SCIENTIFIC REVIEWS AND LECTURES

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# PATHOLOGY OF THE DIGESTIVE SYSTEM IN CHILDREN WITH OBESITY

**ABSTRACT**

The article presents a review of the literature about lesions of the digestive system at metabolic syndrome with clinical, laboratory, instrumental and morphological positions.

Pathogenetic mechanisms of development of the metabolic syndrome, complications of the digestive system are considered against its background, as well as the risk to human health in the presence of abdominal obesity.

Recent studies have shown a high incidence of comorbid complications in adolescents with obesity, which makes it possible to treat MS as an important pediatric problem.

**Keywords:** children, obesity, digestive organs.

## INTRODUCTION

In many countries in recent decades there has been an increase in the number of patients with overweight and obesity, including childhood and adolescence.

According to the world health organization (WHO) in 2014, around 41 million children under the age of 5 were overweight or obese. Overweight and obesity, previously considered typical of countries with high income, are now becoming more common in countries with low and middle income, especially in the cities. In Africa the number of children who are overweight or obese has almost doubled — from 5.4 million in 1990 to 10.6 million in 2014. In 2014 almost half of children under 5 years are overweight or obese lived in Asia [12].

According to forecasts, by 2025 obesity will suffer 40-50% of the world population. The world health organization has recognized the obesity epidemic of the XXI century.

In the Russian Federation also an increase in the number of children and adolescents with overweight and obesity is noted. According to data published in 2014, the study, which involved more than 5,000 children aged 5, 10 and 15 years from Astrakhan, Yekaterinburg, Krasnoyarsk, Samara and St. Petersburg, it was found that among children of both sexes and all age groups, the prevalence of overweight is 19.9%, and the prevalence of obesity was 5.7% [38].

In the 2015-2016 academic year for the first time in Kazakhstan national center for problems of healthy lifestyle conducted a study within the multicenter study of the prevalence of childhood obesity among children according to the methodology of the who COSI. According to the study, the prevalence of overweight, separately for boys and girls 9 years was 12.7% and 12.0%, respectively, obesity among boys and girls 9 years to 7.1% and 5.5%, respectively [3].

Currently a comorbid disease is a topical problem of medicine not only in Russia but throughout the world [2].

It is known that obesity is accompanied by damage to almost all organs and systems, including the digestive system. Fatty tissue affects the digestive system both mechanically and due to the metabolic action [31].

Studies of comorbidity, published in recent years, indicate the correlation of metabolic syndrome with typical gastrointestinal manifestations [24].

According to the data [26] metabolic syndrome (or syndrome of insulin resistance) in the current literature involves complex of metabolic, hormonal and clinical disorders, closely associated with diabetes type 2, and are risk factors for the development of cardiovascular diseases, which is based on insulin resistance (IR) and compensatory hyperinsulinemia (HI).

For the first time this syndrome has been described in the 60-ies of the last century and included a combination of non-insulin dependent diabetes mellitus, gout and hyperlipidemia.

In the 1980-s G. M. Reaven suggested that a combination of violations glucose tolerance, dyslipidemia and hypertension was associated with reduced sensitivity of tissues to insulin – insulin resistance [9, 46, 47].

Unfortunately, up to the present time, no single criteria have been developed to diagnose MS in children. One of the most universal classifications proposed for use in pediatric practice is the classification developed by the International Federation of Diabetes (IDF) in 2007 on the basis of similar criteria for MS for adults.

According to these recommendations MS in adolescents of 10-16 years may be diagnosed at the presence of abdominal obesity (waist circumference more than 90 percentile) in combination with at least two of the following indices:

- triglycerides ≥ 1.7 mmol/l;
- the level of high-density lipoproteins < 1.03 mmol/l;
- increased blood pressure ≥ 130/85 mm Hg. article;
- increase in glucose venous plasma fasting ≥ 5.6 mmol/l or diagnosed DM of the 2nd type and/or other disorders of carbohydrate metabolism [9].

