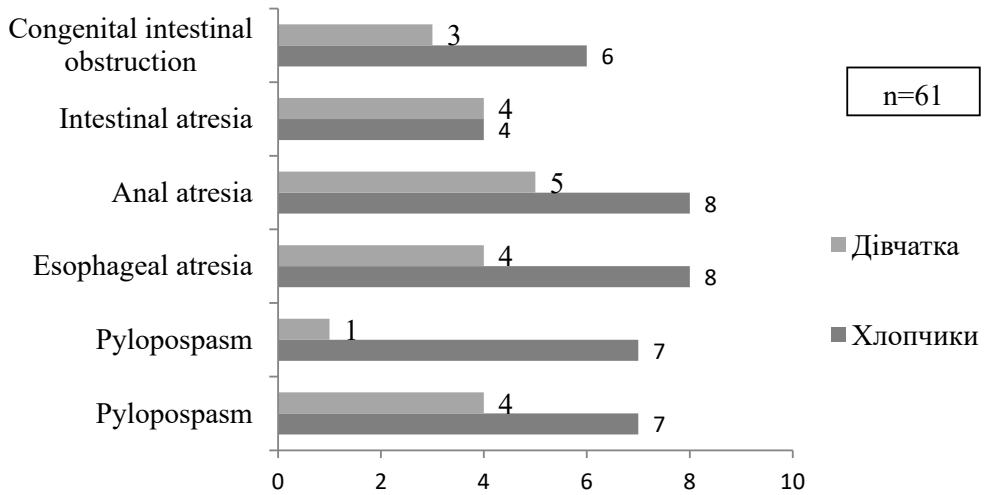

Fig. 1 Frequency and structure of congenital malformations of the gastrointestinal tract in children

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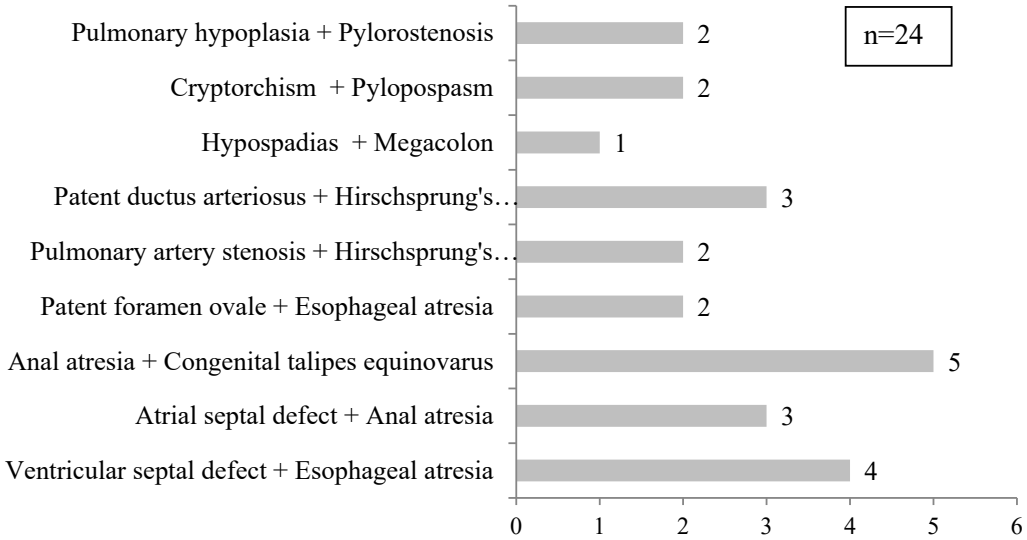

Fig. 2 Variants of combining congenital malformations of various organs

Probable factors for the development of gastrointestinal malformations are given in Table 2. In every third woman, pregnancy with a child with CMGIT proceeded with toxicosis of the first and second trimesters (35.4% and 29.2%, respectively), which was more common than in the group of children without CMGIT (7.3% and 8.3%, respectively).

Anemia of the first half of pregnancy, threatened abortion, and fetoplacental insufficiency occurred more often in mothers who gave birth to children with CMGIT. Every fourth (23.8%) woman during pregnancy with a child with CMGIT had a respiratory tract infection or exacerbation of chronic pathology of other organs and systems. Chronic intrauterine fetal hypoxia was more often documented in patients with CMGIT (14.6%).

