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Comorbidity Index as an Indicator of Comorbidity Effect on the Course of Chronic Gastroduodenitis among Children

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Abstract: The survey results are presented concerning 340 children with Chronic Gastroduodenitis (CGD) at the age of 13-15 years. It was revealed that a higher level of *H. pylori* infection corresponded to large values of Comorbidity Index (CI), the activity of lipid peroxidation processes and a more severe lymphoplasmacytic infiltration in the fundal and antral stomach departments. The signs of atrophy were detected among 33.3% of patients with CI >4 compared with 16.3% of children with CI <3 ($p = 0.038$). The children with CGD and a high CI also had the worst values according to the scale of a personal and a reactive anxiety (45.08±8.81 vs. 32.59±8.03, $p<0.05$ and 31.36±10.28 vs. 21.81±7.81, $p>0.05$), the worst life quality indices.

Key words: Comorbid pathology, comorbidity index, children, chronic gastroduodenitis, worst

INTRODUCTION

Digestive diseases remain important ones due to their high prevalence among children of almost all ages (Kildiyarova *et al*., 2005; Novikova *et al*., 2010). At that most common (more than half of all digestive system diseases) the pathology of an Upper Gastro Intestinal Tract (UGIT) is diagnosed-ulcer disease, CGD, functional dyspepsia with similar clinical manifestations and common elements of pathogenesis with the predominance of CGD detection (Livzan *et al*., 2007; Rusova *et al*., 2015).

One of the risk factors that adversely affects the course and outcome of a primary pathological process is the presence of comorbidities. The patients with comorbid conditions have a higher risk of complications, the resistance to conventional therapy and longer hospitalizations, requiring additional financial costs (Tai *et al*., 2006). According to Belyalov the nature of main pathology and comorbid disease relationship may be conditioned by common causes, risk factors and nonspecific pathophysiological mechanisms. In its turn, the presence of comorbidity contributes to the progression of the main disease and worsens its forecast (Guralnik, 1996).

To assess the impact of comorbid pathology on the main disease course, Charlson *et al.* (1987) suggested the use of CI. Despite the widespread use of CI in therapeutic practice this indicator is used not enough in pediatrics. So, the population-based study (Fenn *et al*., 2005) shows a frequent identification of child pathology under the age of 5 years which increases the likelihood of an unfavorable outcome in the case of acute infectious diseases. The data obtained supporting the close relationship of CI and the Quality of Life (QOL): a negative CI correlation is revealed with the total index of life quality (Van Weel and Schellevis, 2006). Among the studies devoted specifically to the identification of CGD development common risk factors and comorbid conditions the works by Mathers *et al.* (2006) are especially interesting where the researcher indicate a low birth weight, birth asphyxia and birth trauma as the relevant factors.

The purpose of this study is to study the spectrum of comorbid pathology among the children with CGD and the identification of pathogenic characteristics concerning the main disease course, depending on CI.

MATERIALS AND METHODS

We examined 340 children with morphologically proven CGD in the age from 13-15 years. The 90 patients were examined again, 6 months after the successful eradication of *H. pylori* infection. The criteria of children inclusion in the study were presented by morphologically proven CGD. All patients (and/or their legal representatives) gave a free and informed consent to invasive examination methods. CI was determined as the sum of all the comorbid conditions that a child had during

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the examination (Tai *et al*., 2006). Depending on the values of Comorbidity Index (CI) two patient groups were developed: Group 1 (the group of comparison) with low CI values (<3 associated diseases); Group 2 (basic one) with high CI values which included the children with a mean (4-5 comorbidities) and a high index of comorbidity (>6 pathological conditions). Examination methods included in addition to medical history, complaints, objective examination, conventional laboratory tests the conducting of fibro gastroduodenoscopy with the histological evaluation of a stomach mucous Membrane (MB), the research of lipid peroxidation state, the assessment of colon microbial biocenosis, a psycho-emotional status (Spielberg test to assess the levels reactive and personal anxiety) and the quality of life through an adapted SF-36 questionnaire. For the diagnosis of *H. pylori* infection a rapid reduced test and a breath Helic test were used in addition to histological examination. The total oxidant activity of blood plasma and the level of Malondialdehyde (MDA) which is the end product of lipid peroxidation were examined to evaluate the oxidative status. The antioxidant status was evaluated during the study of total antioxidant activity in blood plasma.

Statistical analysis was performed using the Statistical Package SSPS 13.0 for Windows. The resulting study data were analyzed using descriptive statistics with the determination of an arithmetic Mean (M) and a standard deviation (σ). The distribution norm was evaluated using the Shapiro-Wilk test. The evaluation of difference statistical significance for the data with a normal distribution was performed using Student's t-test for dependent samples. The match criterion χ^2 was used and Confidence Interval (CI) was calculated for the Odds Ratios (OR) to compare the incidence of qualitative data in two groups. The comparison of quantitative parameters in both groups was carried out using Mann-Whitney U-test. The obtained results were evaluated as statistically significant at a probability level of $p<0.05$.