The prevalence of diseases of digestive organs, according to official statistics in the Republic of Sakha (Yakutia), 2006-2012 on applications made 90-150 per 1000 of children population.

In the study of Berezkina O. N. [6] of 103 examined children 74 children had chronic *H. pylori* associated gastritis (44 urban students and 30 – SEL). Urban residents prevailed erosive forms (80 %), rural – non-erosive forms of gastritis (70 %).

There were noted diseases of the esophagus: gastroesophageal-reflux disease (7.8 %), reflux esophagitis (18.4 %), and reactive pancreatitis – (63 %), duodenitis (20 % of all patients), dolichosigma (2 %), dyskinesia of the large intestine (4.9 %), malabsorption syndrome (0.9 %). In 3% of children post-traumatic gastritis was reported.

Besides, in Yakutia works for the study of regional features of lipid - metabolic risk factors of cardiovascular diseases were carried out, the association of single-nucleotide polymorphism rs1137101 gene leptin receptor and *rs9939609* gene associated with fat mass in individuals of Yakut ethnicity was investigated [2,19, 20].

According to Sozonova K. K. (2014) in Yakutia the prevalence of abdominal and general obesity (BMI≥30 kg/m2) in the indigenous is lower than that of the non-indigenous.

Level of cholesterol lipoproteid of low density (LDL cholesterol) in the Yakut population is high, but MS is not very different from population values and

values in individuals without MS, which allows to admit the unjustified inclusion of the LDL cholesterol criterion in the list of MS definitions [36,37].

At the same time questions of the MS prevalence among the child population of the Sakha Republic (Yakutia) remain poorly studied, and the pathology of digestive organs in obese children in this territory has not been yet studied.

According to the Central research institute of gastroenterology, nosological structure of diseases of digestive organs in MS patients is represented by the following triad: diseases of the esophagus, including gastroesophageal reflux disease (GERD) – 72% of cases; the liver and biliary tract – 64%; colorectal – 68% of cases [9].

Overweight and obesity are proven risk factors for such diseases of the esophagus like GERD, Barret's esophagus (BE) and adenocarcinoma of the esophagus (ACE).

Gastroesophageal reflux disease is «a chronic inflammatory disease characterized by defined esophageal and outer-esophageal clinical manifestations and a variety of morphological changes of esophageal mucosa due to retrograde reflux of gastric or gastric -intestinal content» [21, 35].

The study of V. G. Borodina, T. V. Stryukova (2014) revealed no strict dependence between the frequency of clinical symptoms of GERD (heartburn, epigastric pain and other dyspeptic complaints) and physical development of children, but with an excess of body weight there was a trend to increased frequency of heartburn at reducing the amount of other dyspeptic manifestations (at 87.5 and 43.7%, respectively) [10, 32].

Obesity is an independent factor in the formation of diaphragmatic hernia. Diaphragmatic hernia is more often diagnosed in patients with symptomatic GERD, as well as in patients with pathological acid reflux. Patients with diaphragmatic hernia often suffer from esophagitis and have a marked decrease in pH in the lower esophagus compared to those without disrupting the function of the lower esophageal sphincter (NPS) [10].

Visceral fat is a metabolically active substance that causes a decrease in the serum level of protective cytokines (adiponectin) and an increase in the level of inflammatory cytokines (TNF-α, IL-1ß, IL-ß) [35].

According to I.Yu. Usanova et al. (2013), in patients with GERD of young age and overweight by the results of pH-metry, alkali reflux occurs in 62% of cases, which can be explained by an increase in intra-abdominal pressure and casting of the alkaline contents of the duodenum into the lumen of the stomach and esophagus [39].