Examination for infection with intracellular pathogens during pregnancy revealed specific IgG in 15.6% (in 5 mothers to CMV, in 12 mothers to HSV-1,2, in 5 to EBV, in 4 mothers to Tox.g).

Signs of morphofunctional immaturity were more frequently observed in children with CMGIT compared to the subgroup without defects (18.8% and 5.7%, respectively). Asphyxia during childbirth was observed in 15.6% of children with CMGIT. Also, mothers of children with CMGIT were more likely to take medications during pregnancy and were more likely to be exposed to occupational hazards.

Discussion. In most leading countries of the world, congenital malformations are among the most common diseases in newborns and children of the first year of life [17, 23]. In the structure of perinatal and infant mortality in Europe and America, congenital malformations take first place [24]. In Ukraine, congenital malformations also occupy second-third place in the structure of causes of death. In the structure of congenital malformations of the gastrointestinal tract, they occupy 4th place. In our study, the frequency of gastrointestinal tract malformations was 2.14 per 10,000, while in Ukraine their frequency ranges from 8.4-9.7 per 10,000 newborns. In the structure of gastrointestinal tract malformations, the conducted study revealed the prevalence of anal atresia, esophageal atresia, and pylorospasm, which coincides with the results of other studies [25].

The causes of CMGIT are diverse, difficult to detect and can be caused by genetic, infectious, environmental factors or have a multifactorial nature. Occupational hazards in parents, according to many authors, are the most significant risk factor for the occurrence of CM, which was confirmed by our studies. It has been proven that there is a direct relationship between an infectious disease in the mother and the frequency of formation of such congenital defects as gastroschisis, omphalocele, small intestinal atresia and rectal atresia. It should be noted the special role of pathogens with an intracellular development cycle (viruses) in connection with their tropism to embryonic tissues, as well as a significant prevalence in the general population in pregnant women. At the same time, a mandatory condition for the formation of CM are periods of intensive intestinal tube organogenesis and the action of an intracellular pathogen combined in time [26, 27].

The uncontrolled use of antibiotics, hormonal drugs, and food additives is of great importance in increasing the prevalence of CM. The teratogenic effect of some drugs has been proven: antimetabolites (aminopterin, 6-mercaptopurine), alkylating compounds (dopamine, cyclophosphamide, thiophosphamide), and antitumor antibiotics (actinomycin, sarcolysin, etc.). Our study confirmed the effect of taking antibacterial drugs on the development of CM, namely, more often atresia of the anus and esophagus.

Prospects for further research. The identification of specific prenatal diagnostic markers of congenital malformations of the gastrointestinal tract is promising in terms of early diagnosis and timely therapeutic correction of this pathology.

Conclusion. Congenital malformations of the gastrointestinal tract are highly prevalent, often combined with other malformations. In the structure of congenital malformations of the gastrointestinal tract, atresia of the anus and esophagus prevail. The identified probable factors of congenital malformations of the gastrointestinal tract include toxicosis of pregnancy, fetoplacental insufficiency, anemia and infections in the mother, bad habits, intrauterine infections, use of medications during pregnancy, morphofunctional immaturity of the fetus, premature birth.

Table 2

Probable factors for the development of gastrointestinal tract defects in children

Indicator	Children with CMGIT (n=96)		Children of the comparison group (n=96)		χ2	P
	Абс.	%	Абс.	%		
Pregnancy:						
First	35	36,4	45	46,8		
Second	30	31,3	42	42,8		
Third	24	25,0	8	8,3		
Fourth and more	7	7,3	3	3,1	1,52	>0,05
The course of pregnancy:						
Toxicosis of the I half	34	35,4	7	7,3		
Toxicosis of the II half	28	29,2	8	8,3		
Anemia of the I half	18	18,8	5	5,2		
Anemia of the II half	15	15,6	2	2,0		
Nephropathy	12	12,5	4	4,2	12,56	<0,01
Threatened abortion	27	28,1	11	11,4	8,67	<0,01
Fetoplacental insufficiency	11	11,5	2	2,1	7,56	<0,05
SARS during pregnancy	23	23,8	8	8,3	7,44	<0,05
Chronic intrauterine infection	14	14,6	5	7,3	8,12	<0,05
Specific IgG:						
to 1 pathogen	15	15,6	5	5,2		
to 2 pathogens	11	11,5	-	-	6,99	<0,05
Childbirth:						
On-term	67	68,7	88	91,6		
Premature	29	30,2	8	8,3	12,43	<0,01
Prematurity						
I	18	18,8				
II	9	9,4				
III	2	2,1	8	8,3	11,67	<0,01
Morphofunctional immaturity	12	12,5	3	3,1	8,23	<0,05
Asphyxia during childbirth	15	15,6	4	4,7	7,41	<0,05
Prolonged jaundice	18	18,8	5	5,7	7,11	<0,05
Intrauterine growth retardation	9	9,4	2	2,1	6,53	<0,05
Medication use during pregnancy (antibiotics, hormonal drugs, NSAIDs)	18	18,8	2	2,1	6,77	<0,05
Occupational hazards	7	7,3	5	5,2	1,66	>0,05
Bad habits	13	13,5	4	4,1	6,18	<0,05

