Assessment of the intestinal microbiota and fecal short-chain fatty acids content in children with non-alcoholic fatty liver disease

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Abstract. Background. Changes in the intestinal microbiome trigger the development and progression of non-alcoholic fatty liver disease (NAFLD). Adverse fluctuations in intestinal microbiota are associated with increased intestinal permeability, activation of mucosal and adaptive immunity, increase in production and intestinal absorption of short-chain fatty acids (SCFA). The ratio of acetic, propionic, butyric acid is an important indicator of the integrity of the microbial community of the intestine. Thus, the study of the gut microbiota composition and short-chain fatty acids production represents a very appealing approach to increasing our knowledge about the mechanisms leading to NAFLD in children. The purpose of the study was to determine the features of the fecal short-chain fatty acids (ISCFA) content and the colonic microbiota composition in children with NAFLD.

Materials and methods. A comprehensive examination of 102 children was provided in the Department of Pediatric Gastroenterology of the Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine. According to the presence of obesity, transient elastography data and alanine aminotransferase levels the patients were divided into four groups: I group — children with simple hepatic steatosis (n = 24); II group — children with nonalcoholic steatohepatitis (NASH) (n = 14); III group — children with obesity without steatosis (n = 48), IV group — children with normal weight (n = 16). Chromatographic study of ISCFA was conducted using gas chromatograph Chromatec Crystal 5000. The microorganisms were identified using a microbiological study of the colon content. Diagnosis of NAFLD was established with FibroScan 502 Touch (Echosens, France) with the determination of the controlled attenuation parameter.

Results. Significant changes in the spectrum of ISCFA were observed in children of the III group with acetic acid content increased by 4.8 times (р < 0.05), propionic acid by 1.5 times (р < 0.001), and butyric acid by 1.7 times as compared to the control group, while in children with NASH, acetic content was 2.5-fold increased, propionic and butyric acid — 1.4-fold in comparison with the control group (р = 0.1). Also, significant anaerobic index decrease was observed in NAFLD patients. The fecal content microbiological examination demonstrated the reduced level of Bifidobacteria strains in 11.8 % patients of group I and in 8.3 % of group III; decreased levels of Lactobacillus were found in 70.6 % children of group I, in all children with NASH, in 70.8 % patients of group III. Overgrowth of bacteria such as Klebsiella was identified in 23.5 % patients of group I and in 8.3 % of group III; decreased levels of Lactobacillus were found in 70.6 % children of group I, in all children with NASH, in 70.8 % patients of group III. Overgrowth of bacteria such as Klebsiella was identified in 23.5 % patients of group I and in 8.3 % of group III; Pathogenic Staphylococcus was detected in 5.9 % patients of group I, in 8.3 % patients of group III. Overgrowth of Candida was detected in 23.5 % children of group I and in 20.8 % children of group III. Pathogenic Staphylococcus was detected in 5.9 % patients of group I, in 8.3 % patients of group III. Overgrowth of Candida was detected in 23.5 % children of group I and in 20.8 % children of group III. Conclusions. Quantitative and qualitative deviation of intestinal microbiota such as a decrease in the number of major symbionts and an increase in the number of opportunistic microflora was observed in children with NAFLD and obesity. Changes in the SCFA spectrum were found in obese children assuming the importance of intestinal microflora disorders at the early stages of NAFLD development. The estimation of the ratio of SCFA fractions with the anaerobic index calculation can be useful to diagnose intestinal dysbiosis in children with NAFLD.