The study of A.S. Asekritova (2015) revealed that in Yakuts with a metabolic syndrome, gastroesophageal reflux disease is characterized by a more severe clinic with a high incidence of dyspeptic and extra-esophageal manifestations compared to Yakuts without MS. Yakut people with GERD, regardless of the presence of MS, are twice more likely to have non-erosive esophagitis than Russians [2].

Diagnosis of GERD in children and adolescents with obesity can be difficult due to the lack of specific complaints. Child's complaints about discomfort and abdominal pain parents can associate with a violation of the quantitative and qualitative characteristics and diet, which, as a rule, take place in the majority of children with excess body weight [4, 8].

At the same time, researchers agree that without correction of body weight in such patients, GERD remission is almost unattainable. In particular, Italian scientists have studied the effect of weight loss on the control of GERD symptoms, as well as the dynamics of the frequency of using proton pump inhibitors against the background of weight loss in 50 patients who were diagnosed with erosive lesions of the esophagus [33].

The presented results indicate a possible relationship of GERD in children with an increase in body weight. Early diagnosis and treatment of GERD, including weight correction, are needed to prevent severe complications of the disease in adults. It is likely that in children, compared with the adult population, in studies to identify signs of reflux, the primary use of non-invasive methods is needed, as well as the use of more sensitive indicators, such as visceral fat assessment [32].

Investigation of the pathology of the gastrointestinal tract with obesity can reveal frequent damage to the stomach (up to 72%) and duodenum (66%). Pancreatic diseases are observed in 18% of patients, and prevail in the female sex (6: 1) [33].

Endoscopic picture at obesity is characterized by the presence of atrophic gastritis, single and multiple erosions, single polyps of the stomach, the formation of ulcers of typical localization.

There is a high incidence of *H. pylori* infection with metabolic syndrome, insulin resistance and diabetes mellitus [12].

*H. pylori* in the body is considered as a trigger switching on a cascade of pathological reactions: it initiates the process of chronic inflammation, promotes the increase in the level of pro-inflammatory cytokines, adhesion molecules, growth factors and acute phase proteins, which in turn stimulate inflammatory and proliferative changes In the walls of the vessels and cause endothelial microvascular dysfunction, exacerbating metabolic disturbances [28, 41].

Regulation 16 of the Kyoto Consensus includes a recommendation to carry out in view of the epidemiological situation scoring against *H. pylori* at the age at which the phenomena of atrophic gastritis and intestinal metaplasia have not yet developed (the degree of recommendation is strong, the level of evidence is moderate, the level of consent - 97.3%). It is noted that such screening is most expedient to be carried out when the probability of occurrence of new cases, *H. pylori* associated gastritis (over the age of 12 years) decreases [42].

Non-alcoholic fatty liver disease (NAFLD) is one of the most common chronic liver diseases in the world. According to the classification of the Russian gastroenterological association (RGA) in 2016 V.T. Ivashkina et al. identified the main clinic-morphological forms of NAFLD: fatty steatosis (hepatosis), which in most cases has a benign course, as well as non-alcoholic steatohepatitis (NASH), characterized by the potential for progression to cirrhosis and hepatocellular carcinoma [18, 46].

Liver steatosis is a pathological deposition of fat droplets inside and outside the liver cells with the development of fatty degeneration of hepatocytes.

Nonalcoholic steatohepatitis (NASH) - necrotic inflammatory changes in hepatocytes due to the action of toxic agents similar to the picture of alcoholic hepatitis in patients not abusing alcohol.

In children and adolescents, NAFLD is characterized by a chronic course and global spread[11, 21].

Recent studies using magnetic resonance imaging and liver histology have shown that liver steatosis is closely related to pancreatic steatosis [21].

It is assumed that both these diseases have a single mechanism of development associated with metabolic changes developing against the background of excessive deposition of visceral fat, whose increased functional activity leads to disruption of autoparaendocrine regulation, the leptin mechanism of

control of food behavior, the development of cytokine-induced Insulin resistance and chronic inflammatory process due to an imbalance between the level of adipo-cytokines with an increase in the concentration of pro-inflammatory leptin and Resistin and a decrease in the level of anti-inflammatory adiponectin, and also causes oxidative stress, which leads to the development of chronic pancreatitis and steatosis [43].

