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Serum biomarkers in the metabolic dysfunction-associated steatotic liver fibrosis diagnosis in children

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Abstract. Background. The COVID-19 epidemic and the war in Ukraine have led to a significant increase in the number of children suffering from metabolic dysfunction-associated steatotic liver disease (MASLD). One of the unresolved problems associated with MASLD is the identification of individuals at risk of rapid disease progression and development of irreversible liver changes. The search for alternative noninvasive markers suitable for the early detection of liver fibrosis in children remains extremely relevant. The aim of the study was to determine the diagnostic value of serum fibrosis markers and their relationship with sonographic and body composition parameters in children with MASLD. **Materials and methods.** The case-control study included 80 children aged 6 to 17 years (mean of 12.15 ± 2.51 years). The presence of steatosis and liver fibrosis was determined by transient elastography (FibroScan® 502 touch F60156, Echosens, France). All subjects underwent anthropometric studies to determine body mass index. If it was within one-two Z-score, overweight was diagnosed. If the body mass index exceeded two Z-score, obesity was diagnosed. According to transient elastography and body mass index, all children were divided into four groups: group I — 27 children with MASLD and fibrosis $\geq F1$, group II — 35 children with MASLD without fibrosis, group III — 18 obese or overweight children without MASLD and without fibrosis. The control group IV consisted of 14 children with normal weight without MASLD and without fibrosis. The groups had no significant differences in age and gender distribution. The study of body composition was performed by bioimpedance analysis using a TANITA MC-780MA analyzer (manufactured by Maeno-cho, Itabashi-ku, Tokyo, Japan). Quantitative determination of the serum concentration of vascular endothelial growth factor (VEGF) was performed by enzyme-linked immunosorbent assay (ELISA) using test systems from Wuhan Fine Biotech Co., Ltd (China) according to the manufacturer's recommendations. The level of serum cytokeratin 18 (CK-18) was evaluated with IDL Biotech AB kits (Sweden) for ELISA. Serum content of transforming growth factor beta 1 (TGF- β 1) was studied using an ELISA test system from IBL International (Germany). Fibrogenesis processes were evaluated by the serum content of free hydroxyproline (HPf), protein-bound hydroxyproline (HPp/b) and glycosaminoglycans (GAG). **Results.** The study revealed a significant increase in the level of CK-18 and TGF- β 1 in children with MASLD-associated liver fibrosis. In children with liver fibrosis, an increase in the ratio of HPf/HPp/b and the level of GAG in the blood serum was observed compared to patients with MASLD without fibrosis and with overweight and obese children. The threshold value of CK-18 for liver fibrosis diagnosis was 90.3 U/l (sensitivity 81.3 %, specificity 76.9 %, AUC 0.843, $p < 0.001$). The sensitivity of the threshold value of serum TGF- β 1 (96.8 pg/mL) in children with MASLD was 80.0 %, specificity 65.7 %, AUC 0.787 ($p < 0.001$). Threshold value of serum GAG (4.24 mmol/L) demonstrated a sensitivity of 70.6 % and a specificity of 69.6 %, AUC 0.743 ($p < 0.01$). CK-18, TGF- β 1, GAG shown a positive correlation with liver stiffness and elasticity, body composition of MASLD children and had high levels of diagnostic accuracy, which allows them to be used in children when screening for MASLD-associated liver fibrosis. **Conclusions.** Children with liver fibrosis are characterized by elevated serum levels of CK-18, VEGF, TGF- β 1, HPp/b and GAG. The threshold values of CK-18 (more than 90.3 U/l), TGF- β 1 (above 96.8 pg/mL) and GAG (more than 4.24 mmol/l) have high sensitivity and specificity, which allows them to be used for the diagnosis of liver fibrosis in children with MASLD. **Keywords:** children; metabolic dysfunction-associated steatotic liver disease; fibrosis; cytokeratin 18; glycosaminoglycans; transforming growth factor beta 1

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Introduction

The COVID-19 epidemic and the war in Ukraine have led to a significant increase in the number of children suffering from metabolic dysfunction-associated steatotic liver disease (MASLD). Physical activity restrictions, social deprivation, and stress-related eating disorders have become promoters of weight gain in children, the development of obesity-related metabolic disorders and comorbidities, including MASLD [1–3].

