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RELATIONSHIP OF FAMILY PREDISPOSITION FOR GASTRIC PATHOLOGY WITH GERD AND EROSIVE-ULCERATIVE LESIONS OF THE GASTRODUODENAL ZONE IN SCHOOLCHILDREN IN SIBERIA

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To study the prevalence of gastroesophageal reflux disease (GERD), erosive and ulcerative diseases of gastroduodenal zone and their association in schoolchildren from different regions of Siberia with hereditary predisposition to stomach pathology, schoolchildren from the Republic of Tyva, Buryatia and Evenkia were examined. The prevalence of GERD among schoolchildren in Tyva was higher than in Buryatia and Evenkia. The destructive process of stomach mucosa and duodemum was also higher in Tyva. In children with erosive ulcerative lesions of the gastroduodenal zone, comorbidity of the esophagus was also more frequently determined.

The significant influence of family predisposition to stomach pathology on the prevalence of GERD, erosive- ulcer diseases of gastroduodenal zone, as well as their association in Siberian schoolchildren was established. At the same time, territorial features influence the severity of these processes.

Keywords: children, gastritis with erosions, ulcer disease, GERD, hereditary predisposition.

Chronic diseases of the upper gastrointestinal tract are mostly classified as multifactorial [4, 5, 9]. Among risk factors, family predisposition plays a major role in their formation [11, 13]. Its realization is carried out under the influence of unfavorable factors of external environment that reflects the level of organism's resistance to their influence. Nutrition, stresses, bad habits, etc. are considered among environmental factors with negative impact on the organism. At the same time by the level of negative influence they can have different significance for the organism, up to failure of its adaptation reserves and disease development [2, 8]. This may be one factor with a pronounced negative impact on the functional systems of the organism, leading to the formation of pathology, or, more often, a complex of adverse factors [12, 17]. At the same time, different regions of the world have their own set of environmental factors with various negative impacts on the human body, which, to a large extent, determine the level of regional risk of disease development [6]. Thus, ecologically unfavorable environment for human habitation and increased risk of gastrointestinal diseases development is considered to be the Far North. Moreover, in Siberia, the structure of diseases of the stomach and esophagus has regional, ethnic, and age-related features [1, 14, 16]. Speaking about these features, it is necessary to note especially presence in the region of territories with extremely high incidence of adult population of stomach and esophagus cancer. In particular, these are the territories of the Tyva Republic and Buryatia [1, 3]. In this connection, the data on the role of specific factors in the development of children's stomach and esophagus diseases, i.e., in the age period of pathology occurrence in the majority of adults, are of interest [1, 3]. In particular, the data on the role of family predisposition in their occurrence, this can be used in preventive measures of formation and progression of pathology.

The **objective** of the research is to study the prevalence of gastroesophageal reflux disease, erosive and ulcerative diseases of the gastroduodenal zone and their association with hereditary predisposition to stomach pathology in schoolchildren from different regions of Siberia.

Materials and methods. The cross-sectional method was used to collect data on gastroenterological complaints in children and anamnestic data on the presence of digestive pathology in children's relatives using standardized questionnaires in various regions of Siberia: in the Republic of Tyva (1535 schoolchildren), Buryatia (790) and Evenkia (1369). A total of 3,694 school children aged from 7 to 17 years were examined. The research in the regions was carried out by the expedition method in localities that are identical in their socio-economic level.

All children over 15 years of age and parents of young children involved in the study gave a written form of informed consent to participate in the experiment, according to the Helsinki Declaration of the World Medical Association, which regulates the conduct of scientific research. The form of informed consent and the research Protocol were reviewed and approved by the ethics Committee of Federal Research Centre «Krasnoyarsk Scientific Centre» Siberian Division of Russian Academy of Sciences, Krasnoyarsk.

Groups of school children were randomly selected from the number of children with gastroenterological complaints in each region and underwent esophagogastroduodenoscopy (FGS). An instrumental study of the upper gastrointestinal tract in Tyva was conducted for 283 children, in Buryatia - 110 and in Evenkia - 205. The gender-age composition of the surveyed schoolchildren in the regions was identical.