Clinical manifestations of pancreatic steatosis are β-cell dysfunction, exocrine pancreatic insufficiency, an increased risk of fistula formation after pancreatic surgery, a high risk of developing pancreatic cancer, a significant severity of episodes of acute pancreatitis [43].

Numerous studies in adult patients indicate the association of pancreas steatosis with old age, higher body mass index, abdominal circumference, the ratio of abdominal circumference of growth, hyperglycemia, hypertension, hypercholesterolemia, and hypertriglyceridemia, hepatic steatosis, increased level of alanine aminotransferase (ALT), A violation of tolerance to glucose and diabetes [16].

In children, pancreas studies at adiposity and metabolic syndrome are single [1, 14].

In the study of E.I. Aleshina, V.P. Novikova (2014) et al., coprologically pancreatic syndrome was detected in 23.3% of obese children and in 7.5% of children with a normal body mass index (BMI). These results are consistent with the indices of feces elastase activity [1].

According to the ultrasound changes of the pancreas in children with obesity significantly more often than in children with normal BMI changes of echostructure and echogenicity of the pancreas, increasing of its size were detected. They also had more increased size of the tail of the pancreas. The incidence of pancreatic steatosis in obese children reached 70% (according pathognomonic term - hyperechogenicity compared with renal parenchyma) [1, 13, 48].

The pathogenesis of non-alcoholic fatty liver disease (NAFLD) is the accumulation of an excessive amount of triglyceride (TG) and cholesterol other derivatives in hepatocytes due to imbalance between the synthesis and utilization of these organic molecules [7].

There is no single well-studied mechanism for the development of NAFLD: it is a complex multifactor process. Insulin resistance and the change in hormone profile - fat metabolism regulators (leptin, adiponectin etc.) are considered as its main component [7, 10, 19, 44].

Numerous clinical studies have shown that metabolic abnormalities in the liver are often associated with disorders of the intestinal microbiocenosis. In the formation of steatosis and steatohepatitis secrete exogenous risk factors - excessive intake of hepatocyte intestinal lipid hydrolysis products (fatty acids), glucose, fructose, galactose, alcohol, and endogenous - increasing con-centration and disruption of fatty acid oxidation in the hepatocyte, the accumulation In hepatocytes of triglycerides, relative or absolute deficiency of apoproteins B, complement components of C1-C3. The maximum expression of bacterial growth is observed in patients with NASH with an outcome in the liver cirrhosis [34, 41].

According to the data of T. A. Bokova (2013) the nature of food has a direct effect on the composition of the microbiota. Thus, the consumption of high-calorie food, characteristic of obese patients, leads to a decrease in the level of bifidobacteria and a shift towards one subspecies of Firmicutes, namely Erysipelotrichi, an increase in the level of endotoxins in intestinal contents and blood [9].

In the study of Kurmangulov A.A., Dorodneva E.F., Isakova D.N. (2016) in all groups with an excess of body weight there was a decrease in the total metabolic activity of obligate microorganisms. With obesity of the 2nd degree, the activity of aerobic populations of microorganisms, mainly facultative and residual strains, increases. MS with obesity of the third degree is accompanied by the most significant changes in the coprological profile of short-chain fatty acids (CLC) with the activation of proteolytic microorganisms [19].

Complaints of patients are nonspecific and do not directly indicate a liver disease, first of all manifestations of asthenic and dyspeptic syndrome, discomfort in the right hypochondrium, hepatomegaly in approximately 50-75% of patients [21].

A family history of NAFLD can also help in diagnosis, because related chains are often found [15].