One of the unresolved problems associated with MASLD is the identification of individuals at risk of rapid disease progression and the development of irreversible liver changes [4]. It has been demonstrated that children with MASLD, in particular, metabolic-associated steatohepatitis (MASH), have significantly higher rates of overall and liver-associated mortality compared to the general population [5]. Advanced fibrosis (\geq F3) is recognized as an independent predictor of liver-related complications and overall mortality in adults with MASLD [6]. A ten-year follow-up of the course of MASLD in a pediatric European cohort confirmed the development of advanced fibrosis in 6 % of children, which indicates the need for early diagnosis of fibrosis for the selection of high-risk patients [7].

Nowadays, histologic evaluation of liver biopsies remains the reference standard for quantifying fibrosis and characterizing zonal distribution of collagen [8]. At the same time, the well-known difficulties associated with biopsy and evaluation of its results, such as the risk of complications, heterogeneous tissue distribution of fibrosis, and subjectivity in data characterization, are becoming obstacles to the widespread introduction of biopsy in pediatric practice [9]. Moreover, liver biopsy is unsuitable for screening in high-risk groups and long-term monitoring of the disease [10].

Numerous non-invasive tests have become an alternative to biopsy, which have been developed to determine the clinical form of the disease and risk stratification, in particular for the diagnosis of steatosis, MASH, and liver fibrosis [6]. Noninvasive methods for quantifying liver fibrosis include imaging techniques such as liver stiffness assessment by elastography [11], serum biomarkers [12], and combined scores [13]. Activated by inflammatory, damage-associated, and metabolic signals, liver stellate cells play a key role in fibrogenesis mechanisms by promoting the overproduction and deposition of extracellular matrix proteins, which leads to the formation of fibrosis with subsequent vascular remodeling [14]. Thus, serological markers that reflect the activity of inflammation, apoptosis, collagen formation and lysis, and angiogenesis can be useful for fibrosis detection, that has been confirmed by experimental and clinical studies [15–18]. At the same time, a comparative study of the diagnostic accuracy of serum fibrosis markers and combined scores for detecting liver fibrosis in adults with MASLD (LITMUS project) showed that none of the studied markers reached the area under the ROC curve (AUC) value acceptable for replacing biopsy [19]. Evaluation of the diagnostic accuracy of combined fibrosis scores in a pediatric cohort also showed no advantages over biopsy and ALT levels [9]. Thus, the study for alternative non-invasive markers suitable for the early detection of liver fibrosis in MASLD children remains extremely relevant.

The purpose of the study was to determine the diagnostic value of serum fibrosis markers and their relationship with sonographic and body composition parameters in children with MASLD.

Materials and methods

The case-control study included 80 children aged 6 to 17 years (mean age (12.15 ± 2.51) years). The inclusion criteria were the presence of MASLD, overweight or obesity. The exclusion criteria were: infectious or other inflammatory acute diseases, the presence of clinical, anamnestic, biochemical and serological signs of chronic viral, autoimmune and drug-induced hepatitis, Wilson's disease.

Verification of the diagnosis of MASLD was conducted following the joint consensus of the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), the European Association for the Study of the Liver (EASL) and others [20]. The presence of liver steatosis and fibrosis was determined by transient elastography (FibroScan® 502 touch F60156, Echosens, France). The threshold value of the controlled attenuation parameter (CAP) for the diagnosis of liver steatosis was 225 dB/m [21], cut-off of the liver stiffness for the diagnosis of liver fibrosis was 5.1 kPa [22]. All subjects underwent anthropometric measurements to determine body mass index (BMI). The assessment of nutritional status was performed according to WHO recommendations in accordance with the sigma deviations (Z-score) of BMI corresponding to age and sex [23]. Overweight was diagnosed if the BMI value was within one-two Z-score. Obesity was diagnosed in case BMI exceeded two Z-score. Body composition was evaluated by bioimpedance using a TANITA MC-780MA body composition analyzer (manufactured by Maeno-cho, Itabashi-ku, Tokyo, Japan). The following parameters of body composition were automatically measured and calculated: body fat mass (BFM, kg), body muscle mass (BMM, kg), total water content (TBW), and physical rating was assessed, taking into account the ratio of body fat to body muscle mass [24].

According to transient elastography and body mass index, all children were divided into four groups: group I — 27 children with MASLD and fibrosis \geq F1, group II — 35 children with MASLD without fibrosis, group III — 18 obese or overweight children without MASLD and without fibrosis. The control group IV consisted of 14 children with normal weight without MASLD and fibrosis. The groups had no significant differences in age and gender distribution.