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Criteria for including children in a study using FGS: 1. Age from 7 to 17 years; 2. Absence of acute inflammatory diseases in children; 3. Absence of chronic diseases of other body systems in the acute stage; 4. Absence of functional insufficiency of organs and body systems; 5. Presence of internal complaints.

The GERD in children was diagnosed in accordance with the children's consensus on pathology [10]. During screening, the presence of weekly heartburn was taken as a criterion for diagnosing GERD. Heartburn was understood as a burning sensation in the retrosternal region. Based on the results of an instrumental study of the upper gastrointestinal tract, two clinical variants of GERD were identified: 1. non-erosive (NERD), based on the presence of weekly heartburn in the child in the absence of erosive and ulcerative changes in the esophageal mucosa and 2. erosive form, diagnosed in the presence of erosive esophagitis.

Statistical analysis of the results was performed using the Statistica 6.1 software package (StatSoft, USA). The analysis of the statistical significance of differences in qualitative characteristics was carried out using the Yates-corrected x^2criterion and the Fischer two-way exact criterion. The statistical significance of differences in features was estimated at $p<0.05$ [7].

Results and discussions. Based on the clinical manifestations of heartburn, GERD was diagnosed among the examined contingent of schoolchildren in 6.4%. Significant territorial differences in the prevalence of pathology in children were noted. In Tuva, 9.5% of schoolchildren had GERD manifestations. These are significantly higher in comparison with the prevalence of the disease among schoolchildren in Buryatia (4.1%; $p = 0.0001$) and Evenkia (4.2%; $p = 0.0001$). The prevalence of GERD in Evenkia and Buryatia was identical ($p = 0.8988$).

The prevalence of GERD in children with a burdened family history of gastric pathology was assessed. It was found that in schoolchildren with a burdened family history, the frequency of GERD increased (in 9.8% compared with 4.6% of the prevalence of the disease among children without a burdened family history; $p = 0.0001$). We consider this result as a consequence of the increased effect of the acid factor, which is inherent in patients with diseases of the stomach and GERD. A connection with a family predisposition for gastric pathology indicates genetic mechanisms for the implementation of the negative impact of this factor in the occurrence of the disease. At the same time, Siberia is a huge territory, which includes various climatogeographic zones, significantly differing in the geochemical composition of soil and water. Extreme environmental factors can enhance the negative role of a family predisposition to the disease in the formation of the pathological process; in particular, which is the basis for the onset of clinical manifestations of GERD. Territorial features of the prevalence of diseases are formed. This is clearly demonstrated by the results of our study. Thus, the association of GERD with a family predisposition to the pathology of the digestive organs in schoolchildren was determined independently of the region and the particular climatic conditions of residence (Table 1). This highlights the special, dominant role of family predisposition in the formation of the disease.

At the same time, differences in the severity of this association in children of different regions draw attention to themselves, which reflects the negative impact of environmental factors. GERD prevalence rates among schoolchildren with a family history of gastric pathology in Tuva were significantly higher (11.8%) than among schoolchildren in Buryatia (6.7%; $p = 0.0001$) and Evenkia (8.4%; $p = 0.0001$). The result, in our opinion, indicates the presence on the territory of Tyva of environmental factors with a more pronounced negative effect on the body. Such factors in Tuva can be pronounced iodine deficiency [15], which is accompanied by hypothyroidism and characteristic motor disorders of the gastrointestinal tract. The alpine climate, which distinguishes Tuva from other territories, can have a negative effect on the function of the gastrointestinal tract. Maybe this is a factor in the specifics of nutrition. It is important that the indigenous people are the titular nations in Buryatia and Tuva. Moreover, the uniqueness of the indigenous population of Siberia lies in their genetic diversity. In this connection, it is impossible to exclude a certain influence, again, of genetic factors characterizing the belonging of a population to a specific ethnic group. All this needs further study.

