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THE COURSE OF METABOLIC COMPLICATIONS UNDER CHILDHOOD OBESITY AND OVERWEIGHT

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Introduction. Obesity is one of the greatest modern health problems among adults and children. Due to the constant significant increase in the prevalence of childhood obesity and overweight, the prevalence of comorbidities is also increasing. Childhood and adolescent obesity significantly raises the risk of cardiovascular disease and premature death, regardless of the presence of this disease and BMI level in adulthood. The metabolic complications of childhood overweight and obesity are asymptomatic and underdiagnosed conditions that lead to their progression and negative impact on the health of young adults.

The research **aim** is to analyze the course of metabolic complications of childhood obesity and overweight.

Materials and methods. The cohort non-intervention study involved 200 children aged 8 to 14 years with obesity criteria and overweight. Children were divided into comparison groups depending on their physical development. Group 1 included overweight children (133 children), and Group 2 included obese children (67 children). The criteria for exclusion from the study were the presence of infectious, endocrine, immune, and genetic diseases that could lead to liver damage.

Results and discussion. As a result of the assessment of all metabolic complications, a high incidence of metabolic-associated fatty liver disease (MAFLD) was found in both groups. Thus, it emphasizes the need to screen for these conditions and prevent the development of metabolic complications not only in obese but also in overweight children.

Conclusions. MAFLD is the most common and, at the same time, poorly studied pathology of the digestive system associated with obesity. Among the most frequent factors that may be associated with the development of metabolic complications in overweight and obese children, a group of factors related to early feeding and eating habits in the future, as well as a sedentary lifestyle, deserve attention. Metabolic-associated fatty liver disease occurs and requires treatment in both obese and overweight children.

Key words: children, obesity, overweight, liver, metabolic-associated fatty liver disease.

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ХАРАКТЕР МЕТАБОЛІЧНИХ УСКЛАДНЕНЬ ПРИ ОЖИРІННІ ТА НАДЛИШКОВІЙ МАСІ ТІЛА У ДІТЕЙ

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Ожиріння є однією з найважливіших сучасних проблем здоров'я дорослих і дітей. У зв'язку з постійним суттєвим збільшенням поширеності ожиріння та надлишкової маси тіла у дітей відповідно зростає і розповсюдженість супутніх захворювань. Метаболічні ускладнення надлишкової маси тіла і ожиріння у дітей є малосимптомними і недостатньо діагностованими станами, що призводить до їх прогресування та негативного впливу на стан здоров'я молодих дорослих. Серед найбільш частих факторів, що можуть мати асоціацію з розвитком метаболічних ускладнень у дітей з надлишковою масою тіла та ожирінням, заслуговує уваги група факторів, пов'язаних з раннім годуванням і харчовими звичками в подальшому, а також малорухомий спосіб життя.

Ключові слова: діти, ожиріння, надлишкова маса тіла, печінка, метаболічно асоційована жирова хвороба печінки.

Introduction. Obesity is one of the greatest contemporary health problems among adults and children. Over the past 40 years, many studies involving more than 130 million children aged 5 to 18 have revealed an increase in the prevalence of obesity among girls from 1% (respectively 5 million) to 6% (respectively 50 million) and among boys from 1% (respectively 8 million) to 8% (respectively 74 million). The total number of children with obesity has increased more than 10-fold over the observation period, from 11 million to 124 million [1]. It should be noted that, according to estimates, 213 million children worldwide are overweight and at high risk of developing obesity [2]. In recent years, the prevalence of obesity and overweight in children has increased not only in high-income countries, but also in low- and middle-income countries [3]. In general, the number of overweight and obese children is expected to outnumber children with moderate and severe underweight worldwide [4]. In developed countries, 25% of adolescents are overweight and 15% are obese. In Ukraine, 18–20 thousand new cases of obesity among children and adolescents are recorded

annually [4]. Due to the ongoing significant increase in the prevalence of obesity and overweight in children, the prevalence of comorbidities is also increasing. Certain co-morbidities that can be observed in obese and overweight children, such as type 2 diabetes mellitus (T2DM) and metabolically associated fatty liver disease (MAFLD), were previously considered 'adult diseases'. But nowadays, they are increasingly seen in obese and overweight children. Obesity in childhood and adolescence significantly increases the risk of cardiovascular disease and premature death, regardless of the presence of this disease and the level of body mass index (BMI) in adulthood [5].

The most common and, at the same time, insufficiently studied pathology of the digestive system associated with obesity is metabolic-associated fatty liver disease. Non-alcoholic fatty liver disease is considered to be a hepatic manifestation of metabolic syndrome associated with central obesity, hypertension, T2DM and/or insulin resistance. In 2020, a consensus of international experts decided to change the definition and nomenclature of non-alcoholic fatty liver disease to MAFLD. These changes should increase the perception and awareness of the pathogenesis of this condition [6].