Quantitative determination of the serum concentration of vascular endothelial growth factor (VEGF) was performed by enzyme-linked immunosorbent assay (ELISA) using test systems from Wuhan Fine Biotech Co., Ltd (China) according to the manufacturer's recommendations. The level of serum cytokeratin 18 (CK-18) was determined using ELISA kits from IDL Biotech AB (Sweden). Determination of the serum content of transforming growth factor beta 1 (TGF- β 1) was performed using an ELISA test system from IBL International (Germany). The ELISA was performed using a Stat Fax 303 Plus ELISA, and the optical density was measured at a wavelength of 450 nm.

Fibrogenesis activity were evaluated by the measurement of serum content of free hydroxyproline (HPf) and protein-bound hydroxyproline (HPP/b) [25] and glycosaminoglycans (GAG) [26].

Table 1 — Serum levels of CK-18, VEGF and TGF-β1 in children of the studied groups, Me (Q1; Q3)

Indicator, unit of measurement	I group (n = 27)	II group (n = 35)	III group (n = 18)	IV group (n = 14)
CK-18, U/l	101.9 (61.5; 169.8)*	73.4 (43.3; 103.0)**	56.5 (33.9; 72.0)**	46.5 (40.5; 53.4)
VEGF, UL/ml	371.1 (207.3; 1157.1)*	296.3 (160.3; 466.2)*	308.0 (177.6; 366.2)*	155.8 (132.0; 279.4)
TGF-β1, pg/ml	153.4 (99.7; 189.1)*	72.4 (53.1; 111.3)**	74.0 (50.6; 99.4)**	56.1 (46.0; 77.4)

Notes: * — $p < 0.05$ — significance of differences in comparison with group IV; ** — $p < 0.05$ — significance of differences in comparison with group I.

Table 2 — Levels of HP and GAG in blood serum in children of the study groups, Me (Q1; Q3)

Indicator	I group (n = 27)	II group (n = 35)	III group (n = 18)	IV group (n = 14)
HPf, mmol/l	11.74 (10.56; 14.08)	14.08 (10.56; 17.60)	16.45 (14.09; 17.62)	13.50 (11.15; 18.49)
HPp/b, mmol/l	244.48 (216.2; 281.9)*	242.42 (206.86; 300.72)*	263.20 (225.6; 375.99)*	206.88 (185.64; 206.88)
kHPp/b/HPf	21.37 (17.62; 26.70)*	20.0 (14.14; 23.15)*	18.29 (13.91; 19.20)*	14.40 (10.61; 19.06)
GAG, mmol/l	4.50 (3.21; 4.60)*	3.82 (3.36; 4.58)	3.66 (3.21; 4.28)	3.56 (3.40; 4.01)

Note: * — $p < 0.05$ — significance of differences compared to group IV.

The results were statistically processed using the Statistica 6.1 software package (AGAR90 serial number E415822FA). For statistical analysis of the data, descriptive statistics were used; comparison of the mean values of the variables was carried out using parametric methods (Student’s t-test) under the normal distribution. In other cases, a nonparametric method (Mann-Whitney U test) was used. The distribution was checked using the Shapiro-Wilk method. The mean values were presented as Me (Q1; Q3). The difference was considered significant if the achieved significance level (p) was below 0.05. Correlation analysis in the conditions of normal distribution of variables and linear relationship between them was performed with the calculation of Pearson’s correlation coefficient, in the conditions of distribution that differed from normal and nonlinear relationship between variables, Spearman’s correlation coefficient was calculated. To assess the diagnostic value of the indicators, ROC analysis was used to determine the AUC and its 95% confidence interval (CI), which were used to determine the quality of the diagnostic model. Optimal thresholds were selected to maximize the sensitivity and specificity, and positive and negative predictive values (PPV and NPV, respectively) were calculated.

All measurement tools used in the study were validated in accordance with the established procedure.

The study was conducted in accordance with the requirements of the Helsinki Declaration, the Convention on the Rights of the Child, the rules of good clinical practice and good laboratory practice, and national regulatory documents in the field of bioethics. Prior to the study, the parents of the patients were informed about the methods and scope of the study and gave their consent. The study protocol was approved by the local Medical and Biological Ethics Committee.