The relationship of family predisposition and GERD in children, the severity of which has certain differences under the influence of environmental factors, forms regional features of not only the prevalence, but also the severity of damage to the esophagus. To a certain extent, this fact is confirmed by the results of instrumental studies of the upper sections of the gastrointestinal tract (Table 2). GERD with erosive esophagitis was mainly diagnosed in schoolchildren with a family history of gastric pathology (in 3 (1.2%) cases versus 1 (0.3%) in schoolchildren without a family history). Significant differences were not obtained, due to the fact that pathology is not widespread in childhood and adolescence compared with adults.

In the course of the study, it was noted that there was no obvious increase in erosive and ulcerative diseases in schoolchildren with a family predisposition to stomach pathology, there was only a tendency in children of Buryatia and Even-

Table 1

Screening for GERD in children with gastrointestinal complaints in Tyva, Buryatia, and Evenkia

Region	Burdened family history of gastric pathology	n	GERD	
			n	%
Tyva	1. Yes	626	74	11,8
	2. No	909	72	7,9
Buryatia	3. Yes	254	17	6,7
	4. No	536	15	2,8
Evenkia	5. Yes	379	32	8,4
	6. No	990	25	2,5
All regions	7. Yes	1259	123	9,8
	8. No	2435	112	4,6
p-level (significance of feature differences)			$p^{1-2}=0,0105$ $p^{1-3}=0,0235$ $p^{1-5}=0,0911$ $p^{3-4}=0,0095$ $p^{5-6}=0,0001$ $p^{2-4}=0,0001$ $p^{2-6}=0,0001$ $p^{7-8}=0,0001$	

Note: GERD - gastroesophageal reflux disease.

kia (Table 3). A similar trend was not observed in Tuva, which is regarded as the result of a pronounced negative influence of external factors, and the significance of the influence of such a factor as family predisposition goes by the wayside. An argument in favor of this may be an extremely pronounced problem with cancer incidence in adult residents of Tyva [1], which is evidence of the existence of factors in the region with an extremely negative effect on health parameters. Another argument may be the highest rates of erosive-ulcerative pathology of the gastroduodenal zone in Tyva and in children without a family predisposition to stomach pathology (17.4%). Moreover, its growth was formed by an increase in almost all nosological units in the structure of erosive-ulcerative pathology.

Analyzing the relationship of GERD and diseases with erosive and ulcerative changes in the mucosa of the gastroduodenal zone, it was noted that the association of these pathological processes increases sharply in schoolchildren with a burdened family history of gastric pathology (Table 4).

Thus, the highest rates of GERD were determined in schoolchildren with a family predisposition in the presence of erosive and ulcerative changes in the gastric mucosa and duodenum. The prevalence of GERD in schoolchildren with erosive-ulcerative lesions of the gastroduodenal zone increased in individuals with a family history of gastric pathology (30.3% versus 18.9% in individuals without a destructive process in the stomach and duodenum; p = 0.1299) and in schoolchildren without a family predisposition to gastric pathology (25.8% versus 7.4% in individuals without a destructive process in the stomach and duodenum; p = 0.0006). This insignificant trend was observed in the populations of schoolchildren examined in all three territories. A closer associative relationship between the diseases was observed in Buryatia and Evenkia. In schoolchildren of these regions, even in the absence of erosive and ulcerative lesions, in the presence of a family predisposition to gastric pathology, clinical manifestations of GERD were more often present. This, in our opinion, indicates the importance of genetic mechanisms in the implementation of pathological processes. Excellent territorial data were established in Tyva, where the influence of family predisposition to gastric pathology on the association between diseases (GERD and erosive ulcers) was not determined. In fact, this strengthens the arguments in favor of the position of the dominant influence of the regional environmental conditions of this territory in the formation of the considered diseases.