Conflict of Interest: No conflict of interest was declared by the authors.

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АНАЛІЗ ЧИННИКІВ ТА СТРУКТУРА УРОДЖЕНИХ ВАД ШЛУНКОВО-КИШКОВОГО ТРАКТУ В ДІТЕЙ

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Резюме.

Уроджені вади розвитку шлунково-кишкового тракту (УВРШКТ) займають четверте місце у структурі вроджених вад розвитку у новонароджених.

Мета – проаналізувати чинники та структуру уроджених вад шлунково-кишкового тракту в дітей.

Матеріали і методи дослідження. Проведено ретроспективне когортне епідеміологічне дослідження УВРШКТ в Чернівецькій області з детальним аналізом ймовірних чинників розвитку вад у 96 дітей із УВРШКТ. Групу порівняння становили 96 дітей без УВРШКТ. Основною одиницею зберігання інформації була «Анкета обстеженої дитини», на якій фіксувалися та

поєднувалися всі дані єдиним кодом, що був автоматично генерованим для кожної дитини і оброблені загальноприйнятими в медицині методами варіаційної статистики. Це дослідження отримало схвалення комісії з питань етики. Дизайн дослідження та всі методи, використані в цьому дослідженні, були розглянуті та схвалені комісією з питань біоетики Буковинського державного медичного університету (протокол № 4 від 12//2024).

Результати дослідження. Серед усіх УВР частка УВРШКТ становила 9,9%. Перше рейтингове місце у структурі УВРШКТ належить атрезії ануса (13,5%), друге – атрезії стравоходу (12,5%), третє – пілороспазму (11,5%). Найрідше траплялися вади підшлункової залози (3,1%), хвороба Гіршпрунга та евентерація петель кишечника (4,1%). У кожної четвертої дитини траплялося поєднання УВРШКТ з вадами розвитку інших органів. За наявності у дитини УВРШКТ вагітність перебігала з токсикозом першої та другої половини (відповідно 35,4% та 29,2%). Анемія першої половини вагітності, загроза переривання вагітності фетоплацентарна недостатність траплялися частіше у матерів, які народили дітей із УВРШКТ. 23,8% жінок під час вагітності дитиною із УВРШКТ перенесли інфекцію респіраторного тракту або загострення хронічної патології інших органів та систем. Обстеження на наявність інфікованості внутрішньоклітинними збудниками під час вагітності виявили специфічні Ig G у 15,6% випадків народження дітей із УВРШКТ. Ознаки морфо-функціональної незрілості та асфіксію під час пологів частіше спостерігали у дітей із УВРШКТ (18,8% та 15,6% відповідно). Матері дітей із УВРШКТ частіше приймали ліки під час вагітності.

Висновок. Уроджені вади розвитку шлунково-кишкового тракту мають високу поширеність, часто поєднуються з іншими вадами розвитку. У структурі уроджених вад шлунково-кишкового тракту переважають атрезії ануса та стравоходу. Виділені ймовірні чинники уроджених вад шлунково-кишкового тракту включають токсикози вагітності, фетоплацентарну недостатність, анемію та інфекції у матері, вживання медикаментів під час вагітності, шкідливі звички, внутрішньоутробні інфекції, морфофункціональна незрілість плода, передчасні пологи.

Ключові слова: діти, уроджені вади шлунково-кишкового тракту, структура та ймовірні чинники вад.

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