Keywords: non-alcoholic fatty liver disease; short-chain fatty acids; intestinal microflora; children; obesity
**Introduction**

In the last 40 years, the prevalence of obesity has increased significantly in the general pediatric population: its global age-standardized prevalence has almost raised by 10 times [1]. The global obesity epidemic is increasing the burden of several non-communicable diseases, including nonalcoholic fatty liver disease (NAFLD), which is now recognized as the most frequent cause of chronic liver disease in adults and children worldwide [2]. Meta-analyses suggested that children and adolescents with overweight/obesity were 26.1 times more likely to have non-alcoholic fatty liver disease [3]. The development of NAFLD is highly dependent on age, gender and ethnicity [4]. Fatty liver in adolescents is more common than in young children and is twice more frequent in boys than in girls [5, 6]. Unfortunately, despite considerable progress in understanding the complexity of the disease, the pathophysiological mechanisms involved in the onset and progression of liver damage in paediatric NAFLD remain unclear [2]. It has been proved that fat accumulation in the liver and insulin resistance, influenced by genetic susceptibility, epigenetic mechanisms, a sedentary lifestyle, and hypercaloric diets are the main factors triggering NAFLD development and progression [7]. However, the gut’s critical role in NAFLD pathogenesis has recently been given consideration. In the latest meta-analysis of Karn Wijarnpreecha et al., a significant association between NAFLD and small intestinal bacterial overgrowth was observed with the pooled odds ratio of 3.82 (95% confidence interval, 1.93–7.59) [8]. The mechanisms by which microbiota propagate NAFLD are complex and thought to relate to a combination of deriving increased energy from dietary sources and promoting increased intestinal permeability via loss of intestinal epithelial barrier integrity, leading to bacterial translocation into the portal circulation, innate immune receptors stimulation and activation of the signaling pathways involved in liver inflammation and fibrogenesis [9, 10]. Additionally, animal models suggest that intestinal microbiota may influence several of the putative processes involved in the development and progression of NAFLD, including choline metabolism, endotoxemia, obesity, liver inflammation, and fibrosis [11]. Moreover, bacterial fermentation of dietary carbohydrates may contribute to augmenting oxidative stress through the production of endogenous alcohol and short-chain fatty acids (SCFA). Further hydrolysis of SCFA, which are produced by different microbial fermentation pathways, leads to the generation of more ATPs and simple carbon molecules that are further utilized for de novo synthesis of lipids and glucose by the host [12, 13]. The vast wealth of animal data suggests that SCFA has an important regulatory role in body weight control and insulin sensitivity through the effects on lipid metabolism and glucose homeostasis [14]. So, altering intake of dietary carbohydrates (and fibre) or the intestinal microbiome composition (particularly the *Bacteroidetes/Firmicutes* ratio) will significantly affect SCFA production and dietary energy and can promote NAFLD development.

Additionally, SCFA synthesis is an important factor in colonization resistance, which ensures the stability of the composition of the intestinal microflora. The ratio of acetate, propionate, butyrate is an important indicator of the integrity of the gut microbial community, which remains constant within a small interval of concentrations. The ratio of the total SCFA content to the acetic acid concentration that is called the anaerobic index (AI) allows evaluating the metabolic activity of anaerobic, indigenous gut microbiota in the total metabolic activity of all microbial tissue complex and can characterize the composition of the microbial community [15]. Nevertheless, only a few reports nowadays illustrate the role of microbiota associated with NAFLD with metabolomics data in children [16]. So, the purpose of our study was to determine the features of the fecal short-chain fatty acids content and the colonic microbiota composition in children with non-alcoholic fatty liver disease.

**Materials and methods**

We provided a comprehensive examination of 102 children treated at the Department of Pediatric Gastroenterology of the State Institution “Institute of Gastroenterology of NAMS of Ukraine”. According to the presence of obesity, transient elastography data and alanine aminotransferase levels, the patients were divided into four groups:

- group I — children with simple hepatic steatosis (n = 24);
- group II — children with nonalcoholic steatohepatitis (NASH) (n = 14);
- group III — children with obesity without steatosis (n = 48);
- group IV — children with normal weight (comparison group) (n = 16).