At physical examination acanthosis nigricans, skin pigmentation, from velvety brown to black or «dirty» areas of the skin is often found. Typical localization is skin folds and nape, shoulders, axillary fossa, in the body in combination with papillomatosis. Acanthosis nigricans can be observed in a greater proportion of children with NAFLD [21].

In contrast, patients with NAFLD have no skin signs typical of other chronic liver diseases, such as palmar erythema or «spider veins» [13].

At steatosis and NASH, there is a moderate increase in the liver, its edge is round, and the consistency is doughy [40].

The activity of alkaline phosphatase (APH) increases in less than 50% of patients, and the level of bilirubin increases even more rarely. The level of albumin in the blood almost always remains within normal limits. Elongation of prothrombin time is not characteristic for NASH. Determination of liver enzymes (AST and ALT) in combination with ultrasound examination of the liver has been shown to all obese patients for screening of non-alcoholic fatty liver disease [22].

At the stage of steatohepatitis, an increase in the activity of transaminases from two to 4-5 norms is possible, but at the stage of steatosis the indices are not changed.

To identify and evaluate steatosis, visualizing methods are recommended: ultrasound, computed tomography, magnetic resonance imaging [5].

Sensitivity and specificity of ultrasound in NAFLD vary depending on the degree of steatosis and range from 60-90% to 90-97%, respectively [17].

The sensitivity and specificity of ultrasound in the pathology of the gall bladder make up 90%. The method allows to assess the condition of the gallbladder wall, its shape, the presence of deformations, visualize the stones in the cavity of the bladder or ducts, determine their size and quantity. In addition, when performing ultrasound, it is possible to diagnose «non-homogeneous bile» and «disconnected» gallbladder [9].

In this regard ultrasound can be a screening method for detecting liver steatosis.

Due to the fact that instrumental methods for NAFLD diagnosing are not strictly specific, one of the important and controversial issues is the need for using liver biopsy in patients with childhood suspected of having NAFLD.

According to Y. Ikura (2014), biopsy is not mandatory for diagnosis if the patient is in the classic case of fatty liver damage - a moderate change in hepatic enzymes, the presence of classical risk factors (obesity, type 2 diabetes, dyslipidemia) and Typical data of ultrasound were revealed [45].

The principles of treatment of GERD within the metabolic syndrome consist in the appointment of adequate doses of proton pump inhibitors (PPI). It should be noted that even long-term therapy with PPI in a sufficient dosage without

correcting the body weight of the patient does not lead to stable remission [10].

Regular exercise of adequate physical exercises leads to an improvement in the histological picture of the liver in NASH even without a clinically significant decrease in body weight, and also contributes to a decrease in serum cholesterol level [30].

It should be remembered that pharmacological preparations are only an addition, not an alternative to changes in diet and physical activity, and the spectrum of medicines used to correct lipid and carbohydrate metabolism disorders in childhood is very limited [5, 25, 27, 44].

According to the recommendations of the International Hepatology Congress EASL (Barcelona April - 2016), the most actual and effective way to treat NAFLD is a lifestyle change that includes a hypocaloric diet, aerobic activity [30].

Treatment of NAFLD should begin with the cancellation of all potentially hepatotoxic drugs, the appointment of hypocaloric diet and correction of excess body weight, which leads to an improvement in the functional state of the liver.

It is necessary to treat the concomitant conditions associated with the development of NASH (type 2 diabetes mellitus, atherogenic hyperlipidemia, hypercholesterolemia, obesity).

Widely are used means of metabolic therapy (alpha-lipoic acid drugs), hepatoprotectors-antioxidants (ursodeoxycholic acid (UDCA), hypo-lipidemic therapy (statins), probiotics (lactulose) [17, 29].

The data obtained suggest the presence of pathogenetic determinants between obesity in MS and microbiota of the intestine. In connection with this, further search for cause-effect relationships of the occurrence and progression of metabolic disorders involving the intestinal microbiota at MS is needed [23].