In general, metabolic complications of obesity pose a significant health problem for young adults, affecting morbidity, quality of life, and premature mortality. The course of some of them, for example, MAFLD in obese and overweight children, is almost asymptomatic or has nonspecific manifestations. That is why, due to the lack of specific clinical manifestations and insufficient screening of liver condition in children, timely diagnosis of this condition along with other metabolic complications in children is both a very urgent and insufficiently studied issue.

The study **aims** to analyze the course of metabolic complications of childhood obesity and overweight.

Materials and methods. A cohort non-interventional study included 200 children aged 8 to 14 years with obesity criteria (body mass index greater than the 97th percentile for age and sex and/or waist circumference greater than the 97th percentile for age and sex) and overweight (body mass index greater than the 85th percentile and less than the 97th percentile for age and sex and/or waist circumference greater than the 85th percentile and less than the 97th percentile for age and sex). Children were divided into comparison groups depending on their physical development. Group 1 included overweight children (133 children), and Group 2 included obese children (67 children). Exclusion criteria were the presence of infectious, endocrine, immune and genetic diseases that could lead to liver damage.

The diagnosis of ALT was made in the presence of increase in ALT levels of more than 22 U/L for girls and 26 U/L for boys (level of evidence A1) for more than two months, the presence of liver steatosis on ultrasound, and the determination of the stage of the disease (steatosis, steatohepatitis, or liver fibrosis/cirrhosis), if possible [7].

The questionnaire used for the study has sections on the nutritional characteristics of the patient's family, with a note on the presence of diseases of family members; the nature of the patient's diet at the time of the examination, indicating the amount and range of food per week, dietary regimen, etc.

Statistical data processing was performed using the Statistica 12 software package. The study was conducted at the clinical base of the Multidisciplinary Medical Centre as part of the scientific work of the Department of Pediatrics of Odesa National Medical University (Protocol of the Bioethics Committee Meeting No. 13 of May, 10 2023). All stages of the study were carried out in accordance with the Declaration of Helsinki on the Ethical Principles for Medical Research, the CoE Convention on Human Rights and Bioethical Aspects, and the laws of Ukraine.

Study results and discussion. According to the criteria of the International Diabetes Association [8], the main components of metabolic syndrome in children are abdominal type of subcutaneous fat distribution (according to percentile tables according to age and sex); increased blood pressure (according to percentile tables for age and sex); elevated glucose levels (more than 5.6 mmol/l) or insulin resistance or type 2 diabetes mellitus or elevated glycated hemoglobin levels; elevated cholesterol or high-density lipoprotein levels (less than 0.9 mmol/l) and elevated triglyceride levels (more than 1.7 mmol/l).

When assessing the complaints of the children under study, the most frequent were changes in food preferences (mainly cravings for foods containing sugar and easily digestible carbohydrates) in 180 children. The gastrointestinal complaints included nausea in 33 children, bitterness in the mouth in 27 children, abdominal pain without clear localization in 82 children, and constipation in 121 children. Anamnesis revealed the following disorders and peculiarities of feeding in the first year of life and at an early age:

– Early artificial feeding (natural feeding for less than 1 month) in 147 children of the study cohort and in the vast majority of obese children;

– Late introduction of solid components of complementary foods (later than 27 weeks of age) in 127 children, most of them in group 1 (57 children).

In general, the presence of eating disorders (consumption of large amounts of carbohydrates, fast food, sweet drinks, etc.) was noted in 165 children of the study cohort (65 children in group 2 and 100 patients in group 1). A decrease in physical activity (less than 60 minutes per day) and an increase in screen time (more than 2 hours per day, including the school curriculum) was observed in 189 children (65 obese children and 124 patients with a normal weight); lack of activities at the sports clubs – in 167 children (60 children in group 2 and 107 children in group 1). The majority of children in the study cohort showed a tendency of changes in physical development towards overweight and obesity from the age of 2 (97 children). Rapid weight gain was recorded in 84 children in the study cohort. Rapid weight gain was defined as a weight gain exceeding +2σ according to the WHO curves [4]. A burdened family history (overweight/obesity, T2DM, changes in eating behavior) was found in 191 families (65 children of group 2 and 126 children of group 1).

Most of the pathological findings identified in the objective clinical examination of children in the study cohort could be attributed to physical development parameters and changes in the distribution of subcutaneous fat (abdominal type), which were found in 84 children,

an increase in waist circumference > 97th percentile (99 children), and BMI > 85th percentile (37 children). Changes in blood pressure depending on age and sex were detected in 5 children (Table 1).

To detect possible metabolic complications of obesity and overweight, all children in the study cohort underwent tests of the activity of alanine aminotransferase (ALT), alkaline phosphatase and the main indicators of carbohydrate and lipid metabolism. Ultrasound examination of the abdominal cavity and kidneys was also performed.

Comparison of the results of laboratory and instrumental studies in overweight and obese children is shown in Table 2.

Obese children (group 1) had significantly more frequent increases in ALT activity, total cholesterol, and NOMA, which is consistent with the data from many studies on the sensitivity and specificity of clinical screening for MAFLD in children [3].

The distribution of patients with metabolic complications of obesity and overweight between the comparison groups in the study cohort is shown in Table 3.

The data of our study on the assessment of life and medical history in a cohort of overweight and obese children indicate the probable high significance of risk factors associated with early artificial feeding, late introduction of solid complementary foods, high sugar intake, easily digestible carbohydrates and subsequent development of metabolic complications. The statistical significance of these factors is evidenced by the results obtained in studies by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition and the American Association for the Study of Liver Diseases [4, 5].

It should be noted that the metabolic complications of obesity and overweight in children of the comparison groups have nonspecific clinical manifestations, which correlates with many European studies [3].

The assessment of all metabolic complications revealed a high incidence of MAFLD both in patients of group 2 and in overweight children, which emphasizes the need to screen for these conditions and prevent the development of metabolic complications not only in obese but also in overweight children. Despite the fact that carbohydrate and fat metabolism disorders are mostly present in obese children, their detection, treatment and prevention are an urgent task in the management of not only obese but also overweight children.

Table 1

Assessment of the frequency of main complaints, changes in anamnestic and objective data in obese and overweight children

Clinical data	Frequency	
	1 group, n=133, %	2 group, n=67, %
Complaints		
Changes in food preferences	88.50	92.38
Constipation	55.50	70.03
Pain syndrome without clear localization	43.50	35.76
Rapid weight gain	22.50	80.46
Nausea	4.50	40.23
Bitterness in the mouth	7.50	25.33
Life and medical history data		
Artificial feeding	65.25	89.40
Late introduction of solid components of complementary foods	50.25	89.40
Early tendency to accelerate the rate of weight gain	30.00	65.56
Presence of obese patients with metabolic complications in the family	94.50	96.85
Reduced physical activity and increased screen time	93.00	96.85
Recorded eating disorders	75.00	96.85
Objective examination data		
Abdominal type of subcutaneous fat distribution	24.00	77.48
Plaque on the tongue	52.50	70.03
Increase in waist circumference	33.75	80.46
Increase in BMI	3.75	47.68
Increase in blood pressure	0.75	5.96

Table 2

Results of laboratory and instrumental studies in overweight and obese children

Laboratory and instrumental data	Group 1, n=133%	Group 2, n=67
Increase in ALT depending on the sex and age norm	23.88	12.03
Increase in alkaline phosphatase	26.67	18.8
Increase in cholesterol levels	33.33	15.04
Increase in triglyceride levels	26.67	14.29
Increase in HDL	23.33	13.53
Increase in glucose levels	37.31	33.83
Increase in glycosylated hemoglobin level	33.33	24.06
Increase in the NOMA index	30.00	15.04
Changes in liver ultrasound examination	53.33	57.14

Table 3

Prevalence of metabolic complications in overweight and obese children

Metabolic complications	Group 1, n=133, % (95% CI)	Group 2, n=67, % (95% CI)
Metabolically associated fatty liver disease	23.88 (13.68–38.88)	15.04 (9.19–23.22)
Prehypertension	0.75* (0.01–4.18)	5.97 (1.62–15–28)
Diabetes mellitus type 2	2.25* (0.46–6.52)	10.45 (4.20–21.53)
Disorders of carbohydrate metabolism / Prediabetes	40.3 (26.56–58.63)	42.11 (31.81–54.68)
Disorders of lipid metabolism	25.37 (14.78–40.62)	15.04 (9.19–23.22)

*The difference between the comparison groups is statistically significant

Conclusions. Metabolic complications of childhood overweight and obesity are asymptomatic and underdiagnosed conditions, which lead to their progression and negative impact on the health of young adults.

Among the most frequent factors that may be associated with the development of metabolic complications in overweight and obese children, a group of factors associated with early artificial feeding and subsequent eating habits, as well as a sedentary lifestyle, deserve attention.

MAFLD occurs and requires treatment in both obese and overweight children.

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