Results and discussion

The level of CK-18 in children of group I was 2.2 times ($p < 0.05$) higher than in the control group (Table 1). In addition, the median CK-18 in patients of group I was 1.4 times ($p < 0.05$) and 1.8 times ($p < 0.05$) higher than in patients of groups II and III, respectively.

The level of VEGF was increased in group I by 2.4 times ($p < 0.05$), in group II — by 1.9 times ($p < 0.05$), in group III — by 2.0 times ($p < 0.05$) compared to the control group. In patients of group I, the content of VEGF was 1.3 times ($p > 0.05$) and 1.2 times ($p > 0.05$) higher than in groups II and III, respectively. The median TGF-β1 content in group I was significantly higher than in children of groups II and III by 2.1 times ($p < 0.05$) and in the control group by 2.7 times ($p < 0.05$).

The median content of HPp/b was increased in children of all groups: in group I by 1.2 times ($p < 0.05$), in group II — by 1.2 times ($p < 0.05$), in group III — by 1.3 times ($p < 0.05$) compared to group IV (Table 2). In parallel with an increase in the level of HPp/b in children of group I, an increase in the content of GAG was observed in 1.3 times ($p < 0.05$), while in children of groups II and III, the content of GAG did not differ significantly from the control group.

The HPp/b/HPf ratio was increased in children of all groups: in group I — in 1.4 times ($p < 0.05$), in group II — 1.4 times ($p < 0.05$), in group III — 1.3 times ($p < 0.05$) compared to group IV (Table 2).

A positive correlation between the level of CK-18, the liver stiffness ($r = 0.468$; $p < 0.05$) and the liver steatosis ($r = 0.357$; $p < 0.05$) was found (Fig. 1). VEGF levels were

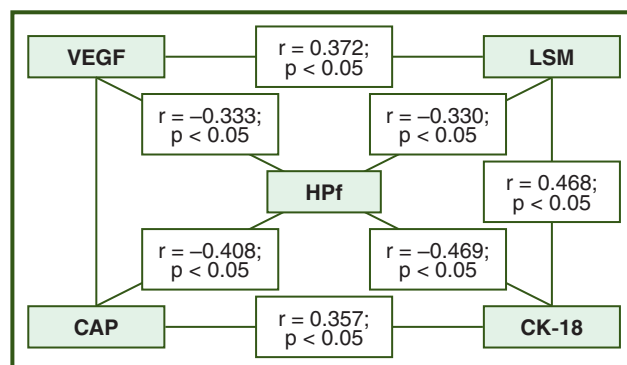


Figure 1 — Correlations of CK-18, VEGF, hydroxyproline with sonographic parameters in children with MASLD

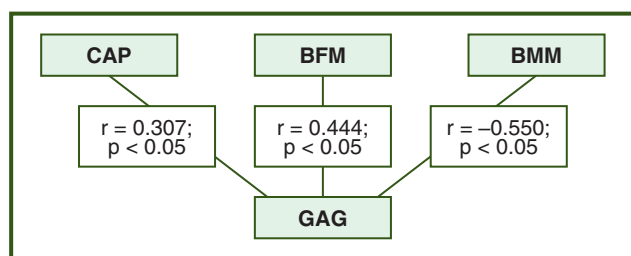


Figure 2 — Correlations of serum GAGs with sonographic and body composition parameters in children with MASLD

also positively correlated with the liver stiffness ($r = 0.372$, $p < 0.05$). Moreover, HPf was negatively correlated with CAP ($r = -0.408$, $p < 0.05$), CK-18 level ($r = -0.469$, $p < 0.05$), and the ratio kHPp/b/HPf had a positive correlation with CAP ($r = 0.307$, $p < 0.05$).

The level of GAG demonstrated a positive correlation with CAP ($r = 0.307$; $p < 0.05$), BFM ($r = 0.444$; $p < 0.05$); negative — with BMM ($r = -0.550$; $p < 0.05$) (Fig. 2).

Based on significant differences in the levels of CK-18, TGF- β 1 and GAG in children with liver fibrosis, and the detection of its stable correlations with liver stiffness and elasticity, and body composition ROC analysis was performed to determine their diagnostic accuracy. The threshold value of CK-18 for the diagnosis of liver fibrosis was 90.3 U/l (Fig. 3). This parameter demonstrated a sensitivity of 81.3 % and a specificity of 76.9 %, with AUC of 0.843 ($p < 0.001$) (Table 3).