Obesity contributes to the emergence and progression of diseases of all parts of the digestive system, characterized by the same type of changes in the digestive system in the form of motor disorders, erosive, and in some cases - severe atrophic lesions, against a background of significant microcirculation disorders; frequent pathology is esophageal leukoplakia or hyperkeratosis, Barrett's esophagus, esophagus polyps, in some cases - adenocarcinoma [34].

## CONCLUSION

Thus, recent studies have shown a high incidence of comorbid complications in adolescents with obesity, which makes it possible to treat MS as an important pediatric problem. Only joint activity of pediatricians with endocrinologists, gastroenterologists, cardiologists will allow fully studying the basic pathogenetic mechanisms of MS formation, to isolate the spectrum of clinical manifestations, while focusing on earlier symptoms, which are predictors of its development in children.

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# RELEVANCE OF RESEARCH ON TREATMENT OF PURULENT SKIN WOUNDS WITH NATURAL SORBENTS

**ABSTRACT**

Review of literature is based on the analysis of sources covering the mechanism of purulent wound progress and choice of effective means of local treatment. We present topical issues for further research of the problem.

**Keywords:** wound process, sorbents, Khongurin zeolite.

Currently wound treatment is one of the most major problems of surgery. With all the success in the development of surgical techniques in recent decades, the number of patients with purulent wounds of different etiologies has not decreased. [1, 17, 31].

The most promising and active of systemic exposures was the use of antibiotics to fight the infection. Unfortunately, removing the infection this way was not prospective, because the microorganisms that cause the infectious process mutate and become resistant to known antibiotics. High resistance to antibiotics and other antimicrobials of many modern strains of bacteria, pathogens of purulent infection dictate the need to find new ways to intervene in the microflora of purulent wound during its topical treatment. [2, 3, 8].

It is known that wound healing process is essential for normal function of the organism. It is a manifestation of biological adaptation, without which complex multicellular organisms could neither evolve nor survive [7, 32]. Clinical, anatomical and pathohistological characteristics of these stages are described in numerous papers by prominent scientists.

Currently we use the classification of M.I. Kuzin (1990): Phase I (inflammation) is the melting of necrotic tissues, their removal, i.e. purification of the wound defect. In the initial phase of inflammation an important part of the defensive reaction of the body is the formation of exudate. Serous exudate to some extent neutralizes the products of cellular and tissue decay, and antibodies and enzymes in the exudate contribute to the disinfection of the pathogenic factor and the removal of nonviable tissues. The process of absorption and digestion of microorganisms and nonviable tissues is the central link of the inflammatory process. The main role in the purification of the wound is performed by leukocytes, lymphocytes, and macrophages, during decay of which about 40 hydrolases enter the wound. In addition, the microbial factor actively participates in the lysis of nonviable tissues and the purification of the wound; it acts as a "biological purifier". Thus, in the first phase of wound healing main efforts of organism defense mechanisms are directed towards removing destroyed tissue from the inflammation area in the wound, as well as toxic products formed in the wound. Phase II (regeneration and maturation of the granulation tissue) begins 2-3 days after injury. Granulation tissue is formed as separate foci at the bottom of the wound and is characterized, firstly, by an intensive neoplasm of capillaries. Their elaboration occurs within 7-9 days. By the end of the second week regenerative processes are nearing completion and, with the increase in collagen fibers, granulation tissue becomes denser. Phase III (scarring and epithelization) occurs by days 19-22, when the wound defect is closed and completely epithelialized. Granulation tissue is converted into mature fibrous tissue, poor on blood vessels, with coarse collagen fibers and fibrocytes [19, 20, 21,30].

Wound shrinkage (contraction) processes play an important role in the reorganization phase. The edges of the wound are reduced thanks to a special area of centripetally-located fibroblasts (miofibroblasts sensu J.Jobiani, 1972) [20, 21].

The mechanism of wound process progress and its clinical picture requires, first and foremost, the use of mechanical removal of altered wound tissues and