A comprehensive assessment of the gut microbiota included the following studies:

- macroscopic examination of feces, its characteristics; microscopic examination of feces, semi-quantitative determination of vegetable muscle fibers, their degree of digestion, fats, fatty acids and their salts, as well as crystals; the presence of iodophilic microflora, fungi, parasites;
- study of the species and quantitative composition of the microflora of the colon content with the determination of *Enterobacteriaceae*, *Bacilli*, fungi;
- determination of SCFA concentrations by gas chromatography by direct introduction of the acidified supernatant of the feces into the evaporator of the chromatograph, followed by separation on a capillary column with detection of the components of the mixture on an ionization detector.

Investigation of the species and quantitative composition of the microflora of the gut contents was performed by the method of serial ten-fold dilutions on a standard set of elective and differential-diagnostic nutrient media for isolation of aerobic and anaerobic microorganisms [17].

SCFA in feces was determined by a chromatographic study using a hardware-software complex for medical research based on the Chromatec-Crystal 5000 gas chromatograph by the method of Guohua Zhao [18]. Quantitative identification of free fatty acids fractions, column calibration and chromatogram calculation were performed using the method of normalization of peak areas and their fractions according to the standards of fatty acids of Sigma-Aldrich (USA).
Statistical analysis of the survey results was carried out using Excel Microsoft Office 2010 and SPSS 9.0 for Windows. Comparisons of the mean values of the variables were performed using the Mann-Whitney U-test. The statistical significance of the difference was estimated to be at least 95.0% (error probability p < 0.05).

Results and discussion

The content of fecal SCFA in children with NAFLD allows evaluating in a short time the structural and metabolic changes in the activity of the gut microflora. Children of group I showed a tendency to increase the content of fecal acetic acid and butyric acid by 1.5 times in comparison with group IV (children with normal weight), but differences were not significant (Fig. 1–3). Comparative analysis of the SCFA content in NASH group indicated a 2.5-fold increase in acetic acid content, a tendency to a 1.4-fold increase in propionic and butyric acids content compared to group IV (Fig. 1–3).

The most profound changes in the SCFA spectrum were observed in children of group III, where acetic acid increased by 4.8 times, propionic acid by 1.5 times and butyric acid by 1.7 times as compared to group IV. These changes may indicate the switching of colon cells metabolism from the Krebs cycle to the anaerobic variant of glycolysis. An increase in propionic and butyric acids content in children indicated the presence of propionic, acetic to a greater extent, and butyric fermentation.

The results of the study of AI values demonstrate the deviation of the anaerobic index value in children with NAFLD and obesity, which reflects the “anaerobization” of the luminal environment. AI value reflects the ratio of strict anaerobes to aerobes, revealed its increase in children of groups I–III that indicates the suppression of strict anaerobic intestinal microflora population in children with NAFLD and obesity (Fig. 4).

Studies of SCFA content in patients with NAFLD of several authors demonstrated inconclusive results. Our data indicate an increase in acetic, propionic and butyric content in NAFLD patients as well as in obesity patients. Adult NAFLD patients (with a median age of 52 years) demonstrate a significant increase in fecal propionic and butyric acids content [15], which may indicate a decrease in the number and activity of obligate microorganisms such as *Bifidobacterium* producing acetic acid and an increase in facultative and residual anaerobic bacteria.

Our findings and literature data suggest that the overweight children have a greater ability to ferment non-digestible polysaccharides compared to healthy ones, which results in increased levels of monosaccharides and SCFA [19]. It is believed that methanogenic bacteria that are able to use hydrogen for the synthesis of methane, which optimizes the processes of bacterial fermentation, are involved in this process. M. Goffredo et al. observed that the butyric acid blood concentration in children had a positive correlation with liver fat deposition [13]. However, another study...
found a decrease in the levels of fecal propionic and butyric acids in obese patients compared to healthy children, which could be explained by increased intestinal absorption [20]. Changes in the composition of the microbiota in favor of an increase in representatives contributing to the production of SCFA cause additional energy extraction from food. Chronic energy excess can lead to fat accumulation in the liver and the development of NAFLD [21, 22].