The sensitivity of the threshold value of serum TGF- β 1 level of 96.8 pg/mL in children with MASLD was 80.0 %, specificity 65.7 %, AUC 0.787 ($p < 0.001$) (Fig. 3, Table 3). An increase in serum GAG content of more than 4.24 mmol/L demonstrates a sensitivity of 70.6 % and specificity of 69.6 %, AUC 0.743 ($p < 0.01$) (Fig. 3, Table 3).

Discussion

The presence and stage of fibrosis are considered to be an important factor in predicting the course of MASLD, the likelihood of developing liver cirrhosis and liver complications, so the search for new non-invasive markers suitable for early screening of liver fibrosis in children with MASLD is crucial [5, 6]. CK-18 currently demonstrates the greatest potential among the biomarkers of MASLD, as it is a direct molecular product of hepatocyte apoptosis, and therefore naturally attracts considerable attention of researchers. A meta-analysis by Xin Zhang et al. (2024) shows that elevated serum levels of CK-18 are associated with a higher risk of mortality or liver transplantation in adults with advanced stages of chronic liver disease [27]. CK-18 has been sufficiently studied as a marker for predicting the development of MASH in adult patients with a pooled AUC value of 0.75 (95% CI 0.69–0.82) for the M30 fragment and AUC of 0.82 (95% CI 0.69–0.91) for the M65 fragment [28]. Pediatric studies have also confirmed the feasibility of determining CK-18 for the diagnosis of MASH in children [29].

Table 3 — Validity of laboratory parameters for the assessment of fibrosis in children with MASLD

Indicators	CK-18, U/l	TGF- β 1, pg/ml	GAG, mmol/l
Threshold value	> 90.3	> 96.8	> 4.24
Sensitivity, %	81.3	80.0	70.6
Specificity, %	76.9	65.7	69.6
AUC	0.843	0.787	0.743
95% CI	0.736–0.950	0.656–0.917	0.626–0.873
P (AUC)	< 0.001	< 0.001	< 0.01
Positive predictive value, %	59.7	49.9	46.2
Negative predictive value, %	90.7	88.5	86.5

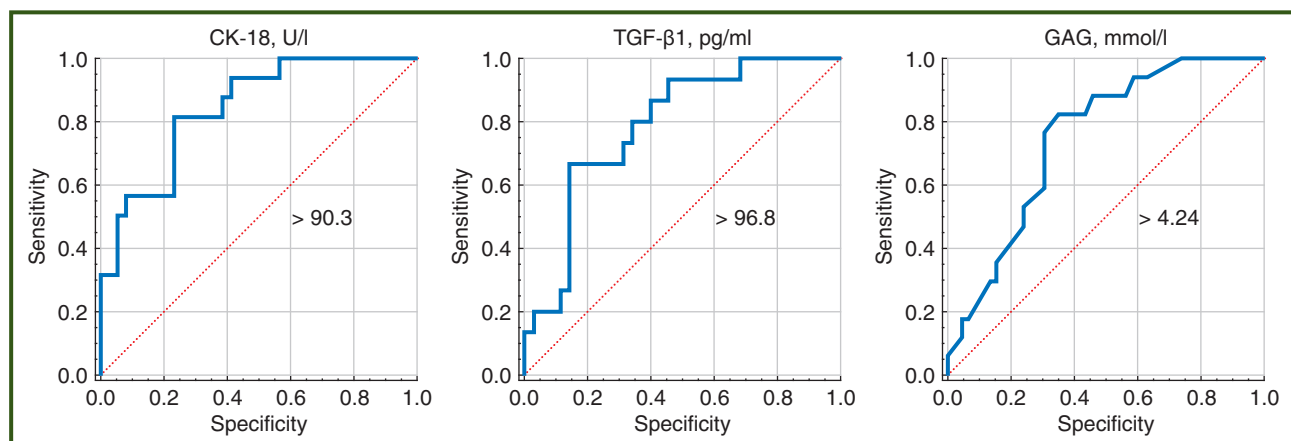


Figure 3 — ROC curves of serum CK-18, TGF- β 1 and GAG levels for the diagnosis of fibrosis in children with MASLD

In our study, a high level of CK-18 significantly distinguished patients with MASLD-associated liver fibrosis, with a threshold level of CK-18 of 90.3 U/l characterized by the highest AUC value of 0.843 compared to other studied parameters. Our data coincide with those of Italian colleagues, but Chetan Mandelia et al. (2016) obtained slightly lower AUC values of 0.75 using liver morphology as a reference [30]. In general, pediatric studies are limited by small sample sizes and the inability to adjust for all influencing factors, so the obtained data need to be validated in large cohorts.