RESULTS AND DISCUSSION

The structure of comorbid diseases included the additional disorders of a gastro in testinal tract and non-gastric-intestinal pathology. Children with CGD in almost 1/3 of cases had the following pathological conditions of the gastro intestinal tract: biliary sludge 28.8%, Oddi sphincter dysfunction of pancreatic type 34.4% of patients, irritable bowel syndrome 30%, chronic constipations 22%. The other (besides gastrointestinal one) pathology was characterized by the changes of the musculoskeletal system (posture disorders amoong 86% of children, scoliosis in 25% of cases); the cardiovascular system (mitral valve prolapse 22%); endocrine system (thyroid hyperplasia of the 1st stage 35.5%, delayed sexual development among 28%); urinary system (metabolic nephropathy 18.4%); autonomic nervous system (autonomic dysfunctions almost in 100% of cases); central nervous system (neurosis and astenoneurotic states 23 and 46%, respectively); dyslipidemia 23% of patients and the violations of nutritional status in the form of excess weight (23%) and an underweight of 1-2 st. (28%). During CI determination the following data were obtained: low CI (up to 3 comorbid conditions) was detected among 55% of patients, average CI (4-5 comorbid conditions) was revealed among 30% of patients, high CI (>6 pathological conditions) was revealed among 15% of children.

The results of stomach morphological change evaluation, depending on CI are shown in Table 1. The detection of *H. pylori* infection was higher among the patients of the 2nd group (78.2% of cases versus 30.6%, $p = 0.036$) and was characterized not only by a greater degree of gastric antrum contamination but by the emergence of a pathogen in the fundal part of a stomach. The prevalence of moderate and severe inflammatory activity among the children of the 2nd group is shown, involving not only the antrum and fundus of a stomach. 1st group children had mainly mild and moderate infiltration of antral department. The fundal department remained virtually intact. The intensity of atrophic changes in gastric MM testifying about disregenerative processes also prevailed in the group of children with >4 CI: the signs of moderate atrophy were detected in 19.5% of cases in the MM of a stomach body and in 33.3% of cases in antrum MM while in 8.33% of cases it was pronounced. Only 16.3% of children who had <3 CI had only mild atrophic changes.

The state of antioxidant status among the children with high CI was characterized by a more pronounced increase of blood plasma and MDA total oxidative activity against the decrease in total antioxidant activity (Table 2). Depending on CI values, the following features of the intestinal microflora state were obtained (Table 3).

When the obtained data are compared the following facts are revealed: the children of the 2nd group compared to the children of the 1st group had greater changes in the microbiota with a reduction of normal flora (bifidobacteria and lactobacilli) an increase of Conditionally Pathogenic Flora (CPF) representatives-yeasts and enter ococci. The evaluation of mental and emotional status showed that

Table 1: Comparative characteristics of gastric mucosa morphological picture among the children with chronic gastroduodenitis and various comorbidity index

	Fundal stomach (%)			Antrum (%)		
Morhological signs	1st group (CI <3) n = 49	2nd group (CI >3) n = 41	p-values	1st group (CI <3) n = 49	2nd group (CI >3) n = 41	p-values
***H. pylori* (+)**						
Weak contamination	0.00	7.3	0.08	18.36	12.2	0.610
Moderate contamination	0.00	4.9	0.34	12.20	19.5	0.590
Severe contamination	0.00	0.0	-	0.00	24.4	0.010
Total	0.00	12.2	0.04	30.60	56.1	0.080
Lymphoplasmacytic infiltration						
Weak	32.60	46.4	0.37	48.9	7.3	0.010
Moderate	0.00	46.4	0.01	44.9	24.4	0.260
Severe	0.00	7.4	0.07	6.2	68.3	0.010
Total	32.60	100.0	0.03	100.0	100.0	-
Atrophy						
Weak	6.12	12.2	0.59	12.2	14.6	0.870
Moderate	0.00	7.3	0.02	4.1	12.2	0.070
Severe	0.00	0.0	-	0.0	8.3	0.018
Total	6.12	19.5	0.30	16.3	33.3	0.060
Intestinal metaplasia						
Weak	0.00	0.0	-	12.2	21.9	0.330
Moderate	0.00	0.0	-	0.0	7.3	0.590
Severe	0.00	0.0	-	0.0	0.0	-
Total	0.00	0.0	-	12.2	29.2	0.150

Table 2: Characteristics of lipid peroxidation among children with chronic gastroduodenitis at various comorbidity index