Conclusion

Thus, a family predisposition to gastric pathology is a significant factor influencing the risk of developing GERD and erosive and ulcerative diseases of the gastroduodenal zone and their association in schoolchildren. This affects the prevalence of pathological processes. In addition to the family predisposition, the external environment has a pronounced effect on the prevalence of these pathological processes in schoolchildren, which forms some regional features of the prevalence of these diseases, as well as their relationship. Moreover, under certain conditions, a family predisposition acts as a factor with a dominant influence on the formation of pathological processes, while in others, the role of unfavor-

Table 2

Frequency and forms of GERD in endoscopically examined schoolchildren in Tyva, Buryatia, and Evenkia with intestinal complaints

Region	Burdened family history of gastric pathology	n	Erosive GERD		Non-erosive GERD	
			n	%	n	%
Tyva	1. Yes	162	3	1,9	36	22,2
	2. No	121	0	0	23	19,0
Buryatia	3. Yes	53	0	0	8	15,1
	4. No	57	0	0	1	1,8
Evenkia	5. Yes	40	0	0	5	12,5
	6. No	165	1	0,6	6	3,6
All regions	7. Yes	255	3	1,2	49	19,2
	8. No	343	1	0,3	30	8,7
p-level (significance of feature differences)					$p^{3-4}=0,0108$ $p^{5-6}=0,0256$ $p^{7-8}=0,0002$ $p^{2-4}=0,0017$ $p^{2-6}=0,0001$	

Table 3

Frequency and structure of erosive-ulcerative pathology in children of Tyva, Buryatia, Evenkia with intestinal complaints

Region	Burdened family history of gastric pathology	n	Erosive-ulcerative pathology		Erosive gastritis		Erosive duodenitis		Gastric ulcer		Duodenal ulcer	
			абс.	%	абс.	%	абс.	%	абс.	%	абс.	%
Tyva	1. Yes	162	23	14.2	12	7.4	9	5.6	2	1.2	5	3.1
	2. No	121	21	17.4	13	10.7	8	6.6	2	1.7	3	2.5
Buryatia	3. Yes	53	6	11.3	4	7.5	1	1.9	0		2	3.8
	4. No	57	2	3.5	2	3.5	0	0	0	0	0	0
Evenkia	5. Yes	40	4	10.0	3	7.5	2	5.0	0	0	0	0
	6. No	165	8	4.8	5	3.0	4	2.4	0	0	2	1.2
All regions	7. Yes	255	33	12.9	19	7.5	12	4.7	2	0.8	7	2.7
	8. No	343	31	9.0	20	5.8	12	3.5	2	0.6	5	1.5
p-level (significance of feature differences)			$p^{2-4}=0.0102$ $p^{2-6}=0.0005$		$p^{2-6}=0.0079$		$p^{2-4}=0.0469$ $p^{2-6}=0.0809$					

Note: GERD - gastroesophageal reflux disease.

Table 4

Association of erosive and ulcerative lesions of the gastroduodenal mucosa and GERD in schoolchildren in Siberia

Region	Burdened family history of gastric pathology	Presence of erosive and ulcerative defects of the stomach and duodenum	n	GERD	
				n	%
Tyva	Yes	1. Yes	23	8	34.8
		2. No	139	31	22.3
	No	3. Yes	21	8	38.1
		4. No	100	15	15.0
Buryatia	Yes	5. Yes	6	1	16.7
		6. No	47	7	14.9
	No	7. Yes	2	0	0
		8. No	55	1	1.8
Evenkia	Yes	9. Yes	4	1	25.0
		10. No	36	4	11.1
	No	11. Yes	8	0	0
		12. No	157	7	4.5
All regions	Yes	13. Yes	33	10	30.3
		14. No	222	42	18.9
	No	15. Yes	31	8	25.8
		16. No	312	23	7.4
p-level (significance of feature differences)				$p^{3-4}=0.0142$	
				$p^{6-8}=0.0144$	
				$p^{14-16}=0.0001$	
				$p^{15-16}=0.0006$	
				$p^{3-11}=0.0402$	
				$p^{4-8}=0.0098$	
				$p^{4-12}=0.0032$	

able environmental factors in their occurrence sharply increases. Obviously, an increase in the association of erosive and ulcerative diseases of the gastroduodenal zone and GERD against the background of an increase in their prevalence can be expected in the face of an increase in the complex effect of these factors.

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