TGF- β 1 is a potent fibrogenic cytokine involved in the activation of hepatic stellate cells and the production of extracellular matrix components [31]. A multivariate analysis in a pediatric cohort demonstrated that plasma TGF- β concentration is associated with the occurrence of hepatic steatosis independently of other covariates [32]. It has been shown that TGF- β 1 levels significantly correlate with the severity of MASLD and may be markers of liver fibrosis [33]. According to our data, TGF- β 1 levels were significantly elevated only in patients with liver fibrosis. Moreover, the threshold value of TGF- β 1 demonstrated a high level of diagnostic accuracy for the detection of liver fibrosis, AUC was 0.787 ($p < 0.001$).

With the development of fibrosis, there is an intensification of the synthesis of extracellular matrix components, in particular, collagen, which in our study was confirmed by an increase in the serum content of HPP/b in children of groups I–III. In children with liver fibrosis, an increase in the ratio of HPF to HPP/b was observed, which, according to scientific studies, is considered as a result of activation of fibrogenesis [34].

At the same time, GAG, as one of the specific markers of fibrosis, tended to increase in all groups of children, but in children with MASLD with fibrosis, the serum level of GAG was the highest compared to patients with MASLD without fibrosis and overweight and obese children.

The detected changes indicate a violation of the dynamic balance between collagen synthesis and degradation, confirm the processes of predominance of synthesis over catabolism, which leads to active accumulation of collagen in children with MASLD with fibrosis. The threshold value of serum GAG of 4.24 mmol/L, according to our data, demonstrated a sufficient level of diagnostic accuracy in the diagnosis of MASLD-associated liver fibrosis in children with an AUC value of 0.743 ($p < 0.01$).

The progression of liver fibrosis is accompanied by angiogenesis regardless of the etiology of liver disease. Hypoxia and inflammation are the main promoters of neovascularization, and VEGF, the main proangiogenic cytokine, plays a central role in angiogenesis, as it is involved in all its stages. Numerous experimental animal models of MASH have demonstrated an increase in the concentration of VEGF in liver tissue [35]. Adult patients with MASLD demonstrate increased levels of angiogenic markers, including VEGF, in serum and liver tissue, and VEGF mRNA expression was higher in cases of simple steatosis, indicating early induction of angiogenesis in MASLD [35]. In our study, the level of VEGF increased in patients of all study groups, but its highest concentration was in children with liver fibrosis, more-

over, the level of VEGF was positively correlated with liver stiffness ($r = 0.372$, $p < 0.05$).

Limitations of the present study include a bias in the formation of the cohort (referral bias), since the selection of patients was carried out in a tertiary care facility, which may limit the extrapolation of the results to the general population. In addition, the cross-sectional nature of the study did not allow us to determine the feasibility of determining serum fibrosis markers for monitoring the course of the disease.

Thus, children with liver fibrosis are characterized by elevated serum levels of CK-18, VEGF, TGF- β 1, HPP/b and GAG. The threshold values of CK-18 (more than 90.3 U/l), TGF- β 1 (above 96.8 pg/mL) and GAG (more than 4.24 mmol/l) have high sensitivity and specificity, which allows them to be used for the diagnosis of liver fibrosis in children with MASLD.

Conclusions

CK-18, TGF- β 1, GAG demonstrate a positive correlation with indicators of liver stiffness and elasticity, body composition of children with MASLD and show high levels of diagnostic accuracy, AUC 0.843, 0.787, 0.743, respectively ($p < 0.05$), which allows them to be used for screening MASLD-associated liver fibrosis in children.

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Сироваткові біомаркери в діагностиці фіброзу печінки в дітей із метаболічно-асоційованою стеатотичною хворобою печінки

Резюме. Актуальність. Епідемія COVID-19 та війна в Україні призвели до значного зростання кількості дітей, які страждають на метаболічно-асоційовану стеатотичну хворобу печінки (МАСХП). Однією з невирішених проблем, пов'язаних із МАСХП, лишається ідентифікація осіб із ризиком швидкого прогресування хвороби й розвитку необоротних змін печінки. Пошук альтернативних неінвазивних маркерів, придатних для раннього виявлення фіброзу печінки в дітей, надзвичайно актуальний. **Мета:** визначити діагностичну цінність сироваткових маркерів фіброзу та їхній зв'язок із сонографічними показниками й параметрами складу тіла в дітей із МАСХП.