Values	CI <3 (1st group) n = 49, M (s)	CI >3 (2nd group) n = 41, M (s)	Healthy children, n = 22, M (s)	p-values
Malondialdehyde (MDA) (mmol L^{-1})	2.75±0.18	3.24±0.26	2.10±0.10	0.001
Total Oxidative Activity (TOA) (%)	24.60±3.80	31.90±7.5	8.15±3.22	0.001
Total Antioxidant Activity (TAA) (%)	34.90±2.70	26.06±6.1	44.13±0.90	0.001

Table 3: The results of faeces examination for disbacteriosis among the children with chronic gastroduodenitis, depending on comorbidity index

Microorganisms (lg mt/g of feces)	Children with CGD, CI <3, n = 49 M (s)	Children with CGD, CI >3, n = 41 M (s)	p-values
Bifidobacteria	5.94±1.300	6.12±0.98	>0.0500
Lactobacilli	6.86±1.100	7.01±1.25	>0.0500
Escherichia coli	19.10±3.800	20.54±4.40	>0.0500
Relative pathogens	0.67±0.050	1.24±0.12	0.0490
Enterococci	0.39±0.040	0.43±0.06	>0.0500
Yeasts	0.45±0.096	1.08±0.08	0.0342
Streptococci	2.52±0.180	2.72±0.62	>0.0500

the mean values according to the scales of personal and reactive anxiety was higher among the children of 2nd group 45.08±8.81 vs. 32.59±8.03, $p<0.05$ and 30.36±10.28 vs. 22.81±7.81, $p>0.05$, respectively. Total performance of life quality assessment among children with high CI was worse than among children with less CI (74.18±11.2 vs. 83.2±10.7, $p<0.01$). The most pronounced changes were shown on the scales characterizing the physical components of health the influence of pain syndrome severity during Regular Performance (RP) but to a greater degree according to the scales that characterize the psychological components of health, Role Emotional functioning (RE), Vitality (VT) and Mental Health (MH) (Fig. 1).

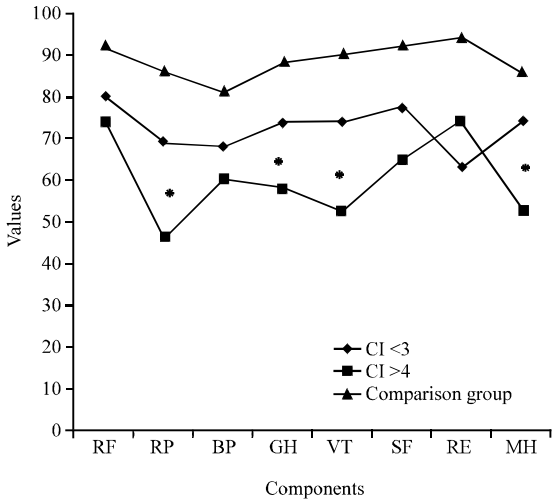

Fig. 1: The quality of life among children with chronic gastroduodenitis, depending on comorbidity index values (on the horizontal axis the quality of life values; PF: Physical Functioning; RP: Role-Physical functioning; BP: Pain; GH: General Health; VT: Vitality; SF: Social Functioning; RE: Role-Emotional functioning; MH: Mental Health; ordinate axis demonstrates points)

Our study revealed that children almost did not have CGD as a single disease. A high frequency of comorbid conditions is recorded at least among half of the children with 3 comorbidities. The most common pathology was the pathology of the autonomic and central nervous system (autonomic dysfunctions, asthenoneurotic states), the changes of the musculoskeletal system (incorrect

posture and scoliosis), cardiovascular and endocrine systems. It was shown that the presence of comorbid conditions (at CI >4) was the additional factor contributing to morphological changes of MM, along with *H. pylori* infection. Furthermore, the combination of CGD and high CI was accompanied by the breach of an antioxidant status with the reduction of total antioxidant activity, the changes in the microbiota intestine with the UPF level increase and the reduction of obligate microorganisms, the changes of psycho-emotional status in the form of increased situational and to a large extent, personal anxiety. The natural results were the worse GI indicators among the children with high CI, characterizing physical and to a large extent, the mental components of health, resulting in a body adaptation ability reduction.

These data substantiate the need for CI use among children with CGD. The children with an average and a high CI (>4) should have a comprehensive survey with the estimation of physical development balance; the states of nutritional and antioxidant status; the states of the intestinal microbiota and psycho-emotional characteristics followed by the appointment of therapeutic measures aimed at the gut microbiota restoration, antioxidant and psycho-emotional status increase.

CONCLUSION

Chronic gastroduodenitis among children takes place with the presence of gastrointestinal and intestinal diseases without gastric ones. The index of comorbidity >4 is a reliable clinical tool, indicating more severe contamination of *H. pylori* gastric mucosa membrane, the intensity of the inflammatory process and the presence of atrophy remaining after a successful eradication of a pathogen. Children with comorbidity index >4 need additional rehabilitation measures aimed at the correction of intestinal microbiota condition, the restoration of antioxidant status activity and the normalization of a psycho-emotional state.

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