Microbiological studies of the colon content in the examined children showed the changes in the qualitative and quantitative composition of the microflora (Table 1, Fig. 5).

Also, a decrease in the level of Bifidobacterium was observed in 4 (16.7 %) patients of group I and in 4 (8.3 %) of group III, whereas a decrease in the concentration of Lactobacillus was detected in 17 (70.8 %) patients of group I, in all patients of group II, in 34 (70.8 %) patients of group III. Conditionally pathogenic Enterobacteria of the Klebsiella group were isolated in 25.0 % patients of group I and in 8.3 % children of group III. Staphylococcus aureus was detected in 8.3 % of patients in group I, in 14.3 % patients of group II and in 20.8 % children of group III, the level of Candida was increased. Besides, in 12.5 % patients of group I and group III, hemolytic strains of Escherichia coli were found, which normally are absent in the colon content. In half of the cases, their dominance over Escherichia coli with normal enzymatic activity was observed.

Table 1 — Colon microflora composition in children of studied groups

| Microorganisms                            | Value, CFU/g | I group, n (%) | II group, n (%) | III group, n (%) | IV group, n (%) |
|-------------------------------------------|--------------|----------------|----------------|-----------------|----------------|
| Bifidobacterium                           | ≥10⁹ (normal values) | 20 (83.3) | 14 (100) | 44 (91.7) | 14 (100) |
|                                           | < 10⁹        | 4 (16.7) | 0 | 4 (8.3) | 0 |
| Lactobacillus                             | ≥ 10⁷ (normal values) | 7 (29.2) | 0 | 14 (29.2) | 7 (50.0) |
|                                           | < 10⁷        | 17 (70.8) | 14 (100) | 34 (70.8) | 7 (50.0) |
| Enterococci                               | < 10⁸        | 3 (12.5) | 2 (14.3) | 2 (4.2) | 0 |
| E. coli                                  | ≥ 10⁷ (normal values) | 18 (75.0) | 12 (85.7) | 36 (75.0) | 7 (87.5) |
|                                           | < 10⁷        | 6 (25.0) | 2 (14.3) | 12 (25.0) | 1 (12.5) |
| E. coli lactose-negative                  | > 10⁴        | 2 (8.3) | 2 (14.3) | 0 | 0 |
| E. coli hemolytic                         | > 10⁴        | 3 (12.5) | 0 | 6 (12.5) | 0 |
| Proteus                                   | > 10⁴        | 0 | 0 | 2 (4.2) | 0 |
| Conditionally pathogenic Enterobacteria  | > 10⁴        | 6 (25.0) | 0 | 4 (8.3) | 0 |
| Candida                                   | > 10²        | 6 (25.0) | 2 (14.3) | 10 (20.8) | 0 |
| Non-pathogenic Staphylococcus             | > 10⁴        | 3 (12.5) | 1 (7.1) | 2 (4.2) | 0 |
| S. aureus                                 | > 10²        | 2 (8.3) | 0 | 4 (8.3) | 0 |
| Pathogenic Enterobacteria                 | –            | – | – | – | – |

Figure 5 — Deviation of intestinal microbiota in children with NAFLD and obesity
So, microbiological examination of the gut content showed the changes in the qualitative and quantitative microflora composition in patients with obesity and NAFLD. NAFLD children presented with a significant decrease in the amount of *Bifidobacterium* and *Lactobacillus*, an increase in hemolytic and lactose-negative strains of *E. coli*, and growth of *Candida*, *Klebsiella*, *Staphylococcus aureus*. This alteration of the intestinal microbiota composition may contribute to the NAFLD development and progression.

Thus, in children with NAFLD, the changes in the intestinal microflora composition by the results of the microbiological study, and in the content of fecal SCFA such as acetate, propionic and butyric acids were observed. Considering the microbial origin of acetate (C2) and its pathological effects on the human body (leading to increased secretion of insulin), increasing of its content may be one of the causes that contributes to the development of NAFLD in children. The detected changes were confirmed by correlation between AI and *Lactobacillus* content ($r = -0.493; p < 0.05$), *Proteus* content and acetic acid concentration ($r = -0.480; p < 0.05$).

Further studies of the influence of the microbiota on the development of NAFLD in children are needed which may contribute to the development of new methods for the diagnosis, prevention and treatment of NAFLD in children.

**Conclusions**

1. Quantitative and qualitative deviations of intestinal microbiota such as a decrease in the number of major symbionts and an increase in the number of opportunistic microflora were observed in children with NAFLD and obesity.
2. The most profound changes in the SCFA spectrum were found in obese children assuming the importance of intestinal microflora disorders at the early stages of NAFLD development.
3. The estimation of the ratio of SCFA fractions with the anaerobic index calculation can be useful to diagnose intestinal dysbiosis in children with NAFLD.

**Conflicts of interests.** Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

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**The contribution of the authors:** Zavhorodnia N. Yu. — conception and design of the study, text editing; Lukianenko O. Yu. — selection of patients, processing of clinical and statistical data, translation of the article into English; Kleinina I.A., Hrabovska O.I. — collection and processing of the material, statistical processing, performance of biochemical studies, writing the article; Tatarchuk O.M., Vishnarevska N.S. — collection and performance of microbiological studies, statistical processing, analysis of microbiological results.

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Оцінка стану інтенсивної мікрофлори та вмісту коротколанцюгових жирних кислот копрофільтрату в дітей з неалкогольною жировою хворобою печінки

**Резюме. Актуальність. Якісні та кількісні зміни стану кишкового мікрофлору сприяють розвитку та прогресуванню неалкогольної жирової хвороби печінки (НАЖХП). Дієтологічна підтримка повинна бути приоритетним напрямом в лікуванні цієї хвороби. Через це у дитячій практиці важливо вивчати особливості метаболічного стану інтенсивної мікрофлори та вмісту коротколанцюгових жирних кислот в копрофільтраті в дітей з НАЖХП.**

**Мета роботи:** Вивчити особливості стану кишкової мікрофлори у дітей з НАЖХП та коротколанцюгових жирних кислот у дітей з навантаженням із розрахунку національного гастроентерологічного центру.

**Матеріали та методи.** Комплексне обстеження 102 дітей було проведено у відділенні дитячої гастроентерології інституту гастроентерології Національної академії медицини України. Відповідно до наявності інфекцій, даних транзієнтної еластографії і рівня аланінамінотрансферази пацієнти були розділені на чотири групи: I група — діти з простим стеатозом печінки (n = 24); II група — діти з неалкогольним стеатогепатитом (НАСГ) (n = 14); III група — діти з ожиріння без стеатозу печінки (n = 48); IV група — діти з нормальною вагою (n = 16). У дітей з НАЖХП виявлено значні зміни спектра коротколанцюгових жирних кислот у розрахунку національного гастроентерологічного центру (КЖК) та вмісту коротколанцюгових жирних кислот у фекаліях дітей з НАЖХП.

**Результати.** У дітей з ожирінням (I група) була заохочена ассоціація КЖК з підвищеним інтенсивним рівнем коротколанцюгових жирних кислот у селективних видів кишкової мікрофлори. Найбільш виражені зміни спектра коротколанцюгових жирних кислот у дітей з НАСГ, у 70,6 % дітей I групи, у всіх дітей III групи. Надмірне зростання Klebsiella виявлені в 23,5 % пацієнтів I групи та у 8,3 % III групи; зниження вмісту Lactobacillus у 70,6 % дітей I групи, у всіх дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи.

**Обговорення.** Незважаючи на патентований стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи. Патогенний кишечник у 70,8 % пацієнтів III групи. Патогенний стафілокок знайдений у 5,9 % пацієнтів I групи, в 8,3 % III групи. Надмірне зростання Candida виявлене в 23,5 % дітей I групи, у 14,3 % дітей II групи та у 20,8 % дітей III групи.

**Ключові слова:** неалкогольна жирова хвороба печінки; коротколанцюгові жирні кислоти; кишкова мікрофлора; діти; ожиріння

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Резюме. Актуальность. Качественные и количественные изменения кишечного микробиома способствуют развитию и прогрессированию неалкогольной жировой болезни печени (НАЖБП). Девиации представительства кишечной микрофлоры ассоциированы с повышением кишечной проницаемости, активацией врожденных и адаптивных иммунных реакций, увеличением продукции и всасывания в кишечнике короткоцепочечных жирных кислот (КЖК). Соотношение уксусной, пропионовой и масляной кислот является важным показателем целостности микробного сообщества кишечника. Таким образом, изучение состава кишечной микрофлоры и продукции короткоцепочечных жирных кислот представляет собой перспективное направление, способствующее пониманию механизмов, приводящих к развитию НАЖБП у детей.

Цель работы: изучить особенности состояния кишечной микрофлоры и содержания фекальных короткоцепочечных жирных кислот у детей с НАЖБП.

Материалы и методы. Комплексное обследование 102 детей было проведено в отделении детской гастроэнтерологии Института гастроэнтерологии Национальной академии медицинских наук Украины. В зависимости от наличия ожирения, данных транзиентной эластографии и уровня аланинаминотрансферазы пациенты были разделены на четыре группы: I группа — дети с простым стеатозом печени (n = 24); II группа — дети с неалкогольным стеатогепатитом (НАСГ) (n = 14); III группа — дети с ожирением (n = 48), IV группа — дети с нормальным весом (n = 16). Хроматографическое исследование КЖК проводилось с помощью газового хроматографа «Хроматек-Кристалл 3000». Идентификация микроорганизмов осуществлялась с использованием микробиологического исследования содержимого толстой кишки. Диагноз НАЖБП подтвержден при помощи аппарата «FibroScan 502 Touch» (Echosens, Франция) с определением контролируемого параметра затухания ультразвука. Результаты. У детей с ожирением (III группа) выявлены значительные изменения в спектре КЖК: увеличение содержания уксусной кислоты в 4,8 раза (p < 0,05), пропионовой кислоты в 1,5 раза (p < 0,001) и масляной кислоты в 1,7 раза в сравнении с контрольной группой. У детей с НАСГ содержание уксусной кислоты в копрофильтрате было увеличено в 2,5 раза, пропионовой и масляной кислот в 1,4 раза по сравнению с контрольной группой (p = 0,1). Также наблюдалось значительное снижение анаэробного индекса у пациентов с НАЖБП. Микробиологическое исследование кала продемонстрировало снижение количества бифидобактерий у 11,8 % пациентов I группы и у 8,3 % III группы; снижение содержания Lactobacillus у 70,6 % детей I группы, у всех детей с НАСГ, у 70,8 % пациентов III группы. Избыточный рост Klebsiella обнаружен у 23,5 % пациентов I группы и у 8,3 % детей III группы; патогенный стафилококк выявлен у 5,9 % пациентов I группы, у 8,3 % пациентов III группы. Избыточный рост Candida был выявлен у 23,5 % детей I группы, у 14,3 % детей II группы и у 20,8 % детей III группы.

Выводы. У детей с НАЖБП и ожирением наблюдаются количественные и качественные изменения кишечной микрофлоры в виде уменьшения численности основных симбионтов и увеличения условно-патогенной микрофлоры. Наиболее выраженные изменения спектра фекальных КЖК были обнаружены у детей, страдающих ожирением, что может свидетельствовать о значимости нарушений микрофлоры кишечника на ранних стадиях развития НАЖБП. Определение соотношения фракций фекальных КЖК с вычислением анаэробного индекса может быть полезным для оценки состояния кишечной микрофлоры у детей с НАЖБП.

Ключевые слова: неалкогольная жировая болезнь печени; короткоцепочечные жирные кислоты; кишечная микрофлора; дети; ожирение