Матеріали та методи. У дослідження «випадок — контроль» включено 80 дітей віком від 6 до 17 років (у середньому $12,15 \pm 2,51$ року). Наявність стеатозу й фіброзу печінки визначали шляхом транзиторної еластографії (Fibroscan® 502 touch F60156, Echosens, Франція). Усім обстеженим проведені антропометричні дослідження з оцінкою індексу маси тіла. При значенні останнього в межах 1–2 Z-score діагностували надмірну вагу, при перевищенні двох Z-score — ожиріння. За даними транзиторної еластографії та індексу маси тіла всі діти були розділені на чотири групи: I — 27 дітей із МАСХП та фіброзом $\geq F1$, II — 35 дітей із МАСХП без фіброзу, III — 18 дітей із ожирінням або надмірною вагою без МАСХП і фіброзу. Контрольну IV групу становили 14 дітей із нормальною вагою без МАСХП та фіброзу. Групи не мали значущих відмінностей за віковим і статевим розподілом. Дослідження складу тіла проведено шляхом біоімпедансометрії за допомогою аналізатора TANITA MC-780MA (виробник Maeno-cho, Itabashi-ku, Токіо, Японія). Концентрацію ендотеліального фактора росту судин (ЕФРС) в сироватці крові визначали за допомогою імуноферментного аналізу (ІФА) з використанням тест-систем фірми Wuhan Fine Biotech Co., Ltd (КНР) відповідно до рекомендацій виробника. Рівень цитокератину-18 (ЦК-18) у сироватці крові оцінювали за допомогою наборів

IDL Biotech AB (Швеція) для ІФА. Уміст трансформуючого фактора росту бета-1 (ТФР- β 1) визначали із застосуванням тест-системи ІФА IBL International (ФРН). Процеси фіброгенезу оцінювали за вмістом у сироватці крові гідроксипроліну вільного (ГПв), гідроксипроліну білковозв'язаного (ГПб/зв) та глікозаміногліканів (ГАГ). **Результати.** Продемонстровано вірогідне зростання рівнів ЦК-18 і ТФР- β 1 у дітей із МАСХП-асоційованим фіброзом печінки. В осіб із фіброзом печінки спостерігалось підвищення співвідношення ГПв/ГПб/зв і рівня ГАГ у сироватці крові порівняно з пацієнтами з МАСХП без фіброзу й дітьми з надмірною вагою та ожирінням. Пороговий рівень ЦК-18 для діагностики фіброзу печінки в дітей із МАСХП становив 90,3 Од/л (чутливість 81,3 %, специфічність 76,9 %, АUC 0,843; $p < 0,001$). Чутливість порогового значення сироваткового рівня ТФР- β 1 (96,8 пг/мл) у пацієнтів із МАСХП для діагностики фіброзу печінки дорівнювала 80,0 %, специфічність — 65,7 %, АUC — 0,787 ($p < 0,001$). Пороговий рівень ГАГ у сироватці крові понад 4,24 ммоль/л демонструє чутливість 70,6 % і специфічність 69,6 %, АUC 0,743 ($p < 0,01$). Продемонстровано позитивну кореляцію ЦК-18, ТФР- β 1, ГАГ із показниками жорсткості й еластичності печінки, компонентним складом тіла дітей із МАСХП та високі рівні діагностичної точності, що дозволяє використовувати їх для скринінгу МАСХП-асоційованого фіброзу печінки в дітей. **Висновки.** Для дітей із фіброзом печінки характерний підвищений вміст ЦК-18, ЕФРС, ТФР- β 1, ГПб/зв та ГАГ у сироватці крові. Порогові значення ЦК-18 (більше 90,3 Од/л), ТФР- β 1 (понад 96,8 пг/мл) та ГАГ (більше 4,24 ммоль/л) мають високі показники чутливості й специфічності, що дозволяє використовувати їх для діагностики фіброзу печінки в дітей із МАСХП.

Ключові слова: діти; метаболічно-асоційована стеатотична хвороба печінки; фіброз; цитокератин-18; глікозаміноглікани; трансформуючий фактор